

# PHARMASCRIP

NEWSLETTER OF THE MARYLAND SOCIETY OF HEALTH-SYSTEM PHARMACISTS

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## Our Future Pharmacists

**James A. Trovato, PharmD, BCOP**  
**University of Maryland School of Pharmacy and**  
**Greenebaum Cancer Center - University of Maryland Medicine**

Back in February I mentioned that my beautiful wife was expanding with our first child. Well, the expanding, labor, and delivery are now a thing of the past. On April 9th at 8:09 PM our son Jacob Cyril Trovato was born. Jacob weighed in at 7 pounds, 5 ounces and was the cutest baby in the nursery (of course I'm not bias). My mom is so delighted because her new grandson is the first child born who will be able to carry on the family name. After speaking with my mom I thought, just like our children are the future of our family, our pharmacy students are the future of our profession. Raising our children requires a lot of time and energy and is often very challenging. In a similar manner, teaching and guiding our students is hard work and challenging as well. All of your imparted knowledge and wisdom pays off in the end. We watch our children grow and accomplish great things and likewise our students become professionals who pave the way with innovative pharmacy practice that will contribute to the strength and growth of our pharmacy profession.

Many of you, as instructors and experiential learning preceptors for the School of Pharmacy, encounter this challenge on a daily basis. I have always felt that the most valuable education for our students takes place outside of the classroom. A student's experience in the world of pharmacy allows them to apply and justify the foundation of knowledge they have acquired in school. Your time and effort in helping to mentor and educate our students is much appreciated.

I encourage those members of MSHP who are not instructors or preceptors to consider becoming one. Many of you practice pharmacy in a variety of health systems. I feel it is important that we make these practice settings available to our students so that they have ample opportunity to experience the multitude of opportunities within the pharmacy profession. As an experiential preceptor you help to facilitate a student's decision making process of pursuing various pharmacy career opportunities. The sharing of your knowledge with our students and their experience at your practice setting is a valuable investment in your future as a pharmacist and the future of our students. Keep in mind that at the same time our students are learning from you, you are also learning from them.

On one occasion I encountered a student who questioned their choice to pursue a career in pharmacy. As a health care professional the student envisioned herself in a position that involved one on one patient counseling, physical assessment, and collaborative medication management. The student began to have doubts and felt that as a pharmacist this type of patient care would not be possible. I assured the student that the position she described does exist in pharmacy practice. The key is to have the initiative, willingness, and know how to prepare yourself for that future position. As educators and preceptors we can help facilitate our students in achieving their desired role as a pharmacist.

The profession of pharmacy is constantly changing for the better. As preceptors we can help take part in preparing our students to adapt to this positive change as they pursue their future career in pharmacy.

On May 26th the class of 2000 will be graduating from the University of Maryland School of Pharmacy. On behalf of MSHP I would like to congratulate them on this great accomplishment. Many of them are already on their way to becoming leaders in our profession. I'm proud to know that I have played a small but important role in preparing them for a career in pharmacy. They are our future pharmacists and I wish them great success.

## Dietary Supplements: Potential Risks

*Ursula K. Hopkins, Pharm.D*  
*Clinical Toxicology Fellow*  
*Maryland Poison Center*

Since the passage of the Dietary Supplement and Education Act (DSHEA) in 1994, the use of herbal products and other dietary

supplements in the United States has been on the rise. In their 1997 study Eisenburg et al<sup>1</sup>, reported that approximately 40% of the adult patients surveyed admitted to the use of an herbal preparation. Additionally, 18% of these patients admitted to the concomitant use of their prescription medications with at least one dietary supplement product. Although these figures suggest a substantial proportion of patients are at a potential risk for an adverse reaction, there is little information regarding the safety or toxicity associated with their use.

Within the Dietary Supplement and Health Education Act, dietary supplements are not held to the same FDA standards as pharmaceutical agents. Because dietary supplements do not require FDA approval prior to marketing, information on the safety and efficacy of these products is limited. While the majority of dietary supplements appear to have minimal toxicity following acute exposures, recent evidence suggests that chronic use of these products may put patients at an increased risk for an adverse event. Surveys of the literature show that there has been an increase in the number of adverse events reported over the last ten years. This review will highlight some of the more recent clinically relevant reactions to these products.

### **Products of Questionable Purity**

The lack of mandated Good Manufacturing Practices (GMP's), has led to the appearance of products with questionable purity on the market. Non-drug potentially toxic contaminants like strychnine, lead, mercury, aconite, ethylene glycol, and bacteria have been identified in various products. Additionally, commercially available drugs like acetaminophen, phenylbutazone, sulfonyleureas, and digitalis have been found in various herbal remedies. Most recently, the California Department of Health Services issued a warning about the contamination of five Chinese herbal products that claimed to treat diabetes with only natural traditional herbs.<sup>2</sup> Investigation of these products was initiated after a diabetic patient experienced several episodes of hypoglycemia following the use of one of the herbals. Laboratory analysis of these 5 dietary supplements revealed that they contained the prescription drugs glyburide and phenformin. Over the years, several other Chinese patent medications and dietary supplements have been found to contain drug contaminants that were not identified on the label. In an attempt to increase the amount of information available on these products, the FDA has mandated that all dietary supplements carry a supplement facts panel however accurate disclosure of ingredients is not actively enforced.

### **Drug-Supplement Interactions**

Despite their widespread use, few large-scale studies characterizing the toxicity of dietary supplements exist. Many of the investigations into drug-supplement interactions have resulted from individual case reports. While well documented drug supplement interactions are few, an increasing understanding of the pharmacodynamic characteristics of these agents has resulted in researchers expressing concerns about certain drug-supplement combinations.

### **Dietary Supplements and Cytochrome P450 Activity**

Recent studies indicate that St John's Wort has CYP3A4 enzyme inducing ability.<sup>3,4</sup> A study of the concomitant administration of St. John's Wort and Indinavir revealed that the herb significantly reduced serum protease inhibitor concentrations. For HIV positive patients, St. John's Wort's inducing effects place these patients at a potential risk for the development of drug resistance. It is thought that similar reactions may be seen between St John's Wort and other drugs that undergo hepatic metabolism by the CYP 3A4 enzyme.

Other herbal products that have been identified as having cytochrome P450 enzyme activity include kava, Ginkgo biloba, valerian, chili pepper, and black pepper.<sup>5</sup> Kava (Piper methysticum) has been found to inhibit the CYP P450 3A4 and 1A2 isoenzymes. Valerian and Ginkgo biloba, chili pepper and black peppers may inhibit CYP 1A2 enzymes. With continued research more cytochrome P450 active agents will be identified and a more complete understanding of the potential risks associated with their use will be derived. Until then, patients taking drugs that are known to be affected by cytochrome P450 activity should be cautioned about the concomitant use of herbal products. Table one is a summary of dietary supplements with known or potential cytochrome P450 activity. It is important to note that while many of these products contain substances that have CYP enzyme activity, there is little documentation of drug-supplement interactions at this time.

### **Dietary Supplements with Antiplatelet Activity**

The best-documented interaction between anticoagulant drugs and dietary supplements involves the herbal ginkgo biloba. Through human volunteer studies, the terpenoid fraction within ginkgo has been found to inhibit platelet aggregation after single doses of ginkgo extracts. Case reports of chronic ginkgo use that resulted in the development of spontaneous bleeding have been documented.<sup>6-10</sup> In many of these cases the patients involved were not concurrently taking an oral anticoagulant drug when the adverse event occurred.

Other dietary supplements thought to have anticoagulant effects include Dong quai and Panax ginseng.<sup>11-13</sup> While Dong quai is thought to have effects on platelet aggregation the exact mechanism of ginseng's effects has not been determined. Case reports suggest that

when these herbals are used concurrently with warfarin increases in INR are observed. Patients who are maintained on an anticoagulant or antiplatelet medications should avoid the use of dietary supplements until more information on the safety of combining these products with therapeutic drugs is determined. Table two is a summary of herbal products with potential anticoagulant activity. It is important to note that while many of these dietary supplements contain substances known to have anticoagulant properties, the number of products that are currently associated with adverse events is few.

The relative paucity of data on the pharmacodynamics of individual dietary supplements has made predicting the quality and likelihood of an adverse event difficult. Adverse reactions to dietary supplements have been observed following all types of use. However, an increased risk for an adverse event has been seen in certain segments of the population. For example, information about the use and safety of dietary supplements in children, the elderly, or patient's with underlying disease states is limited. These groups are at risk for dose-related toxicity as well as supplement-disease state interactions. Another group that is at risk for adverse events are those patients who use supplements at excessive doses or for prolonged periods of time. Additionally, the use of combination products or multiple supplements may also increase a patient's risk potential. Lastly, the addition of a supplement to a patient's current regimen may result in either an additive or deleterious therapeutic effect, based on the supplement's intrinsic activity. Patients maintained on a therapeutic drug regimen are at risk for numerous potential drug-supplement interactions.

There are many resources and references available to practitioners that can aid in the evaluation of a specific dietary supplement product. The FDA has expanded the MedWatch program to include dietary supplements. The Special Nutritional Adverse Event Monitoring System is a searchable database of adverse events that is available via the internet or in a downloadable report (<http://vm.cfsan.fda.gov/~dms/aems.html>). An archive of current and past FDA issued announcements and warnings about dietary supplements can also be found at <http://vm.cfsan.fda.gov/~dms/supplmnt.html>. Consumerlab.com is a new independent research entity that investigates the product quality of commercially available dietary supplements. Currently the site has product evaluations for the following dietary supplements; SAME, Chondroitin, Glucosamine, Gingko biloba, and Saw palmetto. References that may be a helpful addition to a practitioners library include: The Natural Medicine Comprehensive Database (Therapeutic Research Facility, 1999). This reference is available in print format as well as online. Each product has a monograph that includes information on the common and scientific name of the substance, common uses and dosing, safety and efficacy data, pharmacology and active ingredient data, and known/potential adverse reaction/interaction data. Additionally, The Lawrence Review of Natural Products (Facts and Comparisons, 1999), The Complete German Commission E Monographs (American Botanical Council, 1998), and Herbal Medicines: A Guide For Healthcare Professionals (The Pharmaceutical Press, 1996) provide information on individual dietary supplements in a similar monograph format.

In summary, the use of dietary supplements has become commonplace. Therefore it is important that healthcare providers include queries about dietary supplement use in every patient's medication history and identify patients that are at risk for toxicity. The addition of a dietary supplement to a patient's current regimen has the potential to result in an unwanted outcome. There are many online and print resources available to practitioners that can aid in the assessment of a patient's risk for an adverse event. A familiarity with these references can help the healthcare practitioner effectively counsel their patients about the potential for adverse drug reactions and drug-supplement interactions.

**Table One: Dietary Supplements With Known and Potential Cytochrome P450 Activity +**

Cytochrome P450 Enzyme	Effect	Dietary Supplement
1A2	Inhibition	Piper longum (chili pepper), Piper nigrum (black pepper), Grapefruit (quercetin-naringenin), Elder*, Hypericum perforatum (St John's Wort)*, Piper methysticum (Kava)*, Valerina officinalis (Valerian)*, Uva-Ursi*
2D6	Inhibition	Cystisus scorparius (Broom)
3A4	Inhibition	Grapefruit (naringen), Hypericum perforatum (St John's Wort)*, Piper methysticum (Kava)*

\*Contain quercetin which has CYP 1A2 enzyme inhibition ability.  
 Quantities of quercetin vary.  
 + Information on tables adapted from references 3-5,14-17.

**Table Two: Dietary Supplements With Known/  
 Potential Anticoagulant Properties**

Effect	Dietary Supplement
Have been identified to contain coumarin constituents.	Aniseed, Angelica Species (Dong Quai, Chinese Angelica)*, Arinica Species (Leopard's Bane, Mountain Tobacco, Mountain Snuff), Celery, Chamomile (German, Roman), Fenugreek, Ferula Species (Asafoetida)*, Horse Chestnut, Passion Flower, Prickly Ash ( Northern, Southern), Quassia (Picrasma excelsa, Quassia amara), Red Clover, Wild Carrot, Wild Lettuce
Inhibit platelet activity or platelet aggregation	Eugenol (Clove Oil)*, Feverfew, Ginger, Licorice
Anticoagulant Effect	Fucus, Gingko biloba (terpenoids have anti-platelet effects)*, Ginseng Species (Panax ginseng, exact mechanism unknown)*
Interaction with Warfarin	Garlic
Have been identified to contain salicylate constituents.	Willow Bark, Meadowsweet, Birch Bark

\* Documented case reports/series or primary research.  
 + Information on tables adapted from references 6-17.  
*References available upon request.*

## Annual Seminar Committee

The Seminar Committee is hard at work lining up speakers. Dr. Mark Riddle, head of the Research Unit on Pediatric Psychopharmacology at Johns Hopkins, will speak on the topic of drug treatment for behavior disorders in preschoolers. Pharmacist and attorney Michelle Andoll will speak on Board of Pharmacy issues. There will be sessions on men's health and women's health, adverse event reporting, drugs in breast feeding, and other timely topics.

Letters have gone out to potential exhibitors. If you have not received one and are interested in exhibiting, contact Judi Mellendick ([judi@assochq.com](mailto:judi@assochq.com)) at MSHP headquarters.

We look forward to seeing you in Ocean City October 13 – 15.

## Welcome New Members

Tamara Clay June Crosby

Carla Gill            David A.  
                                 Kotzin  
Donna Mondell Nancy Roberts

## **It's Our Money**

(Report from the Treasurer and the Finance Committee)

**Annette Rowden, Chair**

As in our personal lives, money is required in order for the Society to "do the things that it does". We rely upon three basic sources of income: dues, return on investments, and pharmaceutical manufacturers' contributions. All three sources are important for our continued success.

In 1998, under the direction of Finance Committee Chair Babette Duncan, the Finance Committee reviewed our investment strategy and suggested changes to the Board of Directors. The Board approved the proposed changes. In February 1999, we transferred our investments to a Schwab Institutional account with management by Chris Portner of PSA Financial. In 1999, we realized a healthy return on our investment due to the bounding stock market. As a result, the net assets of the Society grew in 1999 and we ended the year on sound financial footing.

In 1999, the Finance Committee also considered how we could increase value of membership to Society members. The financial management seminar presented on April 19, 2000 is the first result. Depending on the success of this program, additional programs may be arranged.

In the year 2000, the Finance Committee will continue to review our investment results. In addition, the Committee will review and approve the year 2001 budget proposal. If you have any questions regarding the Society's financial status or investments, or would like to become involved with the Finance Committee, please contact me at (410) 327-4629.

## **Upcoming Events**

May 18 Board Meeting St. Joe's (8-10 am)

May 18 Monthly Meeting, Diabetes, Stuart Haines

May 28 June *Pharmascript* published

June 4-7 ASHP Annual Meeting

Philadelphia, PA

June 10-13 MPhA Annual Convention - Ocean City

June 15 Board Meeting, St. Joe's (8-10am)

## **Pharmacist of the Year**

Janet Mighty, Chair  
Johns Hopkins Hospital

Your help is needed to identify candidates for MSHP's Pharmacist of the Year Award. Please consider the criteria for nominees listed below (the candidate needs activity in one or more of the following areas):

- An individual's role in providing outstanding pharmacy service within his or her institution OR service to pharmacy at the state or local level
- Participation in research
- Contributions to professional literature
- Other activities or accomplishments reflecting professional excellence

This award is designed to recognize overall contributions with a focus on the preceding calendar year. The award will be presented at an awards ceremony early in 2001. Letters of nomination should be addressed to Janet Mighty through MSHP headquarters. Questions can be directed to: 410-418-4800.

## Call for Nominations

Janet Mighty  
Johns Hopkins Hospital

The MSHP Nominating Committee is now soliciting calls for nominees for the 2000 elections for the following offices:

President-Elect Secretary

Treasurer Board Member at Large

Qualifications include membership in good standing in MSHP, desire to help improve the Society and Pharmacy in general, and the ability to attend and support Board and Society functions. Anyone who is interested in running for any of these offices, or who wishes to nominate someone, should call Janet Mighty at 410-955-6337. Nominations will also be taken from the floor of the September business meeting. Please be sure that your potential officers are willing and able to serve before you nominate them. Also, if you desire to serve MSHP, you can nominate yourself. Don't be shy we appreciate your enthusiasm!

The Nominating Committee is also looking for members to serve as delegates to the 2001 ASHP Annual Meeting. We need to elect four (4) representatives and one alternatives. Current ASHP members who reside in Maryland are eligible to serve in this capacity.

To make any nominations for these positions, or for more information, please call Janet as noted above. You may also make nominations at the September meeting. Thanks for helping make MSHP a strong organization.

## Public Affairs Committee

Shannon Benedetto, Chair

The Public Affairs Committee sponsored National Poison Prevention Week at the Howard County Central Library on March 25th, 2000. A table was set up from 11A.M to 3 P.M. with information for parents and children. Several different informational brochures were available on Emergency Poison Action, Poisonous Plants, Bites and Stings, as well as plenty of Mr. Yuck stickers. A look a like display was prepared to show how many medications can look very similar to candy. Balloons and fun stickers were also given out to the children. Participating in this event were Nancy Clark, Kim Compton, Louise Leach, Deborah Sarama, and Shannon Benedetto.

## *Not Yet Paid Your Dues?*

## *This is the last issue of Pharmascript for Non Paid Members*

Maryland Society of Health System Pharmacists Monthly Meeting

### **Ten Interventions That Will Improve the Lives of People with Diabetes** **Stuart T. Haines, Pharm.D., BCPS, CDE**

Associate Professor, University of Maryland School of Pharmacy  
**Thursday, May 18, 2000**

### **DiMimmo Italian Restaurant**

217 S. High Street, Baltimore (410-727-6876)

### **Sponsored by: Bristol-Myers Squibb**

Directions: From I-95 take I-395 N (exit 53) toward downtown following the signs for Downtown/Inner Harbor. I-395 becomes S. Howard. Make a right onto W. Pratt followed by a right onto Albermale. From Albermarle turn left onto Stiles, then left onto S. High.

FSchedule: 6:00 p.m. Registration and Networking; 6:30 p.m. Business Meeting; 6:45 p.m. Dinner; 7:30 p.m. Dr. Haines' Remarks

The Maryland Pharmacy Continuing Coordinating Council is approved by the American Council on Pharmaceutical Education as a provider of continuing pharmaceutical education for pharmacists. The ACPE Universal program number assigned to the program by CECC is 144-999-00-020-L01.

Objectives - At the conclusion of this session, the participant should be able to:

1. State 10 interventions that will improve the lives of patients with diabetes.
2. Describe the benefit(s) that are likely to be derived from each intervention.
3. Given a detailed patient case, develop a plan of action that includes at least 6 interventions.

Advance registration is required. Please respond by May 13 using either email: [judi@asochq.com](mailto:judi@asochq.com) or fax: 410-418-4805.

Cost: Free for MSHP members, \$30 for non members and guests.

### **MSHP Registration Form - May Meeting**

Name: \_\_\_\_\_

Institution: \_\_\_\_\_ Phone: \_\_\_\_\_

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**Maryland Society of Health System Pharmacists**  
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