Herbal supplementation: practical guidelines for the clinician: a review of the top ten herbal supplements used in the United States

Andrea Marie Tardivo

The University of Toledo

Follow this and additional works at: http://utdr.utoledo.edu/graduate-projects
Herbal Supplementation: Practical Guidelines for the Clinician

A review of the top ten herbal supplements

used in the United States

Andrea Marie Tardivo

The University of Toledo

2008
Dedication

This scholarly project is dedicated to “Dr. Phyll”, my late Grandmother, Phyllis May Tardivo. She was thought of by many as a woman with a healing heart. As a small child, I remember heading down to my Grandmother’s house, so distinctive in smell and humbling warmth, where anyone and everyone was welcomed as family. One memory that I will always share is Grandmother’s many home remedies. Whether is was the vinegar concoction in the mason jar that rid the body of harmful toxins or the warm bowl-fulls of oatmeal and raisins sprinkled with brown sugar in the mornings to aid in cleansing bowel movements. It seems all of us grandchildren would salvage some comic relief after being lovingly persuaded to try these natural cures. At this stage in my life I reflect back on those memories and realize she provided me with a tradition of her love for life and healing. I will forever aim to encompass the character of my grandmother as I continue the pathway of practicing medicine. Further, I will strive to be open-minded about patients’ wants and rights and offer my recommendation to help protect them from harm. I will always try to help my patients realize that being healthy requires an open relationship with their clinician. And I will always remember how my Grandmother thought that she was perfectly healthy and how I know that her heart could have had a lot more ticking to do.
Acknowledgements

I would like to provide my extensive gratitude to Professor Karen Graham, Jolene Miller, Aaron Hoekje, and Megan Tardivo. It was very enjoyable to work closely with the above persons who provided encouragement, constructive criticism, and immeasurable knowledge. This task has taken many long hours; without the above persons this feeling of accomplishment would not have been achievable. Thank you.
Table of Contents

Introduction ..........................................................................................................................1

Ginkgo biloba .......................................................................................................................9

Saw palmetto ......................................................................................................................15

Milk thistle .........................................................................................................................19

Ginseng ................................................................................................................................23

Feverfew ............................................................................................................................32

Kava ...................................................................................................................................35

Garlic ..................................................................................................................................39

Ginger ..................................................................................................................................44

St. John’s wort ...................................................................................................................48

Echinacea ...........................................................................................................................53

Conclusion .........................................................................................................................55

Reference ...........................................................................................................................62

Tables ..................................................................................................................................71

Figures ................................................................................................................................78

Abstract ..............................................................................................................................79
Introduction

*CAM usage on the incline*

A passage from the Hippocratic Oath states, “I will neither give a deadly drug to anybody who asked for it, nor will I make a suggestion to this effect.” Medicine has evolved immeasurably from this traditional practitioner’s oath. As healthcare professional students, the idea to do no harm is embedded in our minds. One aspect of medicine that has not changed is the desire of patients to have control of their own health; to express this autonomy, patients more than ever are choosing alternative medicine. Investigation into alternative therapies should be thorough in order to assess the effects of patients’ independent medical choices. Education and understanding of these therapies is necessary to guide healthcare providers to recommend safe and effective medical treatment to their patients.

Complementary and alternative medicine (CAM) is a broad field that clinicians should recognize. The definition for CAM therapies, as described by the National Center for Complementary and Alternative Medicine (NCCAM), is “a group of diverse medical and health care systems, practices and products that are not presently considered to be part of conventional medicine” (National Center for Complementary and Alternative Medicine, 2007). A national survey conducted by Eisenberg et al. (1998) concluded that visits to alternative medicine specialists increased 47.3% from 1990 to 1997. In 1997, the number of visits made to CAM practitioners exceeded patient visits to primary care physicians, totaling 629 million (Eisenberg et al., 1998). A follow-up study by Eisenberg et al. in 2002 showed that a total of 18.6% of Americans use herbal therapy, making it the most popular alternative medicine modality. Authors agreed that the prevalence of CAM has remained stable from 1997 to 2002 (Tindle, Davis, Phillips, & Eisenberg, 2005). Further emphasis provided by the U.S. National Center for
Health Statistics showed that almost three quarters of the population had used CAM therapies in combination with conventional medicine (Barnes, Powell-Griner, McFann, & Nahin, 2004).

Why patients are choosing to take medicine into their own hands is a question for which the answer remains uncertain. Astin (1998) summarizes three theories explaining why Americans are choosing alternative medicine. To investigate these theories, a total of 1035 randomly selected individuals were asked to respond to a written survey examining the choices of CAM. Three theories resulted, explaining why patients are using alternative medicine. Theory one explains that patients are dissatisfied with conventional treatments due to their ineffectiveness, the possibility of adverse effects, and/or cost alone. The second theory is that patients express a concern for personal control and want to seek sovereignty. For the third theory, Astin addresses the motivation for philosophical congruence. Patients have a variety of intrapersonal needs and want their treatment to reflect their values and religious philosophies (Astin, 1998).

*Clinical knowledge of CAM*

Although it is on the incline, many healthcare providers do not have adequate knowledge of CAM practices. Lack of education and training in this area creates a barrier between the provider and the patient. This is a disservice to patients and one that needs immediate discussion, action and implementation. Over the past 40 years, the proportion of clinical trials has significantly increased, bridging the alternative medicine gap. MEDLINE, a research database, has over 40,000 articles discussing CAM, with 1,500 new articles each year being added to the list (Barnes, Abbot, Harkness, & Ernst, 1999). Research validity has remained under scrutiny by mainstream medicine, and thus is one of the main reasons why many providers hesitate to recommend CAM.
The White House Commission on Complementary and Alternative Medicine Policy (WHCCAMP) decided to take action in March of 2000, with goals of increasing CAM knowledge. The addition of more education and training components at the graduate and postgraduate level were included. Also, WHCCAMP proposed that ensuring safety and efficacy through scientific research was essential for public safety. The policy highlighted that with better designed clinical trials, CAM modalities will be better understood by both the medical and patient community. With this achievement, recommendations for treatment options would be more clinically beneficial and cost effective (Gordon, 2004).

Funding is critical for CAM research goals to be met. In 1998, Congress increased the budget for NCCAM from $20 million to $50 million providing more evidence through research (Marwick, 1998). In 2008, the appropriation provided by Congress totaled $121.6 million (National Center for Complementary and Alternative Medicine, 2008). These statistics reflect the increase in interest regarding CAM.

Many providers agree that the importance of CAM education is essential. In a 2001 study, Houston identifies the need for both physicians and physician assistants (PAs) to be more familiar with CAM therapies. Houston concluded that many physicians express a positive outlook for CAM, however, they admit that their knowledge of the subject matter is poor (Houston, Bork, Price, Jordan, & Dake, 2001). Gordon (1996) stressed that a receptive attitude toward CAM will show the physician’s commitment to their patients, providing an integrative approach to patient care. A suggested 20 to 30 hours of training would be required to adequately build a knowledge base (Gordon, 1996). In addition, Houston highlighted the need for PA programs to incorporate CAM into their curriculum (Houston et al., 2001). The PA profession and CAM practices are rising in tandem. Using figures from the American Academy of
Physician Assistants (AAPA) census information, there is an anticipated growth of working PAs of seven percent from 2007 to 2008, and this number is not expected to plateau (American Academy of Physician Assistants, 2008). It is essential that this occupational growth provides not only access but quality care to patients.

A study identified three cohorts of PA students with different levels of CAM education; 85% of students agreed that clinicians should have knowledge of CAM therapies. However, less than 10% of subjects thought that CAM therapy represents a threat to the safety of patients. The need for more education is crucial since many students are not aware of harmful side effects CAM treatments can produce (Colletti, Robinson, Ostbye, Morgan, & Coniglio, 2006).

Legislature regarding herbal medicines

Statistics illustrate that the sale of supplements more than doubled after enactment of the Dietary Supplement Health and Education Act (DSHEA) in 1994. The DSHEA created a new regulatory category within the FDA, stating that dietary supplements are neither a food nor drug. The legislative objective was to provide a freedom of choice to consumers and to protect development of public health. The legislation defines dietary supplements as products “intended to supplement the diet” and labeled for use to affect the “structure and function” of the body or for “general well being” (Nichter & Thompson, 2006, p.177). A paradox created within this definition is that people ingest food and drugs for the same purposes.

Labeling cannot make claims of diagnosis, treatment, or cure of any disease. However, descriptions of these labels can still be misleading. Manufacturers of these products create substantial ambiguity when claiming the supplement’s intended use. Echinacea is a prime example. For instance, one brand claims that “Echinacea is the world’s best known herb for nutritionally supporting defense system functions.” Yet another portion of the package states
that the product “maintains healthy immune functions.” (Nichter & Thompson, 2006, p.177).
Because the label may be so broadly interpreted, consumers might easily construe that echinacea
will aid in combating an extensive list of infections. The DSHEA’s main objective was to insure
public health safety. Ironically, the legislature created a doorway for many interested buyers of
supplements to misinterpret the labels and experiment based on perceived needs (Nichter &
Thompson, 2006). Manufacturers of herbals historically were not obligated to report evidence
for safety or efficacy, subsequently quality controls from the FDA resulted. The Dietary
Supplement and Nonprescription Drug Consumer Protection Act was signed into law in 2006 in
effort to establish a means of reporting serious adverse reactions experienced by dietary
supplementation. With this law in effect, it is mandatory for manufacturers to submit
information to the FDA regarding such matters (Nisly, 2007).

Though the new legislature has downfalls, Americans are increasingly practicing
preventative medicine. Communication between patients and clinicians regarding the possible
risks associated with herbals is crucial. Patients need to be aware of the potential for adverse
effects and drug interactions (Cupp, 1999). Nearly all herbal remedies have multiple
biologically active ingredients which can create intoxication or risky herb-drug interactions.
Many consumers feel as though herbals are natural and therefore safe, a false impression that
could lead to increased rates of morbidity and mortality (Poppenga, 2002).

*Herbal Medicine: The Controversy*

The Food, Drug and Cosmetic Act (FD&C) defines a “drug by its intended use, as either
articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; or
articles (other than food) intended to affect the structure or any function of the body of man or
other animals” (U.S. Food and Drug Administration, 2007). The DSHEA’s definition of dietary
supplements is similar, stating that the use is to affect “structure and function” of the body, yet supplements are not considered drugs. Consumers take herbals and drugs for either preventative measures or to combat a pathophysiological process. The general public and the medical community should scrutinize herbals and treat them with the same precaution and discretion comparable to prescription drugs.

Since herbal therapies are not FDA regulated, the need to have adequate clinical trials is heightened. Evidence-based medicine is the standard for treating patients. The results from clinical trials will improve the clinician’s ability to accurately discuss herbal use with patients. A 2005 report illustrated a delay between an herb becoming more widely used and the scientific information available for determining efficacy and safety. For example, research for St. John’s wort was performed in 2000 to 2002, although usage of this herbal escalated dramatically from 1998 to 2000 (Hall & Nazir, 2005). This lag time does not allow practitioners to stay current on the most common herbal medicines and therefore, recommendations to their patients are unsatisfactory. It is necessary to identify the popularity of herbals so that research continues to either validate or refute the claims provided by the manufacturers. Ultimately, this would provide a more comprehensive quality assurance approach to direct patients using herbal therapies. Table 1 represents the most recent top ten selling herbal medicines.

Obtaining quality randomized controlled trials (RCT) for herbals is a difficult task. Herbal medicines are not purified and may have a wide range of variations. Herbals may differ due to the part of the plant used, time of harvest and delivery form. The consolidation standards of reporting trials (CONSORT) is a system which provides a structured format regarding the information required for RCT. These guidelines were first published in 1996 and revised in 2001 with expectations to assist investigators, authors, reviewers and editors on the necessary
information to be included surrounding controlled clinical trials. In 2004, CONSORT recommendations were created for reporting of herbal RCT. These elaborations helped extend the quality of information surrounding herbal studies. The additions allowed editors and reviewers to assess internal and external validity, reproducibility, promoting further understanding of safety and efficacy of herbal RCT. CONSORT has been accepted as an appropriate validation model by many medical journals and professional organizations (Gagnier, Boon et al., 2006). One study that interpreted the quality of reports for 206 herbal RCT found that less than 45% of the criteria within the CONSORT recommendations was reported (Gagnier, DeMelo, Boon, Rochon, & Bombardier, 2006). The lack of evidence reported may lead to inappropriate use of herbal medicines.

It is important for herbals to have quality RCT so that interpretation of results can aid clinicians in practice. However, the utilization of herbals may not always be reported by the patient. A 2000 study investigated provider awareness of herbal supplement use. A startling 75% of the patients reported not informing their provider of herbal treatment, and 86% of the patients thought that herbs were safe to use. These patients may not be aware of the possible herb-drug interactions. Thus, some practitioners are practicing blindly, unaware that their patients are using herbals concurrently with prescriptions (Planta, Gundersen, & Petitt, 2000). Harm is imminent if this pattern continues. The FDA received 2,621 reports of adverse effects related to dietary supplements, including death, from 1993 to 1998. Clinicians should include herbal supplement usage as a habitual question during their medical histories (Hudson, Brady, & Rapp, 2001). Patients’ misinterpretation of herbals as safe may make them less likely to volunteer this information.
One reason clinicians are taught to practice evidence based medicine is to minimize the risk of adverse reactions. The US Institute of Medicine (IOM) report of 2005 identified the concerns and implications of CAM. Eisenberg served as one of the 16 committee members responsible for the report and has since summarized many of the issues addressed. The report attempts to create equality for all medicinal therapies regardless of whether they are derived from conventional or CAM based practices. Ideas generated within this report recognize the need for evidence addressing safety and effectiveness of medicinal practices. Without this information and investigation, healthcare providers may not have the knowledge to make appropriate decisions about prevention of healthcare interventions, including CAM (Eisenberg, 2005).

In comparison to the 2001 IOM essay, the 2005 report stressed that CAM needs to be upheld to the same competencies and discipline that encompass conventional medicine practice. Recommendations were made to the National Institute of Health (NIH) and other public agencies to support the research, which included creating a sentinel surveillance system, developing more research centers, sponsoring research and including CAM questionnaires in federally funded surveys to assess prevalence, patterns and perceptions of those therapies. The committee also recommended that the National Library of Medicine to develop a criterion to assess quality and liability of CAM research. The report stressed that with CAM research there is an opportunity for scientific discovery. Examples include the evaluation of herbal therapies and their mechanism of action, interactions with pharmacological therapies, safety, efficacy and cost effectiveness. Furthermore, the report strongly identifies the need for health professional schools to incorporate information about CAM into their curriculum, and include CAM questions on national board certification exams (Eisenberg, 2005).
This literature review will identify the top ten selling herbal products on the market and examine each herbal for RCT. Each herbal will be described, evaluated for efficacy and identified for possible adverse effects and drug interactions. Concluding each herbal section, recommendations for clinical application will be provided.

Herbal RCT will be gathered and analyzed primarily from The Cochrane Collaboration. This not-for-profit collaboration was founded in 1993 by Archie Cochrane. Cochrane was a British epidemiologist who realized that there was a need to have accurate information obtained from clinical trials and that ultimately this research would improve health care. The collaboration aims to provide easy-to-interpret information about the latest healthcare interventions worldwide. The review follows a standard procedure to address each topic thoroughly as well as to develop a protocol for updating reviews continually (Cochrane Collaboration, 2007). The collaboration believes strongly in evidence based medicine and identifies that the definition combines both individual clinical expertise with the best available external clinical evidence from systematic research (Cochrane Collaboration, 2008).
Ginkgo biloba

Description & Background

Ginkgo biloba is an extract taken from the leaves of the maidenhair tree, one of the oldest living tree species. The tree has an amazing capability to survive, thriving for up to 1,000 years through bouts of frosts and aggressive insect and fungal attacks. The leaves are characterized by two lobes termed biloba. The maidenhair tree is now cultivated by profitable plantations ranging from China to South Carolina for the sale of nuts and the proposed medicinal effect of the leaves (Birks & Grimley, 2007).

A variety of health conditions including cognitive impairment and dementia, depression, anxiety, dizziness, acute ischemic stroke, age related macular degeneration, tinnitus and headache have been treated by ginkgo biloba. Its active components contain flavonoids, terpenoids and terpene lactones (ginkgolides and bilobalide). Excluding the terpene lactones, which are specific to ginkgo, the other active ingredients are found in numerous plants. When the leaves are ground together a distinct extract is produced called EGb 761. This compound is one of the top five prescription medicines in Germany and is claimed to have anti-oxidant properties (Birks & Grimley, 2007).

The active ingredients are thought to produce ginkgo’s physiologic effects. The extract is theorized to dilate blood vessels, reduce blood viscosity, alter neurotransmitter systems and reduce the quantity of oxygen free radicals. It is also reported that ginkgo may have an effect on blood clotting. Although this topic is yet to be thoroughly understood, the active ingredient Ginkgolide B is said to be an inhibitor of platelet activating factor (Birks & Grimley, 2007).

The authors from the Cochrane Collaboration investigated ginkgo’s effect on the following conditions: cognitive impairment and dementia, acute ischemic stroke, age related
macular degeneration and tinnitus. The examination for this herb will focus on only those conditions.

Conditions Reviewed

Cognitive impairment & dementia

Birks and Grimely reviewed randomized, double-blind studies on patients with cognitive impairment, including dementia. Subjects were not excluded based upon their degree of severity for these conditions. Subjects were evaluated for improvement comparing the effects of placebo with gingko biloba, with no criteria on dosage or duration. The results were gathered from 35 studies totaling 4,247 participants. Of those 35 studies, only 29 were able to be examined by meta-analyses. Furthermore, from those 29 examined, 15 studies contributed very little data (Birks & Grimley, 2007).

Results showed benefits with a ginkgo dose greater than 200 mg/day at a 24 week time period, as compared to a lower dose. Improvement in cognition was also seen when ginkgo was prescribed at any dose at 12 weeks, but not at 24 weeks. Five studies assessed activities of daily living (ADL) and showed a benefit for ginkgo with a dose less than 200 gm/day compared with a placebo at 12 weeks. Authors concluded that early trials used unsatisfactory methods and that publication bias could not be excluded. Although some results displayed a potential benefit, the authors concluded that there was no clinically significant evidence consistent enough to support that ginkgo improves cognitive impairment and dementia (Birks & Grimley, 2007).

Acute Ischemic Stroke

Chinese traditional medicine has used ginkgo biloba for the treatment of acute ischemic stroke for ages; however, its therapeutic efficacy remains uncertain. Zeng et al. identified 10 trials with a total of 792 patients to incorporate into this review. Evaluation of patients was
performed 14 to 35 days post stroke. These trials consisted of randomized controlled studies or quasi-randomized controlled trials, both of which compared ginkgo with placebo in patients experiencing an acute ischemic stroke (Zeng, Liu, Yang, Li, & Asplund, 2005).

After analysis was completed, the authors reported that ginkgo extract was associated with improvement, although not statistically significant. Only one trial used quality methodology in reporting neurological improvements on an uninterrupted scale. Investigation of higher quality and larger-scaled randomized trials was suggested (Zeng et al., 2005).

Age-Related Macular Degeneration (AMD)

Two trials for AMD were identified totaling 119 participants. Ginkgo was given to patients with either AMD in one or both eyes and compared to placebo. Although some positive effect was seen, the trials reviewed were small in sample size, analyzed for a short duration and lacked control groups. Due to these issues, ginkgo cannot be said with certainty to have positive effects for people with AMD (Evans, 1999). Quality research is needed on ginkgo and AMD.

Tinnitus

The review of tinnitus covered three trials; others proved to have inadequate methodology. Trial samples included adults over 18 years of age complaining of tinnitus and adults with cerebral insufficiency accompanied by tinnitus. The etiology of tinnitus is uncertain, and therefore treatment options are limited. Patients may experience constant or intermittent sounds in absence of external acoustic stimuli. Overall, the authors concluded that too few studies exist, and that currently there is no evidence that ginkgo is an effective treatment for tinnitus (Hilton & Stuart, 2004).
Safety

Patients using ginkgo have reported gastrointestinal upset, headache, allergic skin reactions, dizziness and vertigo. Authors from the Cochrane Collaboration concluded that ginkgo appeared to be safe with little to no adverse events reported. Adverse events were reported in the AMD analysis and included headache, abdominal pain and bloody stools (Evans, 1999). Ginkgo may have possible drug interactions with antithrombotic or platelet therapy (Hudson et al., 2001). Ginkgo has been related to enhancing the effects of anticoagulants (Poppenga, 2002). At least four reports of spontaneous bleeding have been related to ginkgo. One describes a 70 year old who presented with a spontaneous hyphema. The hyphema occurred within one week after the patient self prescribed ginkgo at 40 mg twice daily. The patient was concurrently taking aspirin 325 mg/day, due to CABG surgery three years prior. After the hyphema resolved, the patient continued aspirin therapy. At a three month follow-up the patient presented with no further bleeding episodes. Ginkgo combined with aspirin therapy was determined to be the cause for the bleed (Rosenblatt & Mindel, 1997).

Another case reports a 33 year old woman who had a history of taking ginkgo at 60 mg twice daily for almost two years. Upon admission, she was diagnosed with bilateral subdural hematomas. The patient was concurrently taking acetaminophen and an ergotamine-caffeine preparation. She reported only using those medications for a brief period of time. Her bleeding times had escalated to 9.5 and 15 minutes while on ginkgo supplementation. Thirty five days after ceasing ginkgo, bleeding times returned to normal range (Rowin & Lewis, 1996).

Recommendation

Patients with cognitive impairment and dementia, acute ischemic stroke, age related macular degeneration and tinnitus should be educated on the research provided. Although
gingko may improve certain conditions, there is no clinically significant information that supports gingko’s effectiveness. With this information, the clinician can educate patients regarding ginkgo’s possible benefits as well as adverse effects. This herbal should not be recommended over first line treatment options for the above conditions reviewed. Initial treatment for interested patients should not exceed the standard 60-80 mg two to three times daily (Hudson et al., 2001). Initiation of treatment should be twice per day with a follow up PT/INR value recorded at one week. At this time, if an increase dosage is warranted, follow up again at one week. Once the PT/INR value is within the desired range, follow up should be continued monthly.

Healthcare providers should be aware of the adverse effects of this herb as well as the potential for dangerous drug interactions. Patients should be advised to discontinue ginkgo usage when combining drugs with anti-platelet or anticoagulant effects such as aspirin, warfarin, garlic or vitamin E. Patients should also be cautious and withdraw ginkgo use if unusual bleeding, bruising, visual disturbances or new onset headaches occur (Cupp, 1999).
Saw Palmetto

*Description & Background*

Saw palmetto, also referred to as the dwarf palm plant, is a botanical found in the southern United States. The active ingredients produced by this plant are available in several forms including liquid extract, capsules and tea. This herb is used mainly to treat urinary obstruction, most commonly benign prostatic hyperplasia (BPH). Saw palmetto has also been used to treat conditions such as chronic pelvic pain, bladder disorders and hormone imbalances (National Center for Complementary and Alternative Medicine, 2006e). Wilt et al. reviewed trials specifically related to saw palmetto’s effect on BPH. Of the approximately 30 botanical therapies for BPH, saw palmetto is the most widely used. The mechanism of action for saw palmetto remains unknown. Hypothetical mechanisms consist of alteration of cholesterol metabolism, anti-estrogenic and anti-androgenic effects, anti-inflammatory effects and a decrease in available sex hormone-binding globulin (Wilt, Ishani, & MacDonald, 2002).

*Conditions Reviewed*

**Benign Prostatic Hyperplasia**

Authors review of saw palmetto and its effectiveness incorporated 21 RCT that lasted between four and 48 weeks. Of the trials that meet the specific inclusion criteria, 3,139 male participants were incorporated into the study. Specifications included randomized men suffering from BPH. Male subjects received saw palmetto alone or in combination with other phytotherapeutic agents. Saw palmetto was then compared with a placebo or the BPH medication of choice; finasteride was chosen for these studies. The second criterion was that clinical measures were made using the International Prostate Symptom Scale (IPSS) and urodynamic measurements (Wilt et al., 2002).
Authors concluded that saw palmetto provides improvement to males suffering from BPH. Mild to moderate advances have been recognized for both urinary symptoms and flow measures. Saw palmetto produced greater results than placebo and was comparable to finasteride for improvement of peak and mean flow rates and residual urine volume. In comparison to placebo, male subjects taking saw palmetto were two times as likely to report an improvement in their symptoms. Limitations of the systematic analysis included that most of the studies were performed prior to the development of the urological symptom scale scores and only two studies had a follow-up period of at least 6 months in duration. Therefore, while improvement of BPH symptoms was shown, evidence for long-term success is lacking. A large future RCT study of approximately 3,000 men with a follow-up period of at least four years will be sponsored by The United States National Institute of Diabetes and Diseases of the Kidney. This study will evaluate the efficacy and adverse events of saw palmetto usage and will use IPSS criteria for analysis. The completion of this study should resolve many issues concerning the limitations surrounding the Cochrane Collaborations’ systematic review of saw palmetto (Wilt et al., 2002).

A recent study evaluating BPH symptom improvement examined the effects of saw palmetto, tamsulosin (Flomax) and the combined efficacy of saw palmetto and tamsulosin. A total of 60 men were incorporated into this study ranging from 43 to 73 years of age. Measurements consisted of lower urinary tract symptoms (LUTS) reported and uroflowmetry results. Subjects were given a baseline measurement at day zero and participated in transrectal ultrasonography (TRUS) to measure prostate volume. A serum draw to determine prostate specific antigen (PSA) levels was also performed. Additional randomized visits were made at two, four and six month intervals. Authors concluded that saw palmetto and tamsulosin used
alone were shown equally effective. Combined effects of saw palmetto and tamsulosin did not demonstrate any additional therapeutic benefit (Hizli & Uygur, 2007).

**Safety**

Compared with finasteride, saw palmetto produces similar improvements with fewer adverse effects, such as impotence (Wilt et al., 2002). One study reported that 25% of patients using tamsulosin experienced ejaculatory problems, while saw palmetto did not produce such results (Hizli & Uygur, 2007). Other possible side effects are gastrointestinal upset, headache (rarely) and diarrhea (Hudson et al., 2001). Saw palmetto should not be taken with other hormone therapies or with immune altering or anti-inflammatory drugs (Poppenga, 2002). Saw palmetto has not been shown to interfere with PSA levels (National Center for Complementary and Alternative Medicine, 2006e).

**Recommendation**

Patients with mild to moderate new onset BPH should be educated on the benefit of saw palmetto and should be advised of possible side effects and drug interactions. The patient should be given the option to try saw palmetto instead of standard therapies. Patient follow-up schedules should continue as if a standard therapy was implemented. If symptoms do not resolve with saw palmetto treatment, patients should cease ingestion and be guided to other treatment methods. Standard first line treatment for BPH includes alpha adrenergic antagonists such as terazosin and tamsulosin. Terazosin dosage ranges from one to 10 mg per day, whereas tamsulosin dosage is 0.4 mg per/day (Epocrates, 2008). Saw palmetto’s initial starting dose should be in the range of one to two grams per day, or 320 mg per/day of the lipophilic extract (Hudson et al., 2001).
The trials reviewed made available by the Cochrane Collaboration compared saw palmetto with finasteride, a 5-alpha reductase inhibitor. Additional clinical trials should monitor and evaluate patients choosing saw palmetto over the first line treatment alpha adrenergic antagonist medications. Comparisons made would provide further understanding to guide treatment for BPH patients.
Milk thistle

Description & Background

Milk thistle, *Silybum marianum*, dates back to ancient Greece and is native to the Mediterranean region. The extracts of this herb were used as a remedy to treat ailments of all types, primarily liver pathology (Rambaldi, Jacobs, Iaquinto, & Gluud, 2007). The active ingredient is extracted from the seeds and can be prepared as capsules or as a tea. Milk thistle has other treatment claims that include cholesterol level reduction, insulin resistance reduction in type two diabetics with concurrent cirrhosis, treatment of gall bladder disorders, and reduction in the growth of malignant cells in prostate, breast and cervical cancers (National Center for Complementary and Alternative Medicine, 2005c). The Cochrane Collaboration focused their review solely on the herbs’ ability to aid in the treatment of liver pathologies.

The flavonolignan extracts of milk thistle are collectively known as silymarin. Various animal studies have shown that silymarin has a beneficial effect on the liver. Animal testing showed that protection from hepatotoxins such as acetaminophen, iron overload, radiation, phalloidin and carbon tetrachloride were seen with milk thistle administration. The mechanism behind these protective qualities is based on the idea that silymarin inhibits lipid peroxide formation, reduces the effect of free radicals, changes cell membrane physical properties and limits liver fibrogenesis (Rambaldi et al., 2007).

Conditions Reviewed

*Alcoholic and/or hepatitis B or C liver diseases*

This review integrated 18 randomized clinical trials assessing 1,088 subjects. Unpublished and published trials were reviewed. Patients in these studies had alcoholic and/or hepatitis B or C virus liver diseases. Both acute and chronic hepatic disorders were included.
The trials consisted of subjects receiving milk thistle at any dose or duration versus a placebo or no intervention. Other qualifying trials included design studies of double blind, single blind, or unblind. Testing measurements consisted of mortality rates, complications associated with liver disease and histological evaluation (Rambaldi et al., 2007).

Rambaldi et al. identified the need for more quality randomized clinical trials to be performed. In conclusion, the results of the comparison between milk thistle and placebo, or no intervention, showed no significant evidence to support a decrease in mortality or further complications from hepatic disorders. The systematic review found a general significant reduction of liver-related mortality in all trials, but the high quality trials did not show any decreased risk. The collaboration did not find enough evidence to support or refute milk thistle for treatment of alcoholic and/or hepatitis B or C virus diseases. At this time, the meta analysis needs larger sample sizes to form conclusions (Rambaldi et al., 2007).

Safety

Milk thistle was not shown to produce any increased risk for adverse events during the clinical trials, and few side effects are related to milk thistle supplementation (Rambaldi et al., 2007). Infrequent reports show that milk thistle may produce a laxative effect, nausea and bloating. Patients with hypersensitivity to plants in the same family, (i.e. ragweed, marigold and daisy) are at a higher risk for an allergic reaction when taking milk thistle (National Center for Complementary and Alternative Medicine, 2005c). Drug interactions are linked to the herb’s ability to reduce the hepatotoxic effects of drugs such as acetaminophen, phenytoin and butyrophenones such as haloperidol (Poppenga, 2002).
Recommendation

Treatment options for patients with alcoholic steatohepatitis consist primarily of patient counseling regarding importance of alcohol cessation and a nutritious diet. Pharmacological treatment consists of corticosteroids and pentoxifyllin. These drugs reduce inflammatory mediators and liver-related mortality rates. Duration of treatment is recommended to last four weeks. Depending on the severity of the disease, patients may develop portal hypertension leading to hepatomegaly, splenomegaly and ascites. Liver transplantation is the only treatment that increases survival rates for patients with decompensated cirrhosis (Diehl, 2004).

Patients with a diagnosis of hepatitis B or C, either acute or chronic, have treatment options that may or may not aid in full recovery. For example, hepatitis B and C treatment includes interferon-alpha and other antiviral agents. Hepatitis B has a more positive prognosis than C. Hepatitis C develops into chronic hepatitis C in approximately 70% of cases. Treatment regimens are inconsistent and vary due to staging and progression of the disease. In severe cases, liver transplantation is the only option once end stage liver disease develops (Hoofnagle & Lindsay, 2004).

Due to the varying and inconsistent prognosis for alcoholic and/or hepatitis B or C viral liver diseases other treatment options should be encouraged. Larger scale studies need to include milk thistle as a treatment option as monotherapy or adjuvant therapy so that proper evidence can validate or refute its effectiveness in treating these conditions. Milk thistle should be discussed with patients having these conditions. Treatment options are limited for these patients, and milk thistle reviews show little to no side effects. Milk thistle should be started as a treatment for mild cases and considered in patients with more advanced disease. Dosage formulation would be calculated based upon progression and advancement of disease. At this time, recommended
doses of milk thistle for hepatotoxicity are 280-420 mg daily. Dosages are 140 mg three times daily for acute viral hepatitis and 240 mg twice daily for chronic active hepatitis. (Epocrates, 2008). Follow up appointments should continue, and detection of serological markers of the viral diseases and liver function enzymes should be evaluated at appropriate times based upon the severity of the disease.
Ginseng

Description & Background

Ginseng dates back 5,000 years and is native to China and Korea. The term ginseng refers to the root of several species; \textit{Panax ginseng} is used most extensively. C.A. Meyer, a Russian botanist, combined the Greek words for all and cure into the genus name \textit{Panax}. \textit{Ginseng}, the species name, is derived from the Chinese word for human because the root resembles the human body (Radad, Gille, Liu, & Rausch, 2006).

Today, ginseng use ranks very high and is considered the top selling herbal medicine in the world. Approximately, six million Americans regularly consume ginseng and related products (Radad et al., 2006). Ginseng products contain the active ingredients ginsenosides and can be administered as tablets, capsules, extracts, teas, or as a topical cream (National Center for Complementary and Alternative Medicine, 2005a). Ginseng root preparations can be air dried (white ginseng) or the roots can be steamed (red ginseng) (Radad et al., 2006). Numerous treatment claims include ginseng’s ability in strengthening the immune system, improving mental and physical well-being, treating for erectile dysfunction, treating hepatitis C, alleviating menopausal symptoms, lowering blood glucose levels and lastly, controlling blood pressure (National Center for Complementary and Alternative Medicine, 2005a).

A review by Radad et al. (2006) adds to the list by analyzing ginseng’s effectiveness in treating neurodegenerative disorders, producing action on the cardiovascular system, having anti-inflammatory, anti-allergic, anti-carcinogenic and aphrodisiac effects. The Cochrane Collaboration reviews at this time address ginseng in the treatment of viral myocarditis and heart failure. Ginseng is not taken to treat these conditions in the United States. Additionally, the Cochrane reviews were not exclusive to \textit{Panax ginseng}. The following review will be primarily
taken from Radad’s work evaluating the widespread use of this herb as well as its pharmacological actions. This review will also include RCT from other studies for these conditions.

Ginsenosides, the active ingredients derived from and unique to *Panax*, are also referred to as ginseng saponins. Each of the 30 ginsenosides is thought to have their own specific mechanism and tissue-dependent effects. These active ingredients may vary based upon Panax species, age of plant, part of the plant used, how the herb was preserved, seasonal harvest and how extraction was performed. The most abundant ginsenoside found in the root of the plant is Rb1 and Rg1. Ginseng, is believed to provide resistance to insult so that the body can maintain homeostasis. Specific physiological mechanisms will be more thoroughly examined for each of the following conditions (Radad et al., 2006).

**Conditions Reviewed**

*Neuroprotection*

**Human Studies**

Conclusive studies in humans are minimal at this time. Results from studies in animals and neuronal cell cultures indicate that ginsenosides may have a role in antagonizing factors promoting neuronal death. Factors causing neuronal death include environmental toxins, excitotoxic action of glutamate, an increase in intracellular calcium and an over abundance of free radical and apoptotic events (Rausch, Liu, Gille, & Radad, 2006).

**Animal Studies**

Ginsenosides have been linked to the improvement of neurological function. The extracts are believed to increase neuron cell survival, aid in neurite growth and increase neuronal defense against certain insults. Parkinsonism agents such as methyl-4-1-phenylpyridinium
(MPP⁺) were shown to have less damaging effects on rodents with the administration of ginseng extract G115. Animals treated with ginseng extract suffered less substantia nigra pars compacta loss and the striatal dopamine transporter suffered far less damage. Several reports show that ginseng may inhibit the effects of MPP⁺ on dopaminergic neurons. The exact mechanism of ginseng and its neuroprotective qualities remains uncertain, but lower prevalence rates of Parkinson’s disease in China compared to the United States may indicate that ginseng has the potential to protect against neurodegenerative diseases. Parkinson’s prevalence in the United States is 200/100,000 persons. China has a prevalence of only 44/100,000 persons. Other neurodegenerative disorders have been examined on a smaller scale. Prevention of neuronal loss was also associated with amyotrophic lateral sclerosis (ALS) and Alzheimer’s disease. The theory that ginseng has a beneficial influence on the central nervous system cannot be ruled out entirely (Radad et al., 2006).

**Cognitive Impairment**

**Human Studies**

A systematic review performed by Vogler (1999) identified five studies that investigated the effects of ginseng on psychological functions. Three of those studies reported significant improvements in areas of mental arithmetic, abstract and memory tests. In another study, ginseng was reported to be less effective when compared to the control group (Vogler, Pittler, & Ernst, 1999). Two studies showed that ginseng extract taken by older adults produced significant improvements in neurological and psychiatric symptoms. Furthermore, psychomotor benefits were shown for younger, healthy subjects. In comparison, one study performed on healthy subjects for up to two years showed that ginseng had no effect on memory performance (Radad
et al., 2006). Overall, results are inconsistent for ginseng and cognitive impairment and thus not adequate for recommendation.

**Animal Studies**

Ginsenosides Rb1 and Rg1 have been shown to adjust acetylcholine release and re-uptake primarily in the hippocampus, as well as increase choline acetyltransferase in rodent brains. Memory functioning may improve due to ginseng’s ability to improve cholinergic functioning. Ginseng has also been linked to improving levels of dopamine and norepinephrine in the cerebral cortex. Positive effects seen in this location of the brain would include the improvement in concentration and cognitive processing and a more efficient integration of both sensory and motor functions. One study reports that learning was improved significantly after local administration of ginseng powder on aged and brain-damaged rats (Radad et al., 2006).

**Cardiovascular Effects**

**Human Studies**

A study evaluating the effects of red ginseng on the improvement of hypertension found that increasing nitric oxide (NO) release results in an improvement of vascular endothelial dysfunction. This study incorporated 17 subjects, seven of whom received ginseng therapy. Measurements of forearm blood flow after infusion of acetylcholine, sodium nitroprusside and bradykinin were measured by venous occlusion plethysmography. Overall, flow measurements were statistically higher for the ginseng treated group compared to the normotensive group. On the contrary ginseng’s subject flow recordings did not differ from the control group (Sung et al., 2000). This is the only study evaluating the effect of ginseng on hypertension. The effectiveness of ginseng has not been studied as a treatment for hypertension.

**Animal Studies**
Ginseng has been associated with a wide-range of cardiovascular effects. Animal studies for both rats and rabbits have shown that vasodilation occurs. This reaction has been linked to ginseng’s ability to decrease the degradation of NO and reported after chronic rabbit ginsenoside ingestion. Speculation that ginseng may help the hypertensive patient is based on the theory that ginsenosides reduce plasma cholesterol levels and are platelet activating antagonists. The anti-atherosclerotic mechanism is linked to ginseng’s capability to equalize prostacyclin and thromboxane as well as inhibit the release of 5-HT. Further, active ingredients prolong the conversion of fibrinogen to fibrin. In theory, ginseng would have cardioprotective effects for patients with cardiovascular disease. Ginsenosides have also been linked to angiogenesis which may provide therapeutic benefit for wound healing (Radad et al., 2006).

Anti-inflammatory & Anti-allergic Effects

Human Studies

Vogler (1999) reviewed two studies that assessed ginseng’s immunostimulant properties. One study reported an increase of T lymphocytes and leukocytes. The other found no increase of these cellular makers (Vogler et al., 1999). Additionally, Radad’s (2006) work offers information that supports ginseng’s effects in stimulating the immune system. Enhancements of interferon induction, phagocytosis, natural killer cells and B and T cells were reported in some human studies as well as in mice and guinea pigs.

Animal Studies

Examination of ginseng in animals has shown that extracts of ginseng help to modulate inflammation and allergic stimulants. Rat models identified that saponins from the root of ginseng inhibit IL-B and IL-6 gene expression. Ginsenosides were shown to decrease TNF-alpha levels produced by macrophages. Testing on guinea-pig mast cells identified that
ginsenosides Rb1 and Rc decreased histamine and leukotriene release. An example involving
dairy cows affected with mastitis showed that their recovery was positively influenced by the
addition of ginseng (Radad et al., 2006).

**Anti-carcinogenic Effects**

**Human Studies**

Reports of decreased incidence of cancers including lung, gastric, liver and colorectal are
associated with chronic use of ginseng. Specifically, ginsenoside Rh2 showed a reduction in
proliferation of human cancers involving the breast, prostate, liver and intestinal origin. Various
other ginsenosides Rb1, Rb2 and Rc displayed inhibitory properties for tumor angiogenesis and
metastasis (Radad et al., 2006). One study suggests that ginseng has been shown to have a dose
response relationship to cancer prevention. The results warrant that ginseng extracts should be
investigated in the prevention of certain types of cancer in humans (Yun, Choi, & Yun, 2001).

**Animal Studies**

Animal models also support ginseng’s anti-carcinogenic effects. One study, involving a
topical application of ginseng extract on mouse skin, showed significant reduction in papilloma
formation and suppressed epidermal ornithine decarboxylase activity and mRNA production.
Ginsenoside Rh2 showed a reduction in proliferation of CA in animal cell lines as well (Radad et
al., 2006).

**Erectile Dysfunction**

**Human Studies**

Ginseng has been used in traditional Chinese medicine for the treatment of sexual
impotence. A study involving 45 men with erectile dysfunction (ED) was the basis for the
practice recommendation provided by Price and Gazewood (2003) to use *Panax ginseng* as an
alternative treatment for ED. Subjects had not received any prior treatment for ED. For the purpose of the study ED was defined as the “persistent inability to achieve and maintain an erection sufficient for normal sexual satisfaction” (Price & Gazewood, 2003, p.20). Subjects were classified based upon the Korean version of the International Index of Erectile Function (IIEF) and approximately 70% were labeled as having moderate or severe ED. Further, at least 50% of the men had at least one other co-morbidity, most commonly hypertension or diabetes mellitus. Baseline measurements included the IIEF, self assessment, rigidity and tumescence experience during audiovisual sexual stimulation, penile duplex ultrasonography and response to penile injections of papaverine, phentolamine and prostaglandin E1. Sixty percent of subjects receiving the 900 mg three times daily dose of Korean red ginseng had improvements in their erections as opposed to 20% of the placebo group (Price & Gazewood, 2003).

Animal Studies

Sexual activity has been shown to increase in rat studies with ginseng supplementation. Theories behind the aphrodisiac effect include the same mechanism which helped cardiovascular function. The decrease in degradation of NO improves the ability for blood to fill the corpus cavernosum, therefore improving erectile dysfunction. Other reports suggest that with the addition of ginseng, serum testosterone levels rise, also causing an increase in desire for sexual activity (Radad et al., 2006).

Safety

General side effects associated with ginseng include excitation, headache, insomnia, palpitations, sleeplessness, hypertonia, edema, decreased concentration and possible estrogenic effects (Hudson et al., 2001). The increased psychoactive state can be attributed to ginsenoside’s ability to inhibit phosphodiesterase activity, thus increasing the levels of cAMP. There needs to
be more research because the exact mechanism still remains uncertain. The patient should be advised to avoid consumption of other stimulants, antipsychotic drugs or other hormone treatments. Drug interactions have been suspected with concomitant usage of warfarin and phenelzine (Izzo & Ernst, 2001). A case study of a 47 year old man reported a decline in International Normalized Ratio when taking warfarin and ginseng. The exact mechanism for this is unclear, but patients need to be monitored closely or avoid concurrent use of ginseng with anticoagulants (Cupp, 1999). Patients with diabetes should use extra caution when using ginseng due to its possible ability to lower blood sugar (National Center for Complementary and Alternative Medicine, 2005a). There has been controversial evidence supporting ginseng’s usage in combination with the influenza vaccine. Although no serious effects on the volunteers were seen taking ginseng in tandem with the vaccination, there were eight reports of side effects, primarily insomnia and nausea (Izzo & Ernst, 2001).

**Recommendation**

Because ginseng has numerous treatment claims, it is important for the clinician to make recommendations based on the evidence. Patients should be warned about adverse events or drug interactions. Due to the vague mechanism of action of ginseng and the availability of FDA approved drug regimens for conditions such as Parkinson’s and cardiovascular disorders, medications that have better RCT evidence should be considered first line treatment. Patients interested in lifestyle modifications and improving overall wellness should be made aware of ginseng and its potential positive effects.

Males suffering from ED should be informed of available therapies including the widely used prescription medications and red ginseng. Ginseng provides a more cost efficient and possibly an effective way to improve ED symptoms. The patient has the right to know that
ginseng is an option. Typical dosages are one or two grams of root every day or 100-300 mg of extract three times a day, three to four days per week (Hudson et al., 2001). Some sources advise to discontinue use after three months to decrease the risk of developing side effects (National Center for Complementary and Alternative Medicine, 2005a).
Feverfew

Description & Background

Feverfew, *Tanacetum parthenium*, is native to the Balkan mountains of Bulgaria and eastern Serbia. This herb can now be found throughout Europe and the western hemisphere. (National Center for Complementary and Alternative Medicine, 2006a). Feverfew has been used to treat many ailments including, fevers, inflammatory conditions, psoriasis, toothache, insect bites, rheumatoid arthritis, asthma and stomach aches. Within the last decade, feverfew has been used as a prophylaxis for migraines (Pittler & Ernst, 2004) The extract can be derived by drying the leaves, flowers and or stems of the feverfew plant. Active ingredients are incorporated into capsules, tablets and liquid formulations for administration (National Center for Complementary and Alternative Medicine, 2006a).

The main active ingredient, sesquiterpene lactone parthenolide, is thought to provide the physiological effects of feverfew. In vitro studies suggest that parthenolide inhibits the release of serotonin from blood platelets. This effect would support using feverfew prophylactically to treat migraines. On the contrary, other research does not support this physiologic theory of feverfew. Therefore the exact mechanism of action is not well understood at this time. Authors systematic analysis will be used to review feverfew’s efficacy in the treatment of migraines (Pittler & Ernst, 2004).

Conditions Reviewed

Migraine

The collaboration compiled five double-blind, RCTs for a total of 343 patients. A prior evaluation of feverfew compared with placebo for the prevention of migraines was performed in 2000 by the collaboration. Data from the previous study was inadequate and therefore efficacy
was not addressed. The new review re-evaluated this question and established a safety guideline for persons interested in experimenting with feverfew. These trials administered an oral preparation of feverfew at any dosage. The preparation did not include any other active components (Pittler & Ernst, 2004).

Meta-analysis produced mixed results concerning the efficacy of feverfew in the treatment of migraines with the interpretation that feverfew is not more efficacious than the placebo effect. Efficacy may have been inadequately assessed due to the inconsistency of active constituents produced from granulated feverfew leaves. Of the five trials reviewed, the two with the highest methodological quality demonstrated no favorable effects from feverfew. Four trials had an adequate sample size. In two of the trials, the incidence of associated nausea and vomiting was reduced with feverfew use. Feverfew also has an effect on prostaglandin synthesis. Chrysanthenyl acetate, an oil of feverfew, inhibits prostaglandin synthesis in vitro and displays analgesic effects. Overall, higher quality studies with larger sample sizes are still required to determine feverfew's efficacy (Pittler & Ernst, 2004).

**Safety**

Examination of feverfew identified mild and reversible adverse events. Two studies reported a higher incidence of adverse effects associated with placebo than to feverfew. Of all the RCT analyzed, 12 withdrawals from the study were associated with feverfew while seven were from placebo. Adverse events reported were due to a condition termed post-feverfew syndrome. This syndrome was described by patients who stopped feverfew and started the placebo. Patients complained of rebound migraines, anxiety, insomnia and joint stiffness. Patients taking feverfew for long-term treatment reported gastrointestinal symptoms and mouth
ulceration. More stringent regulations on dosaging and formulations could resolve these issues (Pittler & Ernst, 2004).

Other literature adds that for glossitis and stomatitis can occur if the dosage is not capsulated. At high concentrations feverfew may cause irreversible inhibition of gastrointestinal contractility (Hudson et al., 2001). Feverfew was not shown to affect blood pressure, heart rate, body weight, or hematological status (Pittler & Ernst, 2004). Feverfew should not be taken with concurrent thrombolytics and/or anticoagulants. This herb may potentiate methylsergide and possibly prevent 5-HT release from platelets (Poppenga, 2002).

Recommendation

Headache is a common reason for a healthcare visit. Patients, often try many treatments before finding relief. Clinicians have a time consuming and frustrating task when trying to resolve headache complaints. Patients are subject to trial and error treatments due to personal physiological effects, triggers and severity of headaches. Offering feverfew as a new method of treatment before conventional therapies is not recommended. Healthcare providers may choose to educate patient about feverfew if other standard treatments are failing. Patients should start a dose of 200-250 mg daily for prophylaxis of migraine headache (Hudson et al., 2001). Appropriate patient education of this herbal remedy should include the risk of post-feverfew syndrome, side effects and possible drug interactions. Capsulated pill form is recommended to decrease risk of glossitis and stomatitis. Patients should be monitored closely to adjust dosage based upon success and side effects.
Kava

Description & Background

Kava, *Piper methysticum*, is a native plant of the South Pacific islands. It was traditionally used as a ritual beverage and for medicinal purposes. This herb is obtained from the root and the rhizome, or underground stem, of the kava plant (National Center for Complementary and Alternative Medicine, 2006d). Kava, a member of the pepper family, was originally used to treat gonorrhea, aid in relaxation or sleep and, on the contrary, offset fatigue (Pittler & Ernst, 2003). Kava has also been used for asthma, urinary tract infections and topical analgesia. Today, kava is used principally in the treatment of anxiety, insomnia and menopausal symptoms. Thus far, little is still known about the mechanism of action of kava (National Center for Complementary and Alternative Medicine, 2006d). Some research shows that kava has similar action to benzodiazepines, influencing GABA receptors in the CNS. Kava is also recognized as having dopaminergic antagonistic properties (Izzo & Ernst, 2001). Kava can be used in various preparations such as beverages, extracts, capsules, tablets and topical solutions (National Center for Complementary and Alternative Medicine, 2006d). The following review will be solely taken from Pittler and Ernst meta-analysis of kava’s effectiveness in the treatment of anxiety.

Conditions Reviewed

Anxiety

Anxiety is a common disorder that has a lifetime prevalence rate of approximately 24 percent (Pittler & Ernst, 2003). In the year 2004, a startling estimation of 23 million Americans meet the inclusion criteria to be diagnosed with an anxiety disorder (National Institutes of Health, 2004). Benzodiazepines are a common class of drugs used to treat anxiety disorders but
have high side effect rates. Therefore, alternative therapies are being researched. Adverse
effects may include dependence, sedation and memory impairments. Authors compiled 12 RCT
for a total of 700 subjects to compare kava’s effectiveness compared to a placebo for the
management of anxiety. Time periods of kava treatment ranged from one to 24 weeks. Meta-
analysis included seven studies and measurements were reported using the Hamilton Anxiety
Scale (HAM-A). In these seven studies, 74% of subjects, were diagnosed according to the
standards of the American Psychiatric Association. This is a common scale use to quantify
anxiety symptomatology (Pittler & Ernst, 2003).

Patients receiving kava extract, had a significant lower HAM-A score, indicating less
anxiety, compared to placebo. In addition, the five remaining trials that were not submitted for
meta-analysis strongly support that kava extracts reduce anxiety. Authors add that although kava
seems to produce an effect, the overall significance is low due to small sample sizes. Studies
including larger sample sizes may provide validity to kava’s treatment claim (Pittler & Ernst,
2003).

Safety

Much attention has been focused on kava’s effect on the liver due to its association with
hepatotoxicity. In 2002, the FDA advised consumers of this possible risk. The FDA used
information from Germany, Switzerland, France, Canada and the United Kingdom that reported
25 cases of liver toxicity linked to kava supplementation. Liver effects included hepatitis,
cirrhosis and liver failure. The FDA advised that although this associated side effect is rare,
warnings are still warranted (National Center for Complementary and Alternative Medicine,
2002). The collaboration accumulated a systematic review to evaluate hepatotoxicity prevalence
in 7,078 patients. Patients took kava extract for five to seven weeks with a dosage of 105 mg to
240 mg per day. Hepatotoxicity was not correlated with kava ingestion, leading authors to agree
that hepatotoxicity appears to be a rarity with kava treatment. Liver enzymes were measured from
seven trials and no abnormalities were suggestive of hepatotoxicity. The most frequent adverse
effects were stomach symptoms, drowsiness, restlessness, tremor, headache and tiredness
Overall this systemic review reported that adverse events were mild, transient and infrequent
(Pittler & Ernst, 2003).

Kava usage has also been linked to Parkinson-like symptoms. Patients on kava extract
may display signs of dopamine deficits due to kava’s dopaminergic antagonistic properties (Izzo
& Ernst, 2001). It is important to also recognize that with chronic kava intake, patients may
develop a scaly, jaundiced appearing skin (National Center for Complementary and Alternative
Medicine, 2006d). This condition may also present with erythematous eyes, a sign of kava
toxicity, referred to as kawaism (Poppenga, 2002). Kava is a lipophilic herb and it is theorized
that the extract can accumulate in sebaceous oils and trigger a hypersensitivity reaction (Cupp,
1999).

Kava should not be taken concurrently with CNS depressants such as benzodiazepines
and alcohol. It is important to avoid kava use in Parkinson’s patients because of the
doaminergic antagonistic action against conventional Parkinson’s medication. Patients on
levodopa with concurrent intake of kava would have opposing acting medications, therefore
blocking levodopa’s therapeutic effect (Izzo & Ernst, 2001). Kava should not be taken if the
patient has a diagnosis of depression (Poppenga, 2002). Poppenga (2002) states that
supplementation should be no greater than three months to avoid habituation.
Recommendation

Anxiety is often treated with benzodiazepines. Commonly, alprazolam (Xanax) is prescribed. Due to various adverse effects of benzodiazepines, such as dependence, sedation and memory impairments, kava has been suggested to provide a greater benefit compared to the risk associated with such anti-anxiety medications. Kava has been shown to reduce anxiety levels in RCT and has been linked to adverse effects. Recommendations should be made to patients discussing the risk versus benefit ratio for all anxiolytics. Standard first lines treatments should continue for patients suffering with anxiety due to the low sample size of the kava trials. Patients choosing kava should be started on a typical dosage of 60-120 mg daily. Duration of treatment should be limited to the current studies suggesting that kava is a relatively safe option for short term treatment of one to 24 weeks (Pittler & Ernst, 2003). Trials investigating long term safety profiles are essential for clinicians to agree that long term treatment is safe. Dosages should start low and titrated up to therapeutic levels. Patients with a diagnosis or symptoms of Parkinson’s or depression should not be advised to start kava treatment and should be counseled to cease kava self-medicating.
Garlic

Description & Background

Garlic, *Allium satium*, is part of the onion family. For thousands of years, this herb has been used for both medicinal and culinary purposes. Garlic has been traced back to Babylonian times, found in the tomb of Tutankhamen and used by ancient Greeks and Romans (Meher & Duley, 2006). Common conditions treated with garlic are dyslipidemia, hypertension, various infections and cancer (Bhasale & Lissiman, 2006). Garlic’s antiseptic effect was described by Pasteur, and this supplement was used to prevent gangrene during World War I and World War II (Tattelman, 2005). Many preparations of garlic exist such as powder, tablets, capsules, and oil; it can also be eaten raw or cooked (National Center for Complementary and Alternative Medicine, 2006b).

Allicin is garlic’s main biologically active compound. This extract is formed when garlic is crushed or chewed. A sulphur compound, allin is broken down by an enzymatic process forming allicin (Meher & Duley, 2006). Dried garlic must have an enteric coat to provide any result due to the inhibition of allinase by gastric acid secretions. This enzyme can be deactivated by high temperatures, therefore garlic that is cooked has less of a medicinal effect (Tattelman, 2005). Other garlic extracts have been shown to have biologically active effects but at this time little is still known about these ingredients (Meher & Duley, 2006). Cochrane Collaboration has developed a protocol for future meta-analysis for treating the common cold with garlic and has performed meta-analysis on garlic’s effect on peripheral vascular disease and pre-eclampsia prevention. The following examination of garlic will only include these systematic reviews.
Conditions Reviewed

Common cold

The common cold produces an approximated 40 billion dollar industry each year in the United States (Fendrick, 2003). Children have six to eight attacks of the common cold each year, while adults experience between two and four. Herbal supplementation is used frequently to provide relief to suffering individuals. Viruses are the most common culprit and produce symptoms such as sore throat, cough, nasal congestion, nasal draining, headache and malaise. It is a challenge to isolate particular viruses with varying pathogenetic mechanisms to test garlic’s effectiveness. Due to these challenges, the collaboration has identified a protocol for future studies to investigate the efficacy and safety of garlic for treating this condition (Bhasale & Lissiman, 2006).

Peripheral arterial occlusive disease

Atherosclerotic plaques can prevent normal blood flow through arteries. In peripheral arterial occlusive disease, the major arteries affected are lower extremity. Intermittent claudication is the most common symptom of early peripheral arterial occlusive disease. Garlic is thought to have a lipid lowering effect thus helping to maintain arteriole integrity (Jepson, Kleijnen, & Leng, 2008). Prior meta-analysis concluded that garlic reduced total cholesterol levels by four to six percent compared to placebo administration (Tattelman, 2005). Jepson et al. reviewed a trial that contained 78 subjects, including men and women between the ages of 40 and 75. The trial evaluated both the dried and non-powered preparations of garlic versus a placebo for treatment of peripheral arterial occlusion. The trial assessed subjects after 12 weeks. Measurements taken at this time involved ankle pressures, treadmill evaluation and subjective reports from patients. Results demonstrated that pain free walking distance increased from 161
to 207 meters for the group being treated with garlic. The placebo group’s walking distance increased from 172 to 203 meters. Other reports concluded that there was no difference comparing blood pressures, heart rate, ankle and brachial pressures (Jepson et al., 2008).

A more recent study that included seven systematic reviews and three additional RCTs investigated complementary therapy and its effectiveness in treating peripheral arterial disease. Garlic was one of the dietary supplements examined. This article was consistent with the findings from Jepson et al, concluding that there is no statistically significant evidence that proves that garlic is beneficial for patients suffering with peripheral arterial occlusive disease (Pittler & Ernst, 2005).

*Pre-eclampsia and sequela*

Pre-eclampsia is classified as hypertension (≥ than 140 mmHg systolic or 90 mmHg diastolic) during the second half of pregnancy and is associated with the development of proteinuria. The etiology of pre-eclampsia is uncertain but the complications can be detrimental for both fetus and mother. Sequelae may develop including of eclampsia, stroke, liver or kidney failure and risky preterm deliveries. Garlic’s proposed mechanisms of action involve lowering blood pressures, reducing oxidative stress and inhibiting clot formation. The collaboration reviewed one trial consisting of 100 primigravid women. Women were between 28 and 32 weeks gestation. All women were at moderate risk for developing pre-eclampsia and were either given a dried garlic supplement or placebo. The risk associated with the development of pre-eclampsia was decided by determining a rise in diastolic blood pressure of at least 20 mmHg on two separate readings. Follow-up measurements were reported for all subjects and concluded that there was no clinically significant difference between the garlic and placebo. Larger studies are necessary to evaluate the effectiveness of garlic for this condition (Meher & Duley, 2006).
Safety

Garlic was not associated with any severe side effects in the prior study; subjects did complain of odor associated with garlic (Jepson et al., 2008). Possible side effects include heartburn, nausea and hypersensitivity reactions. Additionally, it is important to remember garlic’s ability to produce an anti-coagulative effect. Do not take garlic with a concurrent anti-coagulant or anti-platelet medication. Patients should cease garlic ingestion before undergoing surgery or other minor procedures where bleeding may occur. Case reports highlight that garlic may cause hypoglycemic effects; this is especially important to discuss with diabetic patients (Izzo & Ernst, 2001). Garlic has also been found to impede the effectiveness of saquinavir. Patients with HIV should avoid garlic if saquinavir or other protease inhibitors have been prescribed for their treatment (National Center for Complementary and Alternative Medicine, 2006b).

Recommendation

No severe adverse events and only minor side effects are associated with garlic supplementation. Clinicians need to be aware of the possibility of certain drug interactions. Garlic should not be recommended as prevention of cardiovascular disease or pre-eclampsia. There is no conclusive evidence that garlic supplementation lowers the risk of developing cardiovascular complications and or gestational hypertension. Although garlic has been studied at length both in animal and human clinical trials, the quality of the human trials has been inconsistent (Tattelman, 2005). Pregnant women interested in adding garlic to their prenatal vitamins should be counseled that reports suggest that this herbal is an anticoagulant and may increase the tendency for bleeding. Although not conclusive, garlic has been linked to improve immune functioning as well as reduce cholesterol and blood pressure (National Center for
Complementary and Alternative Medicine, 2006b). Patients should be advised on the risk versus benefit of garlic supplementation and that the evidence regarding garlic is not statistically significant enough to promote this herbal to improve cardiovascular functioning. On the contrary, patients can be advised that garlic has been linked to improving certain conditions and that the overall risk associated with garlic supplementation is low. Garlic ingestion may reduce the number of upper respiratory infections, although evidence for this is lacking as well. Typical dosages of garlic range from four to 12 mg of allin, between two and five mg of allicin, or two to five grams of the fresh clove (Hudson et al., 2001).
Ginger

Description & Background

Ginger has been used traditionally in Asian medicine to treat gastrointestinal symptoms. This herb is often used to relieve stomach aches, nausea and diarrhea. Ginger is also a common ingredient for culinary purposes. In the United States, many medications used for treating nausea and cold and symptoms contain extracts from ginger as one of the biologically active ingredients. Ginger has been used to treat nausea due to surgery, motion, chemotherapeutic agents and pregnancy. Additionally, there have been suggestions that ginger may be used to treat rheumatoid arthritis, osteoarthritis and musculoskeletal pain (National Center for Complementary and Alternative Medicine, 2006c). Gingerol, a ketone extract from ginger, has been used primarily in research trials to evaluate ginger’s effectiveness. The portion of ginger that is consumed comes from the rhizome of the plant (White, 2007). The rhizome can be prepared in various ways. Extracts can be obtained by eating fresh, raw ginger root or dried root in tablets, capsules, tinctures and teas (National Center for Complementary and Alternative Medicine, 2006c).

Studies have been inconclusive in determining the anti-emetic mechanism of ginger. Although unclear, theories suggest that ginger may inhibit serotonin receptors and produce anti-emetic effects on both the gastrointestinal tract and the central nervous system. It is also reported through testing in vitro human synoviocytes that ginger inhibits the activation of α-TNF and COX-2, producing anti-inflammatory effects (White, 2007). This review will focus on the Cochrane Collaborations meta-analysis involving ginger’s effectiveness for intervention of nausea and emesis in early pregnancy.
Conditions Reviewed

Emesis and nausea in early stages of pregnancy

The meta-analysis performed by the Jewell and Young investigated 28 trials of nausea treatments. These treatments included antihistamine medications, vitamin B6, Debendox, P6 acupressure and ginger. The design of the systematic review began with filtering participants. The randomized trials contained women that were less than or equal to 20 weeks of gestation suffering from chronic nausea and/or vomiting. Varying degrees of severity were incorporated, including women with hyperemesis gravidarum. The etiology of nausea and vomiting associated with early pregnancy has not been identified. Rising levels of human chorionic gonadotropin hormone has been considered to cause these symptoms (Jewell & Young, 2003).

Vutyavanich et al. stresses the significance that ginger may work without side effects compared to other drugs incorporated into this review. Antihistamines work well but produce a sedative effect. Debendox was taken off the market after fetal limb defects were associated with its administration. To provide more direct information regarding nausea and vomiting associated with early pregnancy, 12 trials incorporating 1,557 women were analyzed. Six of those trials totaling 1,309 women had acupuncture therapy, two trials of 416 women used vitamin B6 and one including 70 participants were given ginger extract. All 12 trials produced a combined reduction in nausea and emesis. The ginger trial compared to placebo had a completion rate of 96 percent. An improvement of both nausea and vomiting was found for ginger treatment. Trials identified showed that 28 of 32 subjects had improvement after supplementation of ginger compared to 10 of 35 in the placebo group (Vutyavanich, Kraisarin, & Ruangsri, 2001).
Safety

Jewell and Young did not identify any adverse effects with ginger treatment. Ginger’s active ingredients may vary from one dose to the next. Also, location of the plant and post harvesting factors may differ; this could effect treatment (Jewell & Young, 2003). Ingestion of ginger may cause mild gastrointestinal side effects such as gastroesophageal reflux, diarrhea and hypersensitivities of the oral mucosa. Fibrinolytic activity may be altered with the addition of ginger; therefore, patients should avoid concurrent use of ginger with anticoagulant therapies. Animal studies have shown that ginger may produce arrhythmias. No human studies have shown this effect (White, 2007). It is extremely important to rule out the possibility of teratogenicity concerning this medication.

Recommendation

Ginger’s efficacy regarding the treatment of early pregnancy-associated emesis is promising. Limited side effects are associated with usage, and few drug interactions have been identified. Recommendation of ginger supplementation for women suffering with nausea and vomiting in early stages of pregnancy is advised. Ginger in relation to the treatment of motion sickness has mixed reviews. A review performed by White stated that one study showed it to be superior over dimenhydrinate and placebo for effectiveness. Another study did suggest ginger to benefit seasickness experienced by naval cadets (White, 2007). Other research has not shown that ginger has been statistically significant in treating this condition. If non pregnant patients inquire about other methods besides standard pharmacological treatments to treat motion sickness, ginger should be discussed and suggested. A typical dosage for motion sickness is one gram 30 minutes prior to travel, followed by maintenance dosing of 0.5 to one gram every four hours as needed. The total daily dosage of ginger ranges from two to four grams (Hudson et al.,
Pregnant patients should begin ginger treatment with 250 mg four times per day (Epocrates, 2008).
St. John’s Wort

*Description & Background*

*Hypericum perforatum,* commonly referred to as St. John’s wort, is an herb that has an extensive history in treating a wide range of disorders. The name comes from St. John the Baptist. The flower usually blooms close to his birthday on June 24 (American Cancer Society, 2008). Today, this herb generates much attention because of its potential to treat depression, anxiety and sleep disorders (National Center for Complementary and Alternative Medicine, 2005d). Germany has licensed extracts derived from this herb to treat these conditions. The biologically active ingredients from St. John’s wort can be obtained from its flowering top. The tops are then used to prepare either tablets or teas for ingestion (National Center for Complementary and Alternative Medicine, 2005d). At least seven active of ingredients from St. John’s wort may provide pharmacological effect: naphthodianthrons (hypericins), flavonoids, biflavonoids, xanthons and phloroglucinol derivatives. Although the exact mechanism is unclear, phloroglucinol derivatives such as hyperforin, have been shown to produce anti-depressant activity. Overall, the combined extract produces the greatest anti-depressant effect (Linde, Mulrow, Berner, & Egger, 2005).

Animal models have shown that St. John’s wort produces antidepressant qualities (Linde et al., 2005). Further studies describe the extract’s physiological mechanisms by its ability to inhibit re-uptake of neurotransmitters including serotonin, dopamine and norepinephrine (Cupp, 1999). A German reference recognized hypericin as a possible MAOI (Cupp, 1999). Linde et al. performed a systematic review to investigate St. John’s wort’s efficacy in treating depression. Depression will be the only condition examined.
Conditions Reviewed

Depression

A total of 37 trials were included in this meta-analysis. Trials were combined from 26 experiments (3,320 patients) involving comparison with placebo treatment and 14 trials (2,283 patients) being evaluated against prescribed medications such as selective serotonin inhibitors (SSRI) or other older drugs. Thirteen of those studies provided data describing the efficacy and safety assessment, while six compared St. John’s wort to the SSRI’s fluoxetine and sertraline. Globally, drop out rates for participation were low. Clinical depression noted for subjects was classified as mild to moderate range for most trials. Outcome measures for efficacy were evaluated using the Hamilton Depression Scale (HAMD) and Clinical Global Impression Index (CGI). These scales were used to evaluate changes in symptomatology of subjects.

For mild to moderate depression, hypericum extracts showed a greater improvement of symptoms compared with the placebo. St. John’s wort was shown to be similarly effective as prescribed anti-depressants. Six recent studies compared St. John’s wort’s to placebo and standard therapies for the treatment of major depression. St. John’s wort showed minimal benefits compared to placebo and standard therapies. Other trials suggest that St. John’s wort is comparable to prescribed drugs for the treatment of major depression disorder. Authors conclude that the evidence regarding St. John’s wort is inconsistent and confusing (Linde et al., 2005).

Safety

Risks due to St. John’s wort are minimal and unusual. Analysis of the extract compared to placebo showed that fewer patients taking hypericum terminated the study early due to adverse events. In comparison with SSRIs and older medications, patients were less likely to
report and drop out due to adverse events (Linde et al., 2005). St. John’s wort as a monotherapy has very good safety profiles. Concomitant usage of St. John’s wort with other SSRIs may be a concern. St. John’s wort is metabolized by the CYP monoxygenase enzyme system and, therefore, other drugs that use this mechanism for metabolism may cause problems. Induction of the hepatic enzymes may increase their capacity to metabolize other drugs more quickly producing dangerous side effects. When hypericum is used with other SSRIs such as sertraline and paroxetine, symptoms of serotonin excess may result. This is termed central serotonergic syndrome, and symptoms include tremor, autonomic instability, headache, myalgias, delirium and motor restlessness. St. John’s wort has also been shown to increase the activity of P-glycoprotein causing greater elimination of drugs. It can reduce concentration of warfarin, oral contraceptives, phenprocoumon, cyclosporine, amitriptyline, theophylline, indinavir and digoxin (Izzo & Ernst, 2001).

St. John’s wort has also been described as having MAOI-like capabilities. It is important to remember MAOI like drugs have the potential to react with other drugs or food products, specifically, tyramine rich foods such as aged wine and cheeses. There are no current reports indicating that tyramine rich foods and St. John’s wort can cause an adverse side effect (Cupp, 1999). Acute delirium has been reported as a result of an interaction with St. John’s wort and valerian, although reports of loperamide as a monotherapy have been shown to cause delirium (Izzo & Ernst, 2001).

One example of the possibility of adverse drug interactions is a case of a 50 year old woman. She was taking hypericum at 600 mg per/day for a length of 10 days, and then took one dose of paroxetine 20 mg. She began to complain of malaise and nausea and became incoherent. The woman had been taking the paroxetine 40 mg prior to St. John’s wort ingestion for a period
of eight months. She discontinued the paroxetine when she started taking St. John’s wort. Studies show that hypericin’s half life is 24 to 48 hours. When patients have been taking St. John’s wort and are ready to start a new antidepressant, a conservative safety suggestion is to wait two weeks until implementing the new drug. However, if a patient is very severely depressed, this may not be a plausible proposal (Cupp, 1999).

Other side effects associated with St. John’s wort usage includes dry mouth, dizziness, confusion, gastrointestinal symptoms, hypersensitivity and photosensitivity. A case involving a 35 year old woman self medicating with ground St. John’s wort developed pain on sun-exposed areas. The patient ceased intake of hypericum and symptoms began to resolve. Photoactivation causing demyelination of the woman’s cutaneous axons was theorized to be the cause of her pain (Cupp, 1999). Any medication causing an increase in photosensitivity, such as doxycycline, should be discussed with patients using St. John’s wort (Hudson et al., 2001).

**Recommendation**

Medications used to treat depression should be carefully dispensed due to the possibility of serious effects including dependency and suicidal ideation. A recent study regarding the treatment of depression combined results from 47 clinical trials assessing the efficacy of fluoxetine and paroxetine. Researchers concluded that the placebo effect of these drugs is providing more of a benefit than the medication itself. Patients with mild to moderate depression showed no benefit from medication. Moreover, patients with severe depression only improved minimally. Compared to mild to moderate depression, the treatment of severe depression with these same drugs was shown to have real benefit, though it was still only minimal. The authors conclude that when alternative therapies have failed, new-generation antidepressants should be limited to patients with severe depression (Kirsch et al., 2008).
According to Linde et al, St. John’s wort appears to have greater benefit when compared to standard medication for the patient with mild to moderate depression. However, the evidence is inconsistent and confusing. Health care providers should not base practice on research that is not conclusive, and therefore St. John’s wort should not be recommended at this point in time regardless of the possible therapeutic effects. Clinicians cannot evade the theory that perhaps the treatment of depression, in and of itself, is psychologically therapeutic, regardless of the drug used. Therefore some providers may feel that St. John’s wort may be valued on the same playing field as conventional therapies. St. John’s wort dosaging may begin with as much as 300 mg three times a day, for a duration of eight weeks (Hudson et al., 2001). Any anti-depressant medication should be titrated slowly, and discontinuation should be tapered slowly to avoid serious effects, dependency and suicidal ideation.
Echinacea

Background & Description

Echinacea is a native plant to the North America. Nine species exist with the most commonly used form being, *Echinacea purpurea*, because it is thought to be the most potent. Extracts of this plant have been used to treat or colds, flu, or other infections and are also used prophylactically for the same conditions. Infrequently, echinacea has been used for dermatologic conditions such as acne and wounds. The plant and roots may be used fresh or dried to create teas, juice and extracts for use (National Center for Complementary and Alternative Medicine, 2005b). The collaboration focused its meta analysis on echinacea’s safety and efficacy in treating the common cold. This will be the only condition examined.

Echinacea is produced in a variety of ways based on the part of the plant used, method of extraction and addition of other homeopathic ingredients. It is necessary to standardize echinacea products in order to evaluate efficacy. The mechanism of action for echinacea is indistinct. Extracts may act independently or synergistically. The immunomodulatory effects are related to the extracts alkamides, glycoproteins, polysaccharides and caffeic acid derivates (CADs). Examination in mice showed that alkamides, glycoproteins, polysaccharides enhance activation of macrophages and natural killer cells and display properties of antiviral activity. Alkamides have also been attributed to anti-inflammatory modulation and u-regulation of tumor necrosis factor (TNF) by activating CB2 receptors (Linde et al., 2005). A study performed to investigate echinacea’s effect against cytokine production stimulated by Rhinovirus 14 showed that echinacea reversed most of the inflammatory modulators. Rhinovirus, a very common pathogen of upper respiratory infections, was introduced to human bronchial epithelial cells. Upon induction, 31 related cytokine molecules were released, and echinacea helped combat most
of the cytokines’ inflammatory effects. This study indicates that echinacea may be useful for treating the common cold, coughs and other upper respiratory infections (Sharma, Arnason, Burt, & Hudson, 2006).

**Conditions Reviewed**

**Common cold**

Linde et al. examined 16 trials that included 22 comparisons of echinacea treatment with a control group. Nineteen studies compared echinacea with placebo, two compared echinacea with no treatment, and one compared it with another herbal modality. Results were gathered by measuring the frequency, severity and duration of colds experienced by subjects. Additional measurements evaluated symptomatology reported by patients. Conclusions drawn from this study are as follows. Two trials placed subjects on echinacea treatment for eight to 12 weeks, but these trials showed no benefit in preventing the common cold. The majority of studies investigated echinacea usage after onset of cold symptoms and found that echinacea may shorten and decrease severity of symptoms for adults. However, the decrease was not quantified. Specific preparations of this herb may show to have a greater therapeutic effect than others. For the use of children there is no clear benefit for these purposes at this time.

**Safety**

Side effects in the studies reviewed by the collaboration were rare. In one trial including children rashes were reported. The most significant effect induced by usage of echinacea was hypersensitivity reactions (Linde et al., 2005). Allergic reactions are more common in persons who are allergic to plants in the daisy family such as ragweed, marigolds, chrysanthemums. Additionally, increased sensitivity can be seen with people diagnosed with asthma or atopy. Gastrointestinal side effects such as nausea and vomiting may also occur (National Center for
Complementary and Alternative Medicine, 2005b). There are few studies evaluating the safety of echinacea for long periods of time, and there is no current evidence that long term therapy may potentate risks. Recommendations from the German drug regulatory authority state that echinacea should not be used greater than eight weeks at a time. Parenteral use should not be recommended (Linde et al., 2005). Echinacea and immunosuppressants including cyclosporine and corticosteroids should not be taken concurrently due to the potential of an adverse drug interaction (Hudson et al., 2001).

**Recommendation**

Current treatment for the common cold involves symptomatic treatments. Research does not demonstrate any severe side effects associated with echinacea. Echinacea may be linked to possibly shortening the duration of the illness. Patients need to be educated that the evidence for echinacea is not conclusive and may vary due to preparation of the herb. Patients may choose to supplement over the counter treatments for the common cold with echinacea supplementation. This is should not be a recommendation of the provider due to the lack of evidence and variance surrounding echinacea supplementation. Standard dosages are between two and five grams of the dried root for no more than six to eight weeks. Six to nine ml/day of echinacea juice is an alternative form (Hudson et al., 2001). Currently, there is no research that investigates prophylactic echinacea supplementation during the winter months when the common cold escalates in prevalence.
Conclusion

The need for CAM to be addressed thoroughly by the medical community is clear. Providing recommendations for the use of alternative therapies that lack clinically significant evidence is a controversial issue. Compared to prescription medications, a lack of funding creates a marked shortage of studies that could build evidence to support CAM. Pharmaceutical companies provide monies for research that help to profit their individual corporation. Herbal medicines can be sold under a free market due to their unregulated FDA status. If a pharmaceutical company invested money for herbal remedy research, little to no profit would be seen due to a market that is already saturated with herbal manufacturers. The limited supply of research creates difficulty for health care providers when discussing herbal supplementation with their patients.

European countries create a huge reference for evaluating the safety and efficacy of herbal supplements. Guidelines for usage in those countries are derived from the philosophy of the World Health Organization’s Guidelines for the Assessment of Herbal Medicines. The viewpoint of this organization stresses that in the absence of scientific research, a substance’s historical usage is a legitimate way to document safety and efficacy (Messina, 2006). The United States does not accept this school of thought. A plausible resolution to provide more research would be to increase government allowance to special research groups interested in herbals. Another possibility would be to mandate pharmaceutical companies to research herbals with their own profit gains each year. If more research was performed, the DSHEA would be obligated to create a new regulatory category within the FDA stating that herbals should be considered drugs. Results from this reform would provide the framework for herbals to be
regulated just as any other drug. Herbal therapies would then have standard dose equivalents thus helping to improve patient safety as well as clinical knowledge of herbal medicines.

As health care providers it is necessary to address the needs of all of patients using CAM therapies. Patients, regardless of sex, age, socioeconomic status and race are experimenting with CAM. Results from a national study that surveyed why patients choose alternative medicine reported that users of CAM tend to be more educated and have a holistic perspective concerning their health (Astin, 1998). Planta (2000) investigated the prevalence of herbals in the low-income population and concluded that 56% of the participants were of a low socioeconomic status. Results of that same study also showed that 41% of all users referenced their friends or family members as the primary educator about herbal products (Planta et al., 2000). Another study investigating alternative medicine trends in the United States showed that CAM usage could not be confined to any one portion of society (Eisenberg et al., 1998). With herbal products being used by many cohorts of society, it is the duty of health care providers to become more educated in this field of medicine in order to bridge the communication gap with our patients.

The lack of education about herbal treatments in the curriculum of many health care providers has placed the burden on the clinician. Finding and interpreting the quality of RCT can be a difficult task, especially without having a common knowledge base of the herbal therapy. The reader of RCT must be able to understand complex pharmacotherapies for the herbal being examined and decide if the trial established credibility for its intended use (Margolin, Avants, & Kleber, 1998). Fortunately, the Cochrane Collaboration helps to produce and maintain accurate systematic reviews for CAM, including herbal therapies. The database is updated quarterly with information and conclusions provided at the end of each review to help
combine and summarize evidence for the reader. Although some results may be inconclusive, these systematic reviews are still valuable. The Cochrane Collaboration provides a comprehensive assessment to identify where the current knowledge exists for a given topic and what needs to happen in the future to improve the learning curve (Ezzo, Berman, Vickers, & Linde, 1998).

As a health care provider it is important that evidence based practice guide our clinical decision making. Medicine and practice can no longer be held to the standards of tradition. Patients seek treatments that have evidence supporting effectiveness and safety. Many people attribute the development of epidemiology and the support of evidence based practice (EBP) to Archie Cochrane. The term EBP was coined in the 1980’s at The McMaster Medical School in Hamilton, Ontario. This transition valued research as the basis of learning and consequently practicing medicine (Milton, 2007). This movement affects health care professionals with prescription privileges to the highest degree. Prescribers now more so than ever, are expected to back up their decision making with evidence. An editorial submitted to the British Medical Journal by Simon RJ Maxwell eloquently describes the controversy that surrounds evidence based prescribing. EBP will ultimately lead to safer and more effective prescribing practices although prescribers are left to decide which data is the most accurate and representative. He concludes that health care providers need to skeptical of prescribing medications. “Prescribing will always be too complex for all the answers to be evidence based and ‘grey zones’ will always be there” (Maxwell, 2005, p.248).

Herbal recommendations create even more “grey zones” due to the overall lack of evidence compared to standard FDA approved drugs. An issue that creates even more hesitance surrounding complementary medicine is the risk associated with malpractice liability. The legal
definition of a malpractice is when a therapy is chosen that falls below the standard of care and thereby injures the patient. CAM guidelines are less rigorous than their conventional medicine counterpart. Recommendations need to be based upon both safety and efficacy for health care providers to insure that CAM modalities are not below the standard of care. These guidelines will evolve over time as research continues to provide EBP. Clinicians need to be cognizant of this idea whether they are advocating an alternative therapy or providing advice to patients’ questions concerning CAM (Cohen & Eisenberg, 2002).

Table 3 summarizes the clinical approach to provide adequate standard of care concerning CAM treatments. Theses strategies and risk stratification scale are also intended to reduce the overall risk of malpractice liability.

Continuity of care for patients is imperative. To provide more concise care for patients an integration is needed between conventional and the alternative medicine. A study aimed at overcoming the communication gap between conventional health care and CAM practitioners reported that it is also of equal importance to educate CAM clinicians on the significance of close communication with conventional health care providers. Improved communication from both sides of the medicine spectrum would ultimately bring together alternative and conventional medicine (Frenkel, Ben-Arye, Geva, & Klein, 2007).

Patient-centered care requires an avenue for open communication between the provider and the patient. This cannot happen without practitioners inquiring and patients reporting the usage of herbals. One theory suggests such reluctance from patients may be attributed to their apprehension of a negative response form their health care provider (Planta et al., 2000). Clinicians may not be asking about herbal supplementation as well. For instance, only 58% of physicians involved in a study analyzing physicians’ perception of complementary medicine
admitted to often asking about their patients’ usage of CAM. Fifty percent of physicians from that same study estimated that only 10% of their patients report usage of such alternative therapies (Giveon, Liberman, Klang, & Kahan, 2003). If this pattern of poor communication continues, the obligation to do no harm may be lost. Patients may not consider their herbal supplement a drug. There needs to be an increase in awareness that herbs are non-FDA regulated medications. An incomplete medication record can create problems concerning herb-drug interactions. Polypharmacy is a huge concern in the medical community. Yet there may be questions regarding what medications and over the counter supplements patients are taking.

To facilitate this, when scheduling appointments, patients should be advised to bring a complete list of all current medications as well as over the counter supplements, including vitamins, minerals and herbal remedies to the clinic. This would consume a small amount of time but create far less confusion regarding what the patient is taking. Patients should fill out a standardized form documenting all of their medications at their office visits. The practitioner should then review the form with the patient and place it in their medical chart. The patient should be given a copy of their chart so there is less chance of medication confusion for patient when returning home. Figure 1 is an example of such a form that should be implemented in both conventional and alternative medical practices.

If clinical knowledge of herbal supplementation increased, health care costs would decrease. Patients would be less likely to develop sequlae due to herb-drug interactions. Certain herbals have shown to delay therapeutic benefit by induction of hepatic enzymes and transporters. These metabolizing actions create the potential for alteration of drug activity (Venkataramanan, Komoroski, & Strom, 2006). If these complications were less likely to occur it would result in fewer follow up visits, thus decreasing costs for the patient and insurance
companies. Health care providers with increased knowledge of herbal supplements would be able to advise their patients to avoid spending on ineffective treatments and propose which may help to provide a therapeutic benefit (Gaudet & Snyderman, 2002). Herbal therapies could then be compared with their prescriptive drug counterparts. Patients receiving prescriptions might have the same results using herbals. Cost comparison could be made and patients would choose a treatment based upon personal interest, socioeconomic status and insurance coverage.

This literature review was performed to educate health care providers on the top ten herbal supplements used in the United States with emphasis on the conditions these herbals might treat, to evaluate the efficacy by examining evidence from RCT and to review safety precautions, and to provide an overall recommendation for clinical practice. Recommendations were finalized after careful examination of the RCT evidence; an overall risk stratification was interpreted using Cohen and Eisenberg’s classification scale displayed in Table 3. Recommendations are suggested for healthy, adult use only. It is important to realize that each clinician must evaluate the individual on a case by case basis. Caution is imperative when evaluating patients experimenting with herbs, especially pregnant or nursing women and children (Messina, 2006). Knowledge of herbal medicine will help to provide a more valid foundation for herbal supplement use and identification of disuse in the future.

It is necessary to be cognizant of the patient’s ability to experiment with herbal therapies and, as clinicians, help to guide them to a safe and therapeutic healing process. As providers we should relentlessly work to ensure patient safety and advocate for higher quality, large- scale randomized trials to generate evidence based practice guidelines regarding herbal therapies.
References


*Cochrane Database of Systematic Reviews*(2).


*Cochrane Database of Systematic Reviews*(3).


Table 1.

*Top ten selling herbal supplements in the US*

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Scientific Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo</td>
<td><em>Ginkgo biloba</em></td>
</tr>
<tr>
<td>Saw palmetto</td>
<td><em>Serenoa repens</em></td>
</tr>
<tr>
<td>Milk thistle</td>
<td><em>Silybum marianum</em></td>
</tr>
<tr>
<td>Ginseng</td>
<td><em>Panax ginseng</em></td>
</tr>
<tr>
<td>Feverfew</td>
<td><em>Tanacetum parthenium</em></td>
</tr>
<tr>
<td>Kava</td>
<td><em>Piper methysticum</em></td>
</tr>
<tr>
<td>Garlic</td>
<td><em>Allium sativum</em></td>
</tr>
<tr>
<td>Ginger</td>
<td><em>Zingiber officinale</em></td>
</tr>
<tr>
<td>St. Johns wort</td>
<td><em>Hypericum perforatum</em></td>
</tr>
<tr>
<td>Echinacea</td>
<td><em>Echinacea angustifolia/pupurea</em></td>
</tr>
</tbody>
</table>

Note: Table adapted from (Gagnier, DeMelo et al., 2006)
## Table 2. Practical Guidelines for the clinician: What you need to know concerning the top ten selling herbal supplements in the US

<table>
<thead>
<tr>
<th>Herbal Medicine</th>
<th>Typical Dosage</th>
<th>Potential Indication</th>
<th>Theorized Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ginkgo</td>
<td>60-80 mg leaf extract bid-tid (Hudson et al., 2001)</td>
<td>Cognitive impairment &amp; Dementia; Acute Ischemic Stroke; AMD; Tinnitus Peripheral arterial occlusive disease; vertigo; headache</td>
<td>Dilation of blood vessels, reduce blood viscosity, alter NT systems, reduce quantity of oxygen free radial, inhibit platelet activating factor (Birks &amp; Grimley, 2007)</td>
</tr>
<tr>
<td>2. Saw palmetto</td>
<td>1-2 g/d or 320 mg/d lipophilic extract (Hudson et al., 2001)</td>
<td>BPH Chronic pelvic pain, bladder disorders, hormone imbalances</td>
<td>Alters cholesterol metabolism, anti-estrogenic, anti-androgenic and anti-inflammatory effect, decreases sex hormone-binding globulin (National Center for Complementary and Alternative Medicine, 2006e)</td>
</tr>
<tr>
<td>3. Milk thistle</td>
<td>Based upon progression of disease Tx hepatotoxicity: 280-420 mg/d Acute viral hepatitis: 140 mg tid Chronic active hepatitis: 240 mg bid (Epocrates 2008)</td>
<td>Alcoholic and/or hepatitis B or C Hypercholesterolemia, insulin resistance in DM II, gall bladder disorders, reduce growth of malignant CA in prostate, breast and cervix</td>
<td>Extracts silymarin protect against hepatotoxins, inhibit peroxide formation, reduce free radial, limits liver fibrogenesis (Rambaldi et al., 2007)</td>
</tr>
<tr>
<td>4. Ginseng</td>
<td>1-2 g root qd or 100-300 mg extract tid, 3-4 wk (Hudson et al., 2001)</td>
<td>Parkinsons; Cognitive impairment; Cardioprotective effect; Anti-inflammatory, Anti-allergic, &amp; Anti-carcinogenic effects; Erectile Dysfunction; fatigue</td>
<td>Immunostimulant properties, neuroprotective qualities, improve memory function, reduce plasma cholesterol levels and platelet antagonistic properties, reduce carcinogenic growth, decrease degredation of NO improving erectile dysfunction, increase testosterone levels (Radad et al., 2006)</td>
</tr>
<tr>
<td>5. Feverfew</td>
<td>200-250mg qd as prophylaxis for migraines (Hudson et al., 2001)</td>
<td>Migraine Inflammatory conditions, RA, asthma, psoriasis, stomach aches</td>
<td>Extract parthenolide inhibits release of serotonin from platelets (Pittler &amp; Ernst, 2004)</td>
</tr>
<tr>
<td>Herbal Medicine</td>
<td>Typical Dosage</td>
<td>Potential Indication</td>
<td>Theorized Mechanism of Action</td>
</tr>
<tr>
<td>-----------------</td>
<td>----------------</td>
<td>----------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>6. Kava</td>
<td>60-120 mg qd (Hudson et al., 2001)</td>
<td>Anxiety, Asthma, UTI, topical analgesic, insomnia, menopausal sx</td>
<td>Action similar to benzodiazepines influence GABA receptors in CNS, dopaminergic antagonistic properties (Izzo &amp; Ernst, 2001)</td>
</tr>
<tr>
<td>7. Garlic</td>
<td>4-12 mg of allin, 205 mg of allicin, or 2-5 g fresh clove (Hudson et al., 2001)</td>
<td>Peripheral arterial occlusive disease, pre-eclampsia &amp; sequelae, Common cold, infections, hyptension, cancer</td>
<td>Immunostimulant, lipid lowering effects, lower blood pressure, reducing oxidative stress, inhibit clot formation (Bhasale &amp; Lissiman, 2006; Jepson et al., 2008)</td>
</tr>
<tr>
<td>8. Ginger</td>
<td>Total daily dosage: 2-4 g, Motion sickness: 1 g 30 mins prior to travel, maintenance 0.5 g q 4 hrs pm Emesis with early pregnancy: 250 mg qid (Epocrates 2008)</td>
<td>Emesis/Nausea early pregnancy, Nausea due to various etiologies: surgery &amp; chemotherapeutic agents, RA, OA, muscle pain</td>
<td>Inhibit serotonin receptors produce anti-emetic effect on both GI tract and CNS, inhibit activation of α-TNF and COX-2 (White, 2007)</td>
</tr>
<tr>
<td>9. St. Johns wort</td>
<td>300 mg tid up to 8 wk (Hudson et al., 2001)</td>
<td>Depression, Anxiety, sleep disorders</td>
<td>Anti-depressant activity by inhibiting re-uptake of NT including serotonin, dopamine and norepinephrine (Cupp, 1999)</td>
</tr>
<tr>
<td>10. Echinacea</td>
<td>2-5g dried root qd, no more than 6-8g wk 6-9 ml of juice (Hudson et al., 2001)</td>
<td>Common cold Flu, various infection, prophylactic use to prevent above conditions, acne, wound care</td>
<td>Immunostimulant by enhancement of macrophages, natural killer cells, anti-inflammatory effect, combat cytokine production and up-regulation of TNF (Linde, Barrett, Bauer, Melchart, &amp; Woelkart, 2006) (Sharma et al., 2006)</td>
</tr>
</tbody>
</table>

Key: Indications in bold have evidence that supports recommendation. AMD, age related macular degeneration; NT, neurotransmitter; BPH, benign prostatic hyperplasia; NO, nitric oxide; GABA, Gamma-aminobutyric acid; α-TNF, alpha tumor necrosis factor; COX-2, Cyclooxygenase

Note: Typical dosage is based upon healthy adults only
Table 3. Practical Guidelines for the clinician: What you need to know concerning the top ten selling herbal supplements in the US, cont.

<table>
<thead>
<tr>
<th>Herbal Medicine</th>
<th>Potential Side Effects</th>
<th>Potential Drug Interactions</th>
<th>Recommendation Level (ABCD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo</td>
<td>GI upset, headache, skin hypersensitivities, dizziness, vertigo (Hudson et al., 2001)</td>
<td>Antithrombotic or platelet therapy -enhance effects of anticoagulants (Hudson et al., 2001)</td>
<td>Not recommended as first line treatment Educate patients on research Discontinue ginkgo usage with concurrent antiplatelet drugs such as ASA, Coumadin, Garlic and Vitamin E. Cease treatment if unusual bleeding, bruising, visual disturbances, new headache occur. Initiate lowest dose f/u PT/INR q week, titrate as needed, once at therapeutic range f/u PT/INR monthly (E)</td>
</tr>
<tr>
<td>Saw palmetto</td>
<td>GI upset, headache, diarrhea (Hudson et al., 2001) Compared with finasteride, produces less impotence (Poppenga, 2002)</td>
<td>Hormone therapies, immune altering or anti-inflammatory drugs (Poppenga, 2002) Saw palmetto does has not shown to interfere with PSA (National Center for Complementary and Alternative Medicine, 2006e)</td>
<td>Patients with mild-moderate new onset BPH, patients report improvement in urinary symptoms and flow measures Should be offered as a choice for these patient compared to standard therapies F/u appointments should continue as if standard therapy was implemented (A)</td>
</tr>
<tr>
<td>Milk Thistle</td>
<td>Laxative effect, bloating, hypersensitivities (National Center for Complementary and Alternative Medicine, 2005c)</td>
<td>Herbs ability to reduce hepatotoxic effects of acetaminophen, phenytoin, butyrophenones such as haloperidol (Poppenga, 2002)</td>
<td>Due to the varying and inconsistent prognosis for alcoholic and/or hepatitis B or C this herb should be started as a treatment for mild cases Consider as an adjunctive therapy in patients with advance disease due to the unfavorable prognosis of liver transplantation (E)</td>
</tr>
<tr>
<td>Herbal Medicine</td>
<td>Potential Side Effects</td>
<td>Potential Drug Interactions</td>
<td>Recommendation Level (ABCD)</td>
</tr>
<tr>
<td>-----------------</td>
<td>------------------------</td>
<td>----------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Excitation, headache,</td>
<td>Stimulants, antipsychotic,</td>
<td>Vague mechanism of action,</td>
</tr>
<tr>
<td></td>
<td>insomnia, palpitations,</td>
<td>hormones, warfarin,</td>
<td>should not be considered 1st</td>
</tr>
<tr>
<td></td>
<td>sleeplessness,</td>
<td>phenelzine (MAOI),</td>
<td>line treatment for serious</td>
</tr>
<tr>
<td></td>
<td>hypertonia, edema,</td>
<td>hypoglycemic agents</td>
<td>ailments (E)</td>
</tr>
<tr>
<td></td>
<td>decreased concentration</td>
<td>(Hudson et al., 2001)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and estrogenic effects</td>
<td>(Izzo &amp; Ernst, 2001)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Hudson et al., 2001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feverfew</td>
<td>Post fever-few syndrome, anxiety, insomnia, joint stiffness, glossitis, stomatitis if not encapsulated, irreversible inhibition of GI contractility (Hudson et al., 2001), (Pittler &amp; Ernst, 2004)</td>
<td>Thrombolytics &amp; anticoagulants (Poppenga, 2002)</td>
<td>Patients that cannot find relief with other treatments offer this as an alternative, inform the pt to take the capsulated pill form to decrease chance of SE, f/u to monitor patient progress (E)</td>
</tr>
<tr>
<td>Kava</td>
<td>Linked to hepatotoxicity (rare), stomach ache, drowsiness, restlessness, tremor, headache, tiredness, Parkinson-like sx, skin changes, red eyes (Poppenga, 2002) (Izzo &amp; Ernst, 2001), (National Center for Complementary and Alternative Medicine, 2006d) (Pittler &amp; Ernst, 2003)</td>
<td>CNS depressants (benzodiazepines &amp; alcohol), Parkinson’s medications (levodopa) (Izzo &amp; Ernst, 2001)</td>
<td>Avoid use if diagnosis of Parkinson’s and depression, Kava is suggested to provide a greater benefit compared to the risks associated with anti-anxiety medications such as alprazolam (Xanax), Currently, sample size of studies are small Not recommended as first line treatment May discuss as an alterative choice F/u appointments should continue as if standard therapy was implemented (E)</td>
</tr>
<tr>
<td>Herbal Medicine</td>
<td>Potential Side Effects</td>
<td>Potential Drug Interactions</td>
<td>Recommendation Level (ABCD)</td>
</tr>
<tr>
<td>-----------------</td>
<td>------------------------</td>
<td>-----------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Garlic</td>
<td>Odor, heartburn, nausea, hypersensitivity <em>(Izzo &amp; Ernst, 2001)</em></td>
<td>Anticoagulants or anti-platelets, hypoglycemic agents, protease inhibitors <em>(saquinavir)</em> <em>(Izzo &amp; Ernst, 2001)</em> (National Center for Complementary and Alternative Medicine, 2006b)</td>
<td>Cease garlic ingestion before undergoing surgery or other minor procedures, educate diabetic patients that garlic may cause hypoglycemic agents Patients may choose to use as a preventative medicine, educate patients on research <em>(E)</em></td>
</tr>
<tr>
<td>Ginger</td>
<td>GI upset <em>(GERD, diarrhea, hypersensitivities of oral mucosa)</em> <em>(White, 2007)</em></td>
<td>Antithrombotics Anticoagulants <em>(White, 2007)</em></td>
<td>Recommend to pregnant pts suffering with emesis and nausea in early stages of pregnancy, offer as an alternative choice to help those pts suffering with emesis and nausea due other causes F/u appointments should continue as if standard therapy was implemented <em>(A)</em></td>
</tr>
<tr>
<td>St. Johns wort</td>
<td>Dry mouth, dizziness, confusions, GI upset, hypersensitivity, photosensitivity <em>(Cupp, 1999)</em></td>
<td>SSRIs <em>(sertraline &amp; paroxetine)</em>, reduces concentration of warfarin, OCP, phenprocoumon, cyclosporine, amitriptyline, theophyline, indinavir, digoxin <em>(Izzo &amp; Ernst, 2001)</em></td>
<td>Cease St. Johns wort if used with other SSRIs can cause excessive serotonin symptoms <em>(tremor, delirium, restlessness)</em> Appears to have greater benefit than standard medication for pts with mild-moderate depression, use as 1st line treatment for this patient population, Depression treatment has been attributed to the placebo effect of medicating and its psychological role F/u appointments should continue as if standard therapy was implemented <em>(A)</em></td>
</tr>
<tr>
<td>Echinacea</td>
<td>Hypersensitivity, GI upset Avoid parenteral use Do not use greater than 8 wk at a time <em>(Linde et al., 2006)</em></td>
<td>Immunosuppressants, <em>(cyclosporine &amp; corticosteroids)</em> <em>(Hudson et al., 2001)</em></td>
<td>Pts seeking prophylactic mediation to prevent the common cold should be educated on echinacea, can be taken with other palliative care measures to help to relieve symptoms <em>(E)</em></td>
</tr>
</tbody>
</table>

Note: Recommendations are based upon Cochrane Collaboration trials reviewed when available as well as *(Cohen & Eisenberg, 2002)*
Table 4.

**Clinical strategy and classification of risk level: To provide education and standard of care to patients experimenting with CAM practices**

<table>
<thead>
<tr>
<th>Clinical Strategy</th>
<th>Classification of Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Determine the clinical risk level</td>
<td>A. Evidence supports both safety and efficacy</td>
</tr>
<tr>
<td></td>
<td>* Recommend and monitor</td>
</tr>
<tr>
<td>2. Document the literature supporting the therapeutic choice</td>
<td>B. Evidence supports safety, but evidence regarding efficacy is inconclusive</td>
</tr>
<tr>
<td></td>
<td>* Tolerate provide caution, closely monitor effectiveness</td>
</tr>
<tr>
<td>3. Provide adequate informed consent</td>
<td>C. Evidence supports efficacy, but evidence regarding safety is inconclusive</td>
</tr>
<tr>
<td></td>
<td>* Consider tolerating, provide caution and closely monitor safety</td>
</tr>
<tr>
<td>4. Continue to monitor the patient conventionally</td>
<td>D. Evidence indicates serious risk or inefficacy</td>
</tr>
<tr>
<td></td>
<td>* Avoid and actively discourage</td>
</tr>
<tr>
<td>5. Inquire about the competence of the CAM provider when patient seeks referral</td>
<td>E. Evidence inconclusive both for safety and efficacy</td>
</tr>
<tr>
<td></td>
<td>* Do not recommend as standard therapy, offer patient education a</td>
</tr>
</tbody>
</table>

*Note.* Table adapted from (Cohen & Eisenberg, 2002);  a E subdivision was not taken from the authors work
# Medication Record

Name: _____________________________                                Date: ____________

**Prescription Medications:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Instruction</th>
<th>Condition (Why am I taking this?)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Over The Counter Medications: Include herbs, vitamins, any other supplements**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Instruction</th>
<th>Condition (Why am I taking this?)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1.
Abstract

**Objective:** This literature review examines the randomized controlled trial evidence for each of the top ten selling herbals in an attempt to educate Physician Assistants on the risks and benefits of herbal use. **Method:** The databases used were “MEDLINE”, “PubMed” and “The Cochrane Library.” The search terms used were “herbal supplementation,” “alterative medicine,” “CAM,” and individual herbal names. A compilation of the most recent research for each herbal was obtained. **Results:** The ten most commonly used herbals were evaluated for typical dosage, potential indication, theorized mechanism of action, potential side effects, and potential drug interactions. Based on this information evidence based clinical recommendations are made for each herbal. **Conclusion:** Herbals need to be researched more comprehensively and healthcare providers need to be more aware of what patients are self-prescribing. These evidence based recommendations can guide clinicians in their communication with their patients regarding herbal treatments.