5-2003

The Herbal Supplement Market in the United States: A Look at St. John's Wort

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THE HERBAL SUPPLEMENT MARKET IN THE UNITED STATES: A LOOK AT ST. JOHN'S WORT

By
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Thesis submitted in partial fulfillment
Of the requirements for the degree

of

DEPARTMENT HONORS

in

NUTRITION AND FOOD SCIENCES DEPARTMENT

Approved:

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Thesis/Project Advisor	Department Honors Advisor

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UTAH STATE UNIVERSITY
Logan, UT

2003

ABSTRACT

Herbal supplements have become increasingly popular in United States during the past decade. This trend begs the question: why are so many people turning to supplements?

The increased use of herbal supplementation appears to stem from a public demand for changes in health care. This paper will focus on the regulations placed on the supplement market and the impact that supplementation has on patient care. To illustrate these points, St. John's Wort (SJW) will be examined in detail.

Currently regulation in the United States comes from the Food and Drug Administration (FDA) and voluntary organizations within the supplement industry, such as the United States Pharmacopoeia (USP). To many health care providers, these measures do not adequately ensure the safety and efficacy of supplements.

Many patients feel that practitioners of conventional medicine do not accept herbal supplements as valid treatment options. Failure to inform a treating physician of supplement use can decrease the effectiveness and safety of total care.

All herbal medicines contain more than one active ingredient. Current research lacks necessary information needed to understand how these active ingredients interact with other supplemental and pharmacological preparations. Research conducted on SJW shows that these interactions have severe impact on the quality of overall patient care. The concerns surrounding the herbal industry are profound. Most can be resolved with more research and better regulation.

INTRODUCTION

Botanicals have had a place in medicine much longer than surgery or penicillin. It has been documented that herbs have been used in Chinese medicine for more than 5000 years (1). In fact, until the 1930's the United States Pharmacopoeia was entirely comprised of herbal remedies (2). Western medicine has traditionally shied away from herbal remedies in favor of surgery and manufactured pharmaceuticals. However, herbal products, often referred to as supplements, have become increasingly popular in western nations during the past decade.

There are between 1500 and 1800 herbal preparations currently sold in the United States (3). In a study conducted in 1990, 2.5 percent of the American population reported using herbal supplements within the past year (4). By 1999 that number had jumped to 33 percent (5). The amount of money spent on these products more than tripled during that decade, reaching $17.1 billion in the year 2000 (see Figure 1) (6). This trend begs the question: why are so many people turning to supplements?

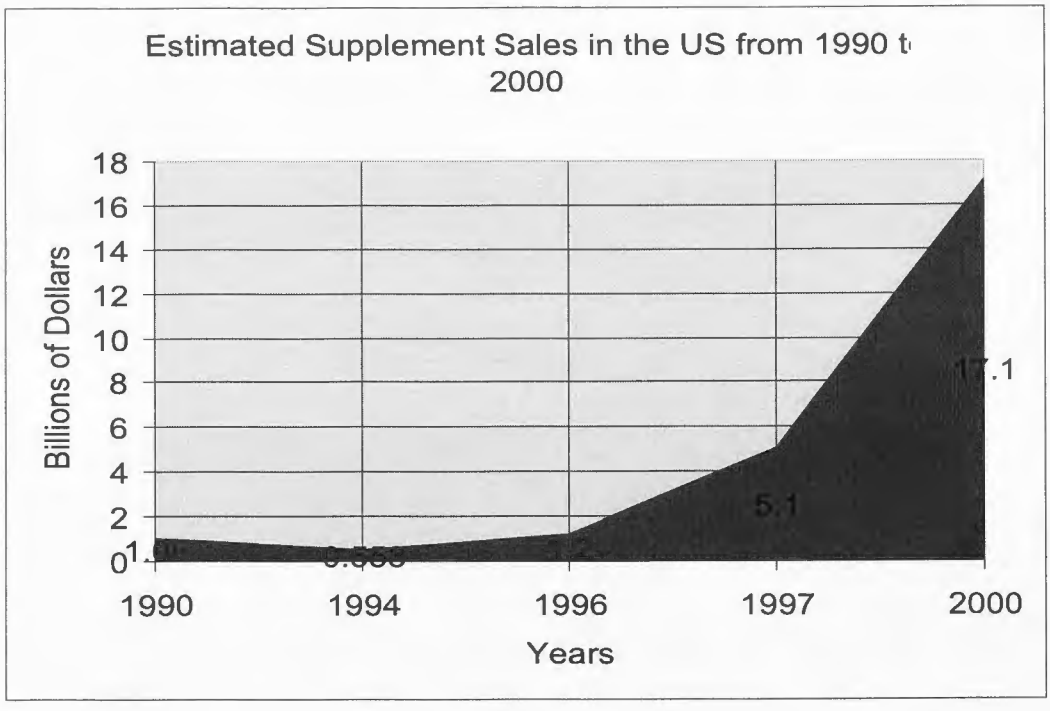

Figure 1. US supplement sales from 1990 to 2000 (4-8).

An article by Dorkrell stated, "This phenomenon is attributed to disenchantment with today's health care system, a lack of control when diagnosed with chronic or incurable conditions, unavailability or cost of traditional health care, cultural factors, and a perception that herbal or 'natural' preparations are safer than pharmaceutical preparations" (7). Another source suggests that the public is dissatisfied with the impersonal methods of many of today's practitioners (9). The increased use of herbal supplementation appears to stem from a public demand for changes in health care. This exponential increase in the use of herbal supplements has prompted many health care organizations to reevaluate patient care practices. It is also alarming to practitioners of conventional western medicine due to the seemingly unscientific nature of the industry (10).

Though doctors may not recommend them, it is evident that nutritional supplements make up a portion of the patient's total care. Therefore, health care workers must be informed about the possible uses of such supplements, the regulations of the supplements, and the impact that supplementation has on the overall care plan of the patient.

This paper will focus on the regulations placed on the supplement market and the impact that supplementation has on patient care. To illustrate these points, St. John's Wort (SJW) will be examined in detail.

REGULATION OF THE SUPPLEMENT MARKET

There is no effective regulation of the supplement industry in the United States. Currently regulation comes from the Food and Drug Administration (FDA) and voluntary regulation within the industry. In 1994 the United States FDA passed the Dietary

Supplement and Health Education Act (DSHEA). This regulatory act established the guidelines by which supplement manufacturers in the United States must abide (11). This act sought to define a supplement. It also established labeling regulations and provided for the establishment of the Office of Dietary Supplements. To many health care providers, this act is too broad (4, 6).

The DSHEA, with some exceptions, defines supplements as any product intended for ingestion as a supplement to the diet. These include vitamins, minerals, herbs, botanicals, and other plant-derived substances; amino acids and concentrates, metabolites, constituents and extracts of these substances. If a manufacturer is cautious with wording, anything can be classified as a supplement. The labeling regulations are little more defined. They state that labels cannot make claims of therapeutic efficacy. They can only claim effects on body structure or function. Thus, it would be legal to state that SJW enhances mood, but *illegal* to state that it effectively treats depression. These laws also require a disclaimer stating that the product has not been evaluated by the FDA and that the product is not meant to diagnose, treat, cure or prevent disease.

Though the DSHEA does not require that supplements be proven effective prior to their marketing, it does place the burden of safety regulation on the FDA. The FDA and the Secretary of Health and Human Services can remove a product from the market only when it is shown to cause a medical problem. Establishment of such evidentiary support requires that individuals taking supplements report any adverse effects to these agencies. Consequently, regulation of the supplement industry is left entirely in the hands of businessmen and patients. Dr. Cassileth of Memorial Sloan-Kettering said, "Now everybody can play doctor and buy anything they want over the counter and treat themselves" (9).

The DSHEA called for the creation of the Office of Dietary Supplements, an office that would be similar to the National Center of Complementary and Alternative Medicines that was established in 1991 within the National Institutes of Health (9). These offices support research into complementary and alternative medicines (CAM). However, funding for CAM research is limited. Unlike the pharmaceutical industry, the supplement industry is not required to conduct research before marketing its products, and their ability to patent the supplements once efficacy is established does not exist. Therefore, the incentive to conduct research about the efficacy and safety of supplements is minimal.

Figure 2. DVSP verification symbol.

Some regulation comes from the private sector. The United States Pharmacopoeia (USP) is a non-government organization that establishes state-of-the-art standards to ensure the quality of medicines for human and veterinary use (12). USP also develops authoritative information about the appropriate use of medicines and supplements. In the year 2000, the USP instituted the Dietary Supplement Verification Program (DSVP) an effort to establish standards of manufacturing within the supplement industry. This program is voluntary. A manufacturer can subject their products to the USP's five-point test designed to verify ingredients, product and manufacturing processes. All products that pass this test display the DSVP symbol on their label (Figure 2). This is a good start, but since it is voluntary, not all manufacturers have their products tested. In fact there are currently only three manufacturers that are affiliated with the DSVP program. For more information on this program, visit www.usp-dsvp.org.

Due to the lack of regulation in this industry, it is the consumer who loses in the end. There is nothing to guarantee that the supplement being purchased contains active ingredients. There is nothing to prove that a supplement will do what it claims to do. There are no guarantees whatsoever in the supplement industry at this time; therefore, many different guidelines for consumers have been developed to help consumers make informed decisions about buying and using supplements. The guidelines can be found in books, on the Internet, and from health care providers.

The Reader's Digest publication *The Healing Power of vitamins, Minerals and Herbs* (13), suggests the following guidelines:

- More is not always better—in fact, it can be worse. Follow the manufacturer's dosage directions.
- Shop safely: because there is not regulation on purity and potency, it is the consumer's responsibly to select products with a reputation for quality.
- Monitor reactions: Stop using the supplement if an adverse reaction is noted or if no response is distinguished (give it about one month).
- Take a break: it is best to take supplements for specified time periods, then stop temporarily to see if the condition has improved.
- Avoid risks: if symptoms of a serious problem arise before or during supplementation do not self-medicate with supplements. See a doctor. Very young and elderly patients, and pregnant or lactating women should also consult a doctor. If taking supplements talk to your doctor about possible interactions with other medications.

These additional guidelines were published in an article in the April 2001 *American Journal of Nursing* (5):

- Avoid combinations of herbs.
- Seek objective and scientific sources of information. Use caution when evaluating claims made by the manufacturer.
- Use only products that are standardized to contain a specific amount of active ingredient.
- Select herbal products that contain the following information on the label: the herb's common and scientific names, the name and address of the manufacture, a batch or lot number, an expiration date, dosing guidelines, potential side effects and details on how quality is ensured.

Health care providers need to be aware of these guidelines, as well as where to look for additional information on supplements that patients may be taking. Good sources of information on supplements are listed in Figure 3.

- CAM on PubMed: www4.ncbi.nlm.nih.gov/PubMed
- National Center for Complementary and Alternative Medicine: http://nccam.nih.gov
- Micromedex: Complementary & Alternative Medicine (CAM): www.micromedex.com/products/healthcare/cam
- American Dietetics Association: www.eatright .org
- National college of Naturopathic Medicine: www.ncnm.edu
- www.quackwatch.com
- www.herbmed.org
- www.consumerlab.com
- http://altmed.od.nih.gov

Figure 3. Sources on Complementary and Alternative Medicine

IMPACT OF SUPPLEMENTATION ON PATIENT CARE

Many patients feel that practitioners of conventional medicine do not accept herbal supplements as valid treatment options (9). Such a belief stops some patients from discussing alternative treatments with their physician. This *don't ask, don't tell* policy that has evolved has a detrimental impact on the quality of complete patient care. The basic problem that arises from this policy is the lack of truthful, open communication between the patient and the care provider. Failure to inform a treating physician of supplement use can decrease the effectiveness and safety of total care.

SJW is one of the top ten most commonly used supplements in the United States. An examination of this supplement will illustrate the impact of supplementation on patient care.

Hypericum perforatum L. has been used for its medicinal properties for over 2000 years (14). This flowering weed is native to many places across the world. English settlers introduced it to the Americas in the 1700's (15). The flower blooms in late June. The red oil that collects on the edges of the petals reminded many pious Christians in the middle ages of blood of St. John the Baptist, as his birthday was June 24th (16). This association is how the perennial received the name St. John's Wort (wort being a Middle English word meaning medicinal plant) (15). Other names for this herb include: Hardhay, amber, goatweed, klamath weed, tipton weed (17).

Over the centuries SJW has been used to treat emotional and nervous complaints such as anxiety, tension, spasticity, insomnia and depression, especially depression associated with menopause (15-18). Tonic preparations of the herb have been used to treat liver and gallbladder problems, and its infused oil has also been touted for its antiviral, anti-inflammatory and antiseptic properties (18). It has also been used as a sedative, an analgesic, a treatment for skin and breast cancer, and a treatment for carpal tunnel syndrome (15). The increased availability of this "wonder-drug" has caused a huge increase in popular demand for the supplement. In fact, the sales of SJW increased by 190 percent from $48 million in 1997, to $140 million in 1998 (19).

All herbal medicines are mixtures of more than one active ingredient (19). SJW is no exception. The herb is made up of several active components. Hypericin and psuedohypericin produce the red color of the oil and are thought to be the main components responsible for the antidepressant and antiviral attributes of the plant (16). These constituents have also been used to treat diarrhea and disorders that cause diarrhea like Crohn's and Irritable Bowel Syndrome. Hyperforin also contributes to the plant's antidepressive characteristics, and it is Hyperforin that contributes to the

antibacterial function of the herb. Flavonoids and tannins found in its composition have been linked to SJW's anti-inflammatory property.

Today SJW is primarily used to treat depression. There have been numerous studies to test it efficacy and safety. One article reported that more than 27 studies, including randomized, placebo studies, retrospective studies, and comparison studies with currently available antidepressant pharmaceuticals, have been completed (16). It has been determined that SJW is an effective serotonin uptake inhibitor (8). It also interacts with the neurotransmitters dopamine and noradrenaline. Used as a monotherapy, it has negligible side effects and can treat mild to moderate depression. (See Table 1.) Patients in studies cited by Barnes et al. in the *Journal of Pharmacy and Pharmacology*, reported side effects at a rate of 26.3 percent for SJW and 44.7 percent for conventional antidepressants (16). In another study, patients reported adverse effects at a rate of 7.4 percent for SJW and 6.2 percent for placebo (16).

Nausea	Dry mouth, headache
Dizziness	Skin rash
Confusion	Frequent urination
Tiredness/sedation	Sexual dysfunction
Rare episodes of photosensitivity and mania	

Table 1. Side effects that have been reported when taking SJW (4, 5, 8, 10).

Though SJW has a seemingly excellent track record for safety and efficacy, it has come to the attention of the medical community that SJW is very reactive with other medications. SJW acts on key hepatic and nervous system enzymes and proteins, including the CYP enzymes, which are responsible for the metabolism of approximately one-quarter of all drugs, P450 enzymes, and P-glycoproteins to alter their level of activity (See Table 2) (3, 4, 14, 19, 20). The resulting altered metabolism of prescription drugs such as warfarin, digoxin, cyclosporin, antidepressants and oral contraceptives must be

discussed with patients. These and other interactions (4, 16, 22, 23) have fueled much of the research conducted to determine the mechanisms involved in SJW's activities

These interactions can and have had severe impact on the quality of overall patient care. Ernst reported on eleven case reports and two case series that clearly linked organ rejection episodes with concurrent self-medication with SJW (10). Ang-Lee et al. (3) reported that "patients undergoing surgery appear to use herbal medications significantly more frequently than the general population". It has been reported in some populations that 22 to 32 percent of the surgical candidates used herbal preparations during the preoperative period (3). This is significant. As the elimination half-lives for hypericin and hyperforin were reported to be 43.1 and 9.0 hours respectively, surgical candidates need to stop taking the supplement at least 5 days before surgery to ensure that it has cleared their system (3).

Analysis of the third National Health and Nutrition Examination Survey revealed that middle-aged and older adults, obese people, individuals with more healthful lifestyles, and those who have a higher alcohol intake are more likely to use supplements (21). As previously stated, the number of individuals using supplements is on the rise, and many patients fail to consult with their primary care providers prior to beginning supplementation regimens. One study indicated that more than 70 percent of patients in a surgical population failed to report their use of herbal supplements during routine preoperative assessment (3). Patient failure to volunteer information about supplement use is widespread (10). There are four reasons that patients may not talk with their physician about supplement use (3). First, patients often believe that physicians are not knowledgeable about herbal medications or that they are prejudiced against their use. Second, fear of admitting to the use of unconventional therapies or, third, a failure to

perceive supplements as medications may prevent a patient from disclosing information about supplement use. Finally, patients may be using the supplements for reasons other than medical and therefore may not connect them with their medical care.

Enzyme System	Effect SJW has on metabolic activities of the enzyme system	Drugs Metabolized by Enzyme System
CYP3A4	Reduces effects of medications metabolized by this system.	oral contraceptives warfarin cyclosporin
P4503A4	Reduces effects of medications metabolized by this system.	quinidine clindomyacin busulfan calcium channel blockers corticosteriods cyclosporin codeine SSRI's (prozac, zoloft)
P4501A2	Reduces effects of medications metabolized by this system.	acetaminophin warfarin tricyclic antidepressants
P4502C9	Reduces effects of medications metabolized by this system.	barbituates losartan phenytoin
P-glycoprotein	Reduces absorption or excretion of medications, thus decreasing therapeutic effects or increasing toxicity	antibiotics antifungals digoxin protease inhibitors spironolactone

Table 2. Effects that SJW has on select enzyme systems (3, 4, 14, 19, 20).

APPLICATIONS

When not used properly herbal medicines have adverse effects and most can interact with prescription pharmaceuticals (10). Recognition of these interactions has

been a driving force behind much of the research conducted to determine the mechanism of action for many herbal preparations. Realization that herbal products are not safe also serves as an example of the need for better regulation of the herbal industry.

The concerns surrounding the herbal industry are profound. Most can be resolved with more research and better regulation. However, current regulatory laws do not demand such action from manufacturers. Without this type of regulation adverse effects, such as those noted when SJW interacts with conventional pharmaceuticals, will continue to assault the American public. As a result of strict regulations imposed by the FDA on pharmaceutical manufactures, we live in a society that is fairly safe when it comes to pharmaceuticals. Today the American public assumes that supplements that *look* like medicines, and *act* like medicines, must be *safe* like medicines, but they are not.

A drug can be defined as a substance that alters the way the mind and body work. As such, herbal supplements are drugs and should be treated as such by both the health care provider and the patient. Until better regulatory laws are drafted, it is up to the health care community to inform the public about the nature of herbal supplements. The public opinion that the health care community is not knowledgeable about herbal products must be refuted. This will require expanding current scientifically-based information by conducting research on the efficacy, safety, and proper use of botanicals. Communication with patients must include taking better medical and medication histories from patients and discussing supplements with patients.

References

1. Reid DP. *Chinese Herbal Medicine.* Boston: Shambhala Publications, Inc; 1987: 10-25.

2. Cohen SM, Rousseau ME, Robinson EH. Therapeutic use of selected herbs. *Holistic Nurse Practitioners.* 2000:14(3):59.

3. Ang-Lee MK, Moss J, Yuan C. Herbal medicines and perioperative care. *Journal of the American Medical Association.* 2001;286(2);208.

4. DeSmet, PAGM. Herbal Remedies. *The New England Journal of Medicine.* 2002; 347(25): 2046.

5. Waddell DL, Hummel ME, Summers AD. Three herbs you should get to know. *American Journal of Nursing.* 2001;101(4): 48.

6. Lashof JC, Margen S, Swatzberg JE. Regulating natural health products. *Science Magazine.*2002;296:46.

7. Dockrell TR, Leever JS. An overview of herbal medications with implications for the school nurse. *The Journal of School Nursing.* 2000;16(3): 53.

8. Kelly BD. St. john's wort for depression: what's the evidence*? Hospital Medicine.* 2001 May;62(5):274-6.

9. Brody JE, Grady D, et. al. *The New York Times Guide to Alternative Health: A consumer Reference.* New York: Henry Holt and Company; 2001:xiii, 2-34, 61-102.

10. Enst E. The risk-benefit profile of commonly used herbal therapies: ginko, st. john's wort, genseng, echinacea, saw palmetto, and kava. *Annals of Internal Medicine.* 2002;136(1):42.

11. Food and Drug Administration: Dietary Supplement and Health Education Act. http://www.hcrc.org/faqs/dshea.html, accessed 3/5/03.

12. United States Pharmacopoeia. http://www.usp.org accessed 3/5/03.

13. Kalyn W. *The Healing Power of Vitamins, Minerals and Herbs.* Pleasantville, New York: The Reader's Digest Association, Inc; 1999: 29.

14. Assemi M. Herbs affecting the central nervous system: ginko, kava, st. john's wort, and valerian. *Clinical Obstetrics and Gynecology.* 2001;44(4):824.

15. Balch, PA. *Prescription for Herbal Healing.* New York: Avery; 2002: 131-133.

16. Barnes J, Anderson LA, Phillipson JD. St. john's wort (Hypericum perforatum L.): a review of its chemistry, pharmacology and clinical properties. *Journal of Pharmacy and Pharmacology.* 2001;53: 583.

17. Anon: *Physician's Desk Reference for Herbal Medicine, 1st ed.* Montvale, New Jersey: Medical Economics Company; 1998: 905-908.

18. Chevallier A. *The Encyclopedia of Medical Plants.* New York: DK Publishing; 1996: 104.

19. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs. *Drug.*2000;61(15):2163.

20. Ernst E. st.john's wrot supplements endanger the success of organ transplantation. *Archives of Surgery.* 2002;137:316

21. Radimer KL, Subar AF, Thompson FE. Nonvitamin, nonmineral dietary supplements: issues and findings from NHANES III. *Journal of the American Dietetic Association.* 2000 Apr;100(4):447-54.

22. Anon: Understanding st. john's wort. *Nursing.* March 2002: 81.

23. Micromedex: Complementary & Alternative Medicine (CAM) http://www.micromedex.com/products/healthcare/cam/ accessed 03/27/03.