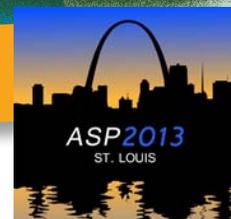




# The American Society of Pharmacognosy

The ASP Newsletter  
Volume 49, Issue 2

## Welcome to St. Louis



## “Natural Products at a Crossroad: Current and Future Directions”

The Annual Meeting of the American Society of Pharmacognosy, “Natural Products at a Crossroad: Current and Future Directions” will be held July 13-17, 2013, in St. Louis, Missouri. Conference registration, hotel information, and the latest conference updates are now available at [www.asp2013.org](http://www.asp2013.org).

By Drs. Ray Cooper & Mark O’Neil Johnson

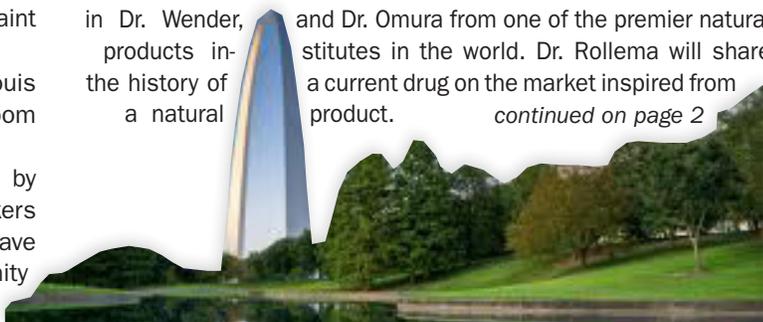
**W**e are almost there! The 54<sup>th</sup> Annual Meeting is ready to kick off! The organizers have a terrific meeting planned in St. Louis, Missouri, centrally located in the middle of the United States. The conference will be held in the heart of downtown Saint Louis by the mighty Mississippi River.

The conference venue is the Hyatt Regency Hotel St. Louis at the Arch, with attractive rates of only \$135/room, but room space is limited at these prices.

We have arranged three outstanding workshops followed by four days of great science talks and posters; with guest speakers from the USA and all five continents around the world. We have participation by a broad and diverse natural products community

involved in industry, academia and education: leaders in the field covering natural products synthesis, marine, microbial and plant chemistry, and a lot, lot more. Our theme, “Natural Products at a Crossroad: Current and Future Directions,” embraces the fact that natural products touches on many scientific disciplines.

Starting on Saturday we offer three outstanding workshops: Metabolomics, NMR Techniques and Microbiology. On Sunday morning we kick off with four terrific lectures: Drs. Paul Wender, Peter Raven, ASP Award Lecture given by President Satoshi Omura, of the Kitasato Institute, Tokyo, and Dr. Hans Rollema. This is a wonderful opportunity for the ASP to hear of the contributions from a true “hero of the planet” in Dr. Raven, a pre-eminent synthetic chemist in Dr. Wender, products in the history of a natural and Dr. Omura from one of the premier natural institutes in the world. Dr. Rollema will share a current drug on the market inspired from product. *continued on page 2*



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## EDITOR'S CORNER



The first days of summer are upon us, and for the ASP we are drawing close to our 54<sup>th</sup> Annual Meeting to be held in St. Louis, Missouri, from July 13-17, at the Hyatt Regency. I hope to see many members at what should be an outstanding meeting. Our lead article discusses many of the final logistics of the meeting, and we hope you will visit the meeting website [www.asp2013.org](http://www.asp2013.org).

The Organizing Committee has organized a great overall conference. Scientifically, the Annual Meeting will include plenary lectures, contributed talks, and posters. There are also a number of social activities planned that include an opening reception on Saturday evening at the Hyatt, an evening Monday at the world-famous Missouri Botanical Garden, and a closing banquet at the Hyatt. The Younger

Members will enjoy a visit to the Anheuser Busch Brewery. If you are looking for ways to spend your free time, like our free Tuesday afternoon, please see the article by members of the Organizing Committee that gives a local perspective on fun things to do in St. Louis.

Also in homage to the St. Louis meeting, "From the Archives" columnist Ms. Devhra BennettJones dug up a fascinating 1901 correspondence between Mr. William Trelease, former Director of the Missouri Botanical Garden (1889-1912), and Mr. Curtis Gates Lloyd, a co-founder of the Lloyd Library. In the early 20<sup>th</sup> Century, scientific advancement often required the time-consuming process of mail correspondence. Mr. Trelease worked with Mr. Lloyd to exchange samples and other information. The Lloyd stationary that we see showcased in this archival piece is a work of art itself, showing the exterior and interior of the original library building.

A doctoral student from my university (City University of New York) has contributed one of our lead articles on crofelemer, the second complex botanical to be approved as a drug by the United States Food and Drug Administration (FDA). Crofelemer was developed with the help of ASP member Dr. Steven King and is approved for the treatment of non-infectious diarrhea in HIV/AIDS patients. This may herald a shift in how the FDA will regard drugs from botanicals that are comprised compound mixtures.

Our regular columns continue to provide the backbone to the *Newsletter*. I was recently in Washington, D.C., and I had a chance to have a lovely extended visit with Dr. Georgia Perdue, a longtime ASP member who pens our column "Brief News from Washington." As many ASP members know, Dr. Perdue published the newsletter *Washington Insight* for years, dedicated to scientists interested in natural products. She generously gave me some old issues of this classic publication, and I have enjoyed reading these and coming up with ideas for the ASP Newsletter. Dr. Perdue never ceases to impress me with her knowledge of Washington and current science policy, as well as her dedication to our Society.

Other regular columns include "Meet a New ASP Member," now written by Younger Member (and my doctoral student), Mr. Dan Kulakowski. Dr. Huzefa Raja from the University of North Carolina, Greensboro, provides a comprehensive view of his work and why he is interested in the ASP. In our "Behind the Scenes" article we learn more about Dr. Leng Chee Chang's research on withanolides, and her lab's inspirational and altruistic motto.

I hope you have a great summer, and I look forward to meeting you in St. Louis soon.

*Dr. Edward J. Kennelly*

## EMPLOYMENT SERVICE

The Society offers a placement service to aid our members in seeking positions or employees. This service is available only to ASP members and is free to both the applicant and the employer.

For more information see the services website.

[www.pharmacognosy.us/?page\\_id=163](http://www.pharmacognosy.us/?page_id=163)

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## Welcome to St. Louis

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We continue the scientific program with advanced analytical technologies emphasizing their importance to the long term success of natural products and the traditional topics of natural products in drug discovery, marine and microbial natural products, botanicals and ethnobotany.

This year's plenary lectures will also highlight remarkable successes involved in natural product synthesis, recently commercialized drugs inspired from natural products and a one-of-a-kind perspective of the evolution of NMR over the last 70 years. Several noteworthy sessions include new anticancer therapeutics derived from natural products and natural products enhancing the experience of pet foods.

### THERE WILL BE PLENARY LECTURES, CONTRIBUTING TALKS AND POSTERS IN ALL THE FOLLOWING KEY AREAS

Spectroscopic Technique in Natural Products Chemistry

Frontiers of Discovery Through Spectroscopy

Natural Products: Drug Research and Current Drugs  
on the Market

Application of Natural Products for Pet Foods

Chemistry, Biology and Ecology of Marine Natural Products

Botanicals: The Road to the Clinic

Natural Products as Anti-Cancer Agents

Ethnobotany and Botanical Discovery

Botanicals and Foods

New Innovations in Agrochemical/Biotechnology

**Are you paddling downriver?  
Are you heading our way?**

**For registration, hotel and the latest details**

**<http://www.asp2013.org/>**

**We are almost there! The 54<sup>th</sup> Annual  
Meeting is ready to kick off!**

The ASP welcomes you to join for a diverse and exciting science meeting at the beautiful Hyatt Regency St. Louis at the Arch, on the banks of the mighty Mississippi River.

**Check out the Hyatt Regency Hotel St. Louis  
at the Arch.**

Hurry! Hurry! Only a few rooms remain at the terrific conference rate of \$135/night.

For the entire conference, we have secured one entire floor of the Hyatt allocated to the meeting with lecture halls, and a large adjacent area for the exhibitors the poster sessions and break-out gatherings. The hotel and venue for the annual meeting is situated next to the famous St. Louis Gateway Arch. Within walking distance, and at the hotel, there are many restaurants both casual and upscale: including Starbucks; the Brewhouse in the



Hyatt lobby; Charlie Gitto's; TGI Friday's; Bamboo Bistro; Zuzu Handmade Mexican; Ruth Chris Steakhouse in Hyatt lobby; Mike Shannon's Steaks & Seafood; Gio's Italian.

### GETTING TO ST. LOUIS

St. Louis Lambert International Airport is the main airport. A host of major airlines offer daily service and excellent taxi service and the Metro link light-rail service running to the downtown area make the arrival transfer to the conference venue very convenient.

### SOCIAL ACTIVITIES

For the conference, we have planned several exciting social activities. Our Young Investigator Event will be a visit to the famous Anheuser-Busch Brewery. The traditional Saturday opening mixer will be at the Hyatt, to meet and greet old friends, make new acquaintances and welcome guests to the Party. On Monday evening we have arranged an "Evening" at the fabulous Missouri Botanical Gardens. On Tuesday Afternoon we are planning a free afternoon for you to spend time at some of the local attractions, such as the famous Arch, the St. Louis Zoo (free admission), and many local Museums (mostly free admissions). There is

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Missouri botanical gardens historic site: A view of Seiwa-en, the largest Japanese garden in North America.



## Welcome to St. Louis

*continued from page 3*

Mississippi river access and attractions, including a riverboat cruise. Other attractions include the Scott Joplin House State Historic Site and Museum, the Downtown Jazz Club, microbreweries and a wonderful vodka bar in the hip Central West End. The famous Souard Farmers Market (open Wednesday-Saturday) is well worth a visit, as well as the Glassblowing Factory, a stroll down Washington Street, and lots of cafes, eateries, breweries and an authentic English tea shop. There are also local casinos in the St. Louis area.

Within driving distance, there is the Historic City of St. Charles where you can stroll the old cobblestone town shops and restaurants on the Missouri River. Also close is Hannibal, a true American experience featuring the Mark Twain Museum, and home to Tom Sawyer and Huckleberry Finn right on the Mississippi River. Drive out to the countryside, wineries, and visit the largest underground cellars in the United States.

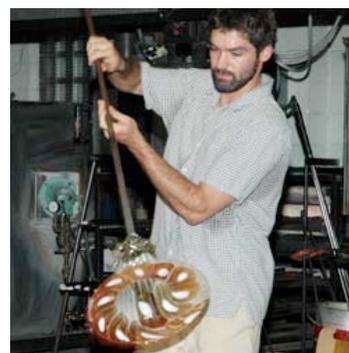
On behalf of the Scientific Organizing Committee, we are delighted to have the opportunity to create a wonderful ASP program and we look forward to seeing you in St. Louis. ■

***On behalf of the Scientific Organizing Committee, we are delighted to have the opportunity to create a wonderful ASP program and we look forward to seeing you in St. Louis.***

### SCIENTIFIC ORGANIZING COMMITTEE

- Drs. Ray Cooper and Mark O'Neil-Johnson, Co-Chairs
- Dr. Barbara Timmermann – University of Kansas
- Dr. John Beale – St. Louis College Pharmacy
- Dr. Amy Wright – Harbor Branch Oceanographic Institute
- Dr. Ikhlas Khan – University of Mississippi
- Dr. Veronica Butterweck – University of Applied Sciences, Northwestern Switzerland
- Dr. Judith Rollinger – University of Innsbruck
- Dr. Nick Oberlies – University of North Carolina at Greensboro
- Dr. Rainer Bussmann – Missouri Botanical Garden (MOBOT)
- Dr. Jim Gloer – University of Iowa
- Dr. Melany P. Puglisi-Weening – Chicago State University
- Dr. Toni Kutchan – Donald Danforth Plant Science Center
- Dr. Roy Okuda – San Jose State University
- Dr. Ed Kennelly – CUNY

Photos clockwise:  
The Gateway Arch, St. Louis's trademark, The Spice Shop at the Souard Farmers Market, 3<sup>rd</sup> Degree Glass Blowing Factory, Scott Joplin House State Historic Site, Home Grown Fruits and Vegetables for Sale at the Souard Farmers Market



# Visiting St. Louis: Local Recommendations



**Dr. Edward Kennelly: Lehman College, City University of New York (Attended graduate school in St. Louis from 1987-1993).**

**What is the ideal night out in St. Louis?**

Walking in University City and enjoying the lively neighborhood and nightlife.

**What are some things travelers should pack for a stay in St. Louis?**

Cool clothes—it can be hot and muggy in St. Louis in the summer. But bring layers since the hotel and other indoor venues are sure to be over air-conditioned.

**If you could only eat one meal in St. Louis, where would you go?**

Little Italy (The Hill)—lots of nice restaurants and home to the famous deep-fried ravioli, not to be missed!

**What is a hidden gem of St. Louis that only a local would know?**

I always enjoy crossing the Mississippi River and driving along Great River Road to the lovely town of Elsah, Illinois;  
<http://www.elsah.org>.

**What is the one thing a traveler should avoid in St. Louis?**

Walking in bad neighborhood.

**Dr. Mark O'Neil-Johnson: Sequoia Sciences.**

**What is the ideal night out in St. Louis?**

Sub Zero Vodka Bar.

**What are some things travelers should pack for a stay in St. Louis?**

Warm weather clothing.

**If you could only eat one meal in St. Louis, where would you go?**

Tani Sushi Bistro in Clayton.

**What is a hidden gem of St. Louis that only a local would know?**

It is not hidden, but Forest Park.

**What is the one thing a traveler should avoid in St. Louis?**

East Saint Louis strip clubs!

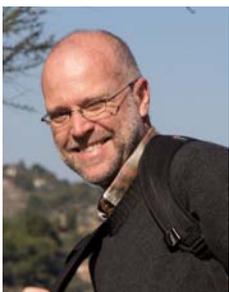


**Dr. Rainer Bussmann: Missouri Botanical Garden.**

**What is the ideal night out in St. Louis?**

Dinner at Five Bistro Restaurant on The Hill.

**What are some things travelers should pack for a stay in St. Louis?**



Lots of light clothing for 100°F degree heat and a sweater for indoor cold.

**If you could only eat one meal in St. Louis, where would you go?**

Five Bistro Restaurant on The Hill.

**What is a hidden gem of St. Louis that only a local would know?**

Tower Grove Park.

**What is the one thing a traveler should avoid in St. Louis?**

Walking alone around downtown at night.



**Dr. Ray Cooper: Phytoscience, Inc.**

**What is the ideal night out in St. Louis?**

The Hilton rooftop sports bar on Cardinals night.

**What are some things travelers should pack for a stay in St. Louis?**

Sun glasses.

**If you could only eat one meal in St. Louis, where would you go?**

Top of the Riverfront Restaurant at the top of Millennium Hotel. It overlooks the arch.

**What is a hidden gem of St. Louis that only a local would know?**

Ted Drews Frozen Custard.

**What is the one thing a traveler should avoid in St. Louis?**

Rush-hour traffic.

**Dr. Wendy L. Applequist: Missouri Botanical Garden.**

**What is the ideal night out in St. Louis?**

In summer, the ideal night out is to have a picnic and enjoy live music at the Missouri Botanical Garden's FREE Whitaker Music Festival, Wednesday evenings at 7:30pm. You can buy picnic food and drinks or bring a basket.



**What are some things travelers should pack for a stay in St. Louis?**

An umbrella (you never know), a sweater (they love their air conditioning here), and if you are going to the Whitaker festival, a blanket to sit on.

**If you could only eat one meal in St. Louis, where would you go?**

Pho Grand (Vietnamese) or Meskerem (Ethiopian) on Grand, or Rigazzi's or one of the many other fine Italian restaurants on the Hill.

**What is a hidden gem of St. Louis that only a local would know?**

Forest Park- the art museum is wonderful and free, and the zoo is free except for parking.

**What is the one thing a traveler should avoid in St. Louis?**

Do not leave valuables visible in a car; break-ins are common in many popular areas.

# FDA Approves Second Botanical Drug in History

By Annie Virnig

**O**n New Year's Eve 2012, the United States Food and Drug Administration (FDA) approved Fulyzaq™ for symptomatic relief of non-infectious diarrhea in HIV/AIDS patients on anti-retroviral therapies (1). The second botanical drug in FDA history, derived from the latex of *Croton lechleri*, is both closely tied to ethnobotanical studies and to socially responsible drug development. When viewed in combination with the approval of the first United States botanical drug, *Camellia sinensis* derived Veregen®, the approval of Fulyzaq™ challenges conceptions of drugs in the US and resurfaces the debate regarding the relevance of natural product research to drug development.

## **Fulyzaq™: an oral medication from *C. lechleri* for relief of anti-retroviral therapy affiliated diarrhea**

As the first oral botanical drug approved in the United States, Fulyzaq™ merits attention for its unique mechanism of action, efficacy in relieving secretory diarrhea in the HIV/AIDS population, and potential to address diarrheal symptoms of globally devastating infectious diseases such as cholera (2-4). At the same time, its development at the hands of long time ASP member Dr. Steven King provides an excellent example of ethnobotanical development of natural product drugs. The *C. lechleri* from which Fulyzaq™ is isolated, referred to colloquially as dragon's blood or sangre de drago, has been known in traditional medicinal systems for centuries (5). Used by indigenous groups as well as urban and mestizo populations in Bolivia, Colombia, Ecuador, Mexico, Paraguay, and Peru, *C. lechleri* oozes a bright red latex when cut (5). Traditional uses of the latex include treatment of bone cancer, cholera, cough, dysentery, diarrhea, flu, stomach ulcers, to speed healing after childbirth, and as a liquid bandage to heal cuts (6).

Initial studies by Shaman Pharmaceuticals into the ethnobotany of *Croton lechleri* exhibited remarkable breadth of attention, devoting resources to evaluating the ecology of the tree, intellectual property rights of Indigenous groups, and pharmaceutical development. From the onset, the group established intellectual property and benefit sharing agreements with the National Peruvian Indigenous Peoples Organization of the Amazonian Region built long-term management plans with local governments, and partnered with the Peruvian Ministry of Agriculture to document and enhance sustainable production systems of *C. lechleri* latex as an income source for local communities (5, 7).

At the same time as establishing these ecologically and sociopolitically sound policies, Shaman Pharmaceuticals also proceeded with studies to isolate, purify, elucidate the structure, and analyze the bioactivity of what become known as Fulyzaq™. The Shaman group developed a seven-step scaleable isolation protocol reliably able to extract the active heterogeneous proanthocyanidin oligomers from the latex of *Croton lechleri* at a yield of approximately 1% (5). Detailed analyses identified the average formula for Fulyzaq™ as  $(C_{15}H_{12}O_{6.5})_n \cdot 8H_2O$ , with an average

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STEVEN R. KING

Above:  
One of Cesar Lozano's reforestation team reforesting a wild collected *Croton lechleri* sapling in the secondary forest near Chimbana, Peru.

Right:  
Manuel Ortiz, a local person living near the city of Iquitos, Peru with the red latex of *Croton lechleri* in his hand that he maintains as part of his living pharmacy for his families health needs in his kitchen garden behind his home.



STEVEN R. KING

## FDA Approves Second Botanical Drug in History

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MICHAEL POWERS



BETO BORGES

Top: Cesar Lozano, a forestry expert who has been working on the reforestation and sustainable management of *Croton lechleri* since 1996 with Steven King, holding a cultivated *Croton* tree in the Huallaga River region of the Northern Peruvian Amazon.

Bottom: A recently planted wild *Croton lechleri* sampling, planted by teams under the direction of Peruvian botany expert Franklin Ayala, who has been collaborating with Shaman and then Napo since 1990 on the Napo river in the Northern Peruvian Amazon.

age chain length of seven monomers and an average molecular weight of 2,100 atomic mass units (5). The monomer subunits were determined to be (+)-catechin, (+)-gallocatechin, (-)-epicatechin, and (-)-galloepicatechin; a flavylium anthocyanidin moiety present in less than one percent of the isolate produces the reddish color of the isolate (5).

The first Phase II clinical trial, completed by Shaman, was a multicenter, double-blind, placebo-controlled, randomized study that demonstrated safety and efficacy of orally administered Fulyzaq™ for treatment of diarrhea in HIV/AIDS patients (8). A Phase III trial, entitled study 210, likewise provided strong proof of efficacy, but failed to meet FDA-mandated statistical significance

(9). Shaman's declaration of bankruptcy shortly thereafter, with its licenses and assets flung to all corners of the pharmaceutical and dietary supplement industries, left the case for ethnobotanical drug discovery grim.

The development and eventual approval of Fulyzaq™ can be traced to the persistence of two people, Ms. Lisa Conte, the entrepreneur who created Shaman, and ethnobotanist Dr. Steven King, both of whom weathered Shaman's bankruptcy and stock delisting and yet still found the investors and scientific staff to launch Napo Pharmaceuticals and buy the intellectual property of its predecessor (10). Napo, according to CEO Ms. Conte: "was created to continue all that Shaman had begun, and to provide global access to the products we developed. Napo added a business model that focused on every country, every population, and every channel of distribution — regardless of socio-economic relevance (11)".

Notably, Napo embraces a fundamentally different business model than most pharmaceutical companies, a fact that may have aided in its survival. Dr. King, Senior Vice President of Sustainable Supply and Ethnobotanical Research, comments on the company's resilience, noting the influence of ASP founder, Dr. Norman Farnsworth: "We have persisted because we believe in the mission of Napo and we have had tremendous support from ethnobotanists and scientists from many different but related disciplines. The mentorship of Dr. Norman Farnsworth and [noted ethnobotanist] Dr. Richard Evan Schultes has profoundly influenced us, leading to our perseverance to sustain this values- and mission- driven company (12)".

Thus, following the demise of Shaman, further studies run under Napo's dollar completed the final molecular research and provided needed clinical trials. Whereas most treatments for diarrhea are either supportive, involving replacement of fluid and salt losses, or halts intestinal peristaltic action, *in vitro* cell culture and *in vivo* animal studies conclusively show that Fulyzaq™ demonstrate a unique mechanism of action. Fulyzaq™ inhibits both the cystic fibrosis transmembrane regulator and calcium activated Cl<sup>-</sup> channels in the intestinal epithelium, leading to an inhibition of cAMP-dependent Cl<sup>-</sup> secretion (4, 13). This mechanism is particularly pertinent given the pathogenesis of both bacterial enterotoxins and the mechanisms of diarrhea in HIV/AIDS patients taking anti-retroviral therapies, both of which are thought involve excessive fluid and Cl<sup>-</sup> secretion in the intestine (14).

Clinical trials, designed and initiated by Napo, were continued by Salix Pharmaceuticals. A Phase III ADVENT trial of Fulyzaq™ demonstrated reduction of secretory diarrhea in HIV/AIDS patients over a six-month period with side effects at a similar level to that of the placebo (3). This trial decisively paved the way for Fulyzaq™'s New Drug Application (NDA) approval for symptomatic relief of non-infectious diarrhea in HIV/AIDS patients on anti-retroviral therapy. As Napo desires to groom the drug for treatment of neglected infectious diseases, trials related to this patient group are ongoing with promising Phase II results (2).

Despite its December 2012 approval, over 20 years in the mak-

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## FDA Approves Second Botanical Drug in History

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ing, the market delivery of Fulyzaq™ has been delayed, one of the subjects of an ongoing lawsuit between Napo and Salix. The genesis of this suit dates to Salix's slow acquisition of approval despite its FDA granted NDA fast-track and "priority review" status (15) and has only been aggravated by slow market delivery following approval. At the time of writing it remains unclear whether Fulyzaq™ is available to fill prescriptions with a recent news article citing Salix representatives stating that the drug is fully stocked at Walgreens, Napo receiving information from physicians to the contrary, and Walgreens declining to comment for the story (16).

### Veregen®: A topical ointment from green tea for treatment of external anogenital warts

Six years prior to the debut of Fulyzaq™, the approval of Veregen® stands as a monument in United States drug policy as the first FDA certified botanical drug. Veregen® is a 15% ointment obtained from green tea leaves (*Camellia sinensis*) for the treatment of external anogenital warts (condyloma acuminata) in adults (17). As Veregen® represents a non-ethnobotanically derived botanical drug, the contrasting discovery and development of Veregen® and Fulyzaq™ provide a means to contextualize changing FDA policy toward natural product drugs.

The culture of green tea influencing both daily life and medicinal practice extends back over 5,000 years to its inception in China (18). Despite extensive use of *Camellia sinensis* in Traditional Chinese Medicine, Veregen® cannot be said to be strictly the result of ethnobotany, given its prescription for a previously undocumented use. The drug consists of eight different catechins documented to be 85-95% by weight with unidentified compounds making up the remainder (19). Although the exact mechanism of action of the drug is not understood it is thought that the catechins, particularly epigallocatechin gallate, induce immunostimulatory activity leading to the release of pro-inflammatory cytokines at the site of infection (20).

The long human history of green tea use, combined with extremely low concentration of catechins in Veregen® (0.1 gram, or 1/30<sup>th</sup> of the content of a single cup of tea) (19), meant that clinical questions of safety were not as difficult to address for Veregen® as in the case of Fulyzaq™. Phase I trials had already been conducted at the time of the original patent application for Veregen® precursor Polyphenon® E (21). Investigators were therefore left primarily with a burden of providing proof of efficacy in the larger Phase II and Phase III trials, a fact that was conclusively shown (22-24), leading to the groundbreaking FDA approval on Halloween, 2006 (19).

### The future for botanical drugs in the United States

It is not only the precedent set by Fulyzaq™ and Veregen® but also the prevailing attitude of senior members of the FDA Center for Drug Evaluation and Research division that truly points to a new era in drug development in the United States. The firm endorsement by FDA researchers that botanical drugs will "eventually lead to new therapies derived from complex natural mix-



ELSA MEZA

Forestry technician Elulogio Pachco, in the Selva Central of Peru in mixed agroforestry site where 4 year old *Croton lechleri* trees (sangre de drago) are cultivated with Simarouba amara (marupa) trees.

tures that will satisfy unmet medical needs" implies a huge step forward for an institution that, until seven years ago, had never approved such a botanical drug (17).

As Dr. King comments: "the development and approval of natural product derived drugs demonstrates the importance of the discipline of pharmacognosy for drug development. There is no doubt that there are many important therapeutic compounds yet to be discovered through natural product research. The recent large scale production of a semi-synthetic artemisinin combination drug for the treatment of malaria also shows the importance of pharmacognosy research to addressing paramount issues in global public health (12)".

Whether discussing Veregen®, Fulyzaq™, or any future botanical drugs, one of the most relevant facts is that botanical drugs are derived from complex natural products, a fact that has implications for quality control of batch-to-batch variation (25). ASP President, Dr. David Newman, notes: "Botanicals are a product of their environment at a particular moment in time, so one must be very careful about how they are harvested, processed, and how efficacy is judged (26)". This is a critical factor to account for, and must be taken account in approval processes.

Amendments within the FDA itself complement new technological developments that allow for analysis of botanicals to ensure efficacy and safety is consistently maintained in new drugs. Development of a Botanical Review Team specifically for review of botanically derived drugs, as well as the publication of a guide for working with botanical products, represent monumental shifts in FDA policy (17, 27). The approval of both Veregen® and Fulyzaq™ thus perhaps herald a new era in drug development. The increased interest in natural product and ethnobotanical drug discovery over the past 20 years can now definitively be said to be reflected by established policies within the FDA. Whether the dominant pharmaceutical companies embrace a natural product approach to drug development, however, remains a question that will only be answered with time. ■

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# FDA Approves Second Botanical Drug in History

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## PHARMACEUTICAL COMPANIES ASSOCIATED WITH THE DEVELOPMENT OF FULYZAQ™

### Shaman Pharmaceuticals



Formed in 1989 by Ms. Lisa Conte as a socially responsible company using an ethnobotanical approach to drug discovery. This company began initial studies into the use of *Croton lechleri* for treatment of HIV/AIDS-associated diarrhea.



### Napo Pharmaceuticals

Formed in 2001 by former Shaman CEO Lisa Conte following Shaman Pharmaceutical's bankruptcy. Napo bought all intellectual property rights held by Shaman as well as their botanical library. Napo continued clinical trials and basic research to bring Fulyzaq™ to approval both independently and in partnership with Salix.



### Salix Pharmaceuticals

Granted intellectual property rights and product testing information in the developed world for HIV/AIDS-associated diarrhea by Napo. Napo receives equity investments and royalties from Salix. Salix submitted and received FDA approval for the Fulyzaq™ NDA.

BRAND NAME	Veregen®	Fulyzaq™
GENERIC NAME	Sinecatechins	Crofelemer
OTHER NAMES	Polyphenon® E Kunecatechins	SP-303 NP-303 Provir
FDA APPROVAL	2006	2012
PRESCRIBED USES	Treatment of external anogenital warts ( <i>condyloma acuminata</i> )	Treatment of HIV/AIDS anti-retroviral associated non-infectious diarrhea
MODE OF USE	Topical ointment	Orally administered
SPECIES	<i>Camellia sinensis</i>	<i>Croton lechleri</i>
PLACE AND BOTANICAL ORIGIN	China: Green tea leaves	South America: Sangre de drago (dragon's blood)
CULTURAL ANCESTRY	Traditional Chinese Medicine (TCM)	Indigenous groups throughout Latin America, popular modern usage
ADMINISTRATION	Applied 3 times a day; for no more than 16 weeks	125 mg tablets two times daily; long-term usage
SIDE EFFECTS	Erythema, pruritus, burning, pain, erosion or ulceration, and edema	Cough, flatulence, high bilirubin, bronchitis, and upper respiratory tract infection
PRESCRIPTION	Veregen	New Fulzaq



continued on page 10

## FDA Approves Second Botanical Drug in History

continued from page 9

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# 2012 Schwarting and Beal Award Winners Announced

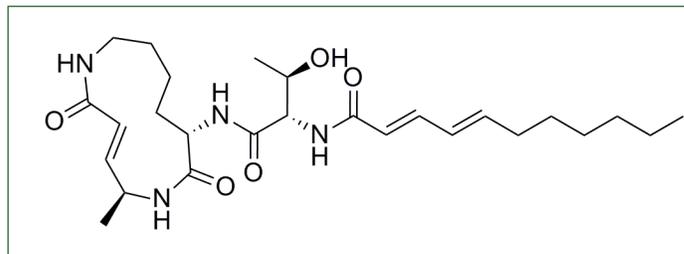
By Dr. Amy Keller

The 2012 Jack L. Beal and Arthur E. Schwarting Awards have been announced, and the award-winning publications are “Nontargeted Metabolomics Approach for Age Differentiation and Structure Interpretation of Age-Dependent Key Constituents in Hairy Roots of *Panax ginseng*,” by Nahyun Kim, Kemok Kim, DongHyuk Lee, Yoo-Soo Shin, Kyong-Hwan Bang, Seon-Woo Cha, Jae Won Lee, Hyung-Kyoon Choi, Bang Yeon Hwang, and Dongho Lee, and “Luminmycins A–C, Cryptic Natural Products from *Photobacterium luminescens* Identified by Heterologous Expression in *Escherichia coli*,” by Xiaoying Bian, Alberto Plaza, Youming Zhang, and Rolf Müller, respectively.

The award-winning publications are “Nontargeted Metabolomics Approach for Age Differentiation and Structure Interpretation of Age-Dependent Key Constituents in Hairy Roots of *Panax ginseng*,” by Nahyun Kim, Kemok Kim, DongHyuk Lee, Yoo-Soo Shin, Kyong-Hwan Bang, Seon-Woo Cha, Jae Won Lee, Hyung-Kyoon Choi, Bang Yeon Hwang, and Dongho Lee, and Luminmycins A–C, Cryptic Natural Products from *Photobacterium luminescens* Identified by Heterologous Expression in *Escherichia coli*,” by Xiaoying Bian, Alberto Plaza, Youming Zhang, and Rolf Müller.

ASP member Dr. Lee told the *Newsletter*, “We are surprised and honored to receive Jack L. Beal award. We identified key constituents showing age-dependent variations by analyzing metabolites of *Panax ginseng* using ultraperformance liquid chromatography/quadrupole time-of-flight mass spectrometry with statistical analysis. In particular, it was interesting to analyze and determine structures of minor metabolites using mass spectrometry. Again, we are very grateful to ASP for this award.”

In 2001, the Foundation Board of the ASP began a new initiative, resulting in the Arthur E. Schwarting and Jack L. Beal Awards for best papers in the *Journal of Natural Products*. In this manner, two former distinguished editors of the *Journal* are

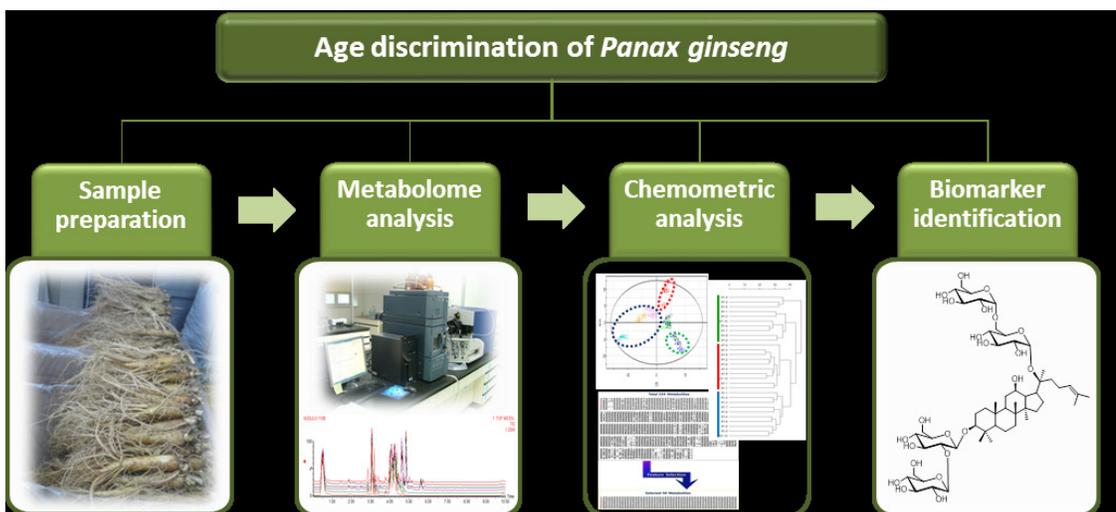


Luminmycin A1 from *Photobacterium luminescens*.

fondly remembered. The Schwarting Award is open to all papers published in the *Journal* within a given year (either in print or electronically). In turn, the Beal Award is awarded to younger investigators defined as those within 12 years of receiving their Ph.D. degree or within 10 years of gaining their first professional appointment such as Assistant Professor or an equivalent position in industry or government.

Dr. Müller relates, “We are delighted to receive this prestigious award as it shows how well received our work is towards establishing tools and methods for heterologous expression of complex microbial natural product biosynthetic pathways. Our recent successes in expressing pathways that are seemingly cryptic in their natural hosts help in setting the stage for the future exploitation of the enormous genomic potential found in microorganisms.”

The corresponding authors of these papers have been invited to the banquet at the 54<sup>th</sup> Annual ASP Meeting in St. Louis, on July 18, 2013, to receive a check and a plaque in honor of this achievement. The above-mentioned papers may be accessed freely from the home page of the *Journal of Natural Products* (<http://pubs.acs.org/JNP>). Congratulations to Drs. Lee, Müller and their co-authors! ■



DR. NAHYUN KIM

The work flow used to analyze metabolites of *Panax ginseng*.

# ACS Honors Moore with Arthur Cope Scholar Award

By Dr. Amy Keller

ASP Vice President Dr. Bradley Moore is the 2013 recipient of the American Chemical Society's (ACS) Arthur Cope Scholar Award that recognizes and encourages excellence in organic chemistry.

Dr. Moore told the *Newsletter*, "I am very honored to have been selected as a recipient of a 2013 Cope Scholar Award from the ACS. It is a wonderful recognition of the creativity and dedication of my remarkable research team over the years who have explored the chemical wonders of how microbes synthesize complex organic molecules."

ASP President Dr. David Newman related, "I have had the pleasure of knowing Brad since his days at the University of Washington (having first met him during his "undergraduate sojourn at the University of Hawai'i in his father's lab"). If one simply looks at the trajectory of just two of his earlier post-doctoral fellows, Drs. Joern Piel and Christian Hertweck, one can see that he chose them well and trained them exceedingly well. This record is definitely continuing, as seen by a perusal of his more recent publications with Alessandra Eustaquio and Amy Lane. His publications in the field of biosynthesis of natural products, predominately based upon microbial products and their genomic control, are very well cited with over 170 citations to just one paper on the *Salinispora tropica* genomic biosynthetic clusters, to say nothing of other papers on similar topics where the citation records are in the 50 to 70+ level in the last three to four years. This Cope Award is very well deserved for work at the frontiers of natural product chemistry and biology."

Dr. Moore will present his work at the ACS meeting this September 8-12, 2013, in Indianapolis, Indiana. Dr. Moore plans to speak about emerging methods for quickly connecting genes to molecules. "I am particularly captivated with our latest DNA cloning approach to directly capture large, orphan natural product biosynthesis gene clusters from genome sequenced microbes in order to rapidly engineer and express them in surrogate host strains for the production of new natural product chemicals. We have already discovered by this approach a powerful new antibiotic from a refactored biosynthetic gene cluster derived from a marine microbe. This new technology has dramatically altered the general



ANDREW SCHULTZ

Dr. Moore in La Jolla, California.

thinking of my research lab and the way in which we now approach the genome mining of microbes for the directed discovery of new natural product molecules," he related.

When asked about other highlights of his work, Dr. Moore said, "I continue to take great pleasure in learning about how nature assembles natural product molecules. This basic knowledge can inform us about new enzymatic reactions, facilitate the bioengineering of designer molecules, and support mechanism of action studies. I have

been so very fortunate over my career to collaborate with a number of natural product chemists who have generously shared their microbial resources to support my research program. Right now we are exploring how marine microbial products, such as salinosporamide, marinopyrrole, chlorizidine, ammosamide, and merochlorine, are constructed. Each story presents a unique challenge and because of their exceptional chemical structures, they regularly surprise us with new concepts in biosynthesis. The biosynthetic enzymes that continue to inspire us are the flavoproteins that have such diverse synthetic functions, such as in favorskii rearrangements, oxidative aromatic coupling reactions, bizarre halogenation reactions, and C-H activation reactions. Really cool stuff!"

Dr. Moore advises younger ASP members to have fun with science. "Do not take the well-traveled and safe path; rather, venture into new directions. Regularly read the literature, especially from other scientific disciplines, and fold new concepts and techniques back into your own research program. There are so many new and exciting technological advances to exploit in the natural products field. Find your inspiration and run with it." ■

**"Do not take the well-traveled and safe path; rather, venture into new directions."**

# Hot Topics in Pharmacognosy: Acutumine, An Old Alkaloid With New Potential

By ASP President David Newman

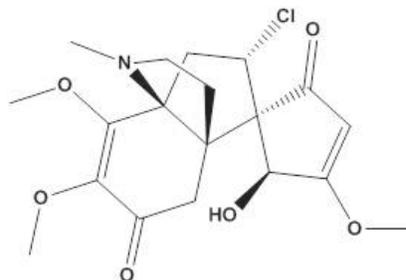
There are many, many unsolved mysteries in the mammalian immune system, to say nothing of the manifold differences and similarities between the human system and comparative processes in the other domains of life. Even the simple metazoan (the marine sponge) has an immune system of sort, to say nothing of more complex invertebrates and the plant kingdom.

In 1929, a group in Japan (Goto, K. and Sudzuki, H., *Bull. Chem. Soc. Jpn.* **1929**, 4, 220) reported the isolation of what we now know to be an unusual alkaloid, with an empirical formula of  $C_{20}H_{27}O_8N$  or  $C_{21}H_{27}O_8N$ , together with a suggestion of a ketone, a carboxyl, an N-methyl and three methoxyl groups in the structure; we now know this to have an unusual tetracyclic structure.

The compound, together with others was isolated from a species of Menispermaceae, *Sinomenium acutum* Rehd. et Wils, with the Japanese name of Oh-tsuzurafuji. There the story languished until a report from the original scientist and colleagues in two papers in *Tetrahedron Letters* in 1967, where they demonstrated that the compound was also isolable from *Menispermum dauricum* DC (Japanese name Kohmori-kazura) in addition to the original source (Tomita et al., *Tet. Lett.* **1967** (25), 2421 and 2425).

With the improved analytical techniques available in comparison to those in 1926, a novel tetracyclic structure was proposed which included a chlorine atom in the molecule and a revision of the empirical formula to  $C_{19}H_{24}O_6NCl$ . These papers were followed by a much fuller report in 1971 (Tomita et al., *Chem. Pharm. Bull.* **1971**, 19, 770).

The story might have finished there, with the report of a novel chlorine-containing tetracyclic alkaloid, coupled to some further studies of a phytochemical nature. However, this plant was well known in Traditional Chinese Medicine as a source of antipyretic and analgesic activities. Thus in 2002, Chinese scientists in Shanghai and Hong Kong reported on the biological activity of acutumine and four closely related alkaloids (two being the des-chloro derivatives).



Acutumine structure as of today.

What was found was not expected. Of the five closely related compounds, only acutumine demonstrated cytotoxic activity against T-cells with no activity against other cell types (Yu et al., *Phytochem.* **2002**, 61, 439). It also was reported in a patent in 2006 to “improve object and social recognition in a Wistar rat model” (Qin

et al., US 2006/0167076 A1, 27JUL2006).

A number of groups have reported various routes to synthesis of this molecule with the first synthesis by Castle's group in 2009 (Li et al., *J. Amer. Chem. Soc.* **2009**, 131, 6674 & *J. Org. Chem.* **2009**, 74, 9082), and then in 2013, Herzon's group at Yale reported the synthesis of both acutumine and the first reported synthesis of the des chloro analogue (King et al., *Angew. Chem. Int. Ed.* **2013**, 52, 3642), a follow-on from their 2011 paper describing the parent molecule's synthesis (Herzon et al., *Angew. Chem. Int. Ed.* **2011**, 50, 8863).

Thus, 85 years after the original report and 11 years after its identification as a potential lead for treatment for T-cell malignancies, the compound is now accessible, using some very elegant catalytic chemistry and stereo-control of addition of various substituents. A much more thorough evaluation can now be performed as to the biological activities of this class of alkaloids.

A take-home lesson from this story may well be that “there are many rough diamonds” in the phytochemical literature from tens of years ago that have interesting structures but whose structures, availability and biological activities are still waiting for “stardom!” ■

## ASP Election Results

By Dr. Amy Keller

The results of the recent ASP elections determined Dr. Phil Crews to be the Vice President during 2013-2014 with 144 votes, and Dr. Barry O'Keefe will be the Executive Committee Member with 146 votes. The incoming Secretary will be Dr. Bill Keller, and there were no constitution or bylaws amendments in this election.

According to the report compiled by the ASP Tellers Committee, chaired by Dr. Bill Keller, from 1,001 ballots sent to ASP members in April, 2013, 261 were sent back, resulting in voting participation by 26% of membership. ■

# Behind the Scenes in Pharmacognosy: Team Spirit Leads the Way

In January of 2013, the *Journal of Natural Products* published work from ASP member Dr. Leng Chee Chang and colleagues at the University of Hawai'i, Hilo, Hawai'i entitled, "Biologically Active Withanolides from *Withania coagulans*." Dr. Chang shares her work on the vegetable rennet, as well as her inspiring laboratory motto. This article is among the top read articles in JNP from January to March of this year. Please read the full article in the *Journal of Natural Products*, 2013;76: 22–28. doi.org/10.1021/np300534x.

By Dr. Amy Keller

## How did you become interested in working with *Withania coagulans* compounds, and how did you come to focus on their potential anti-cancer activity?

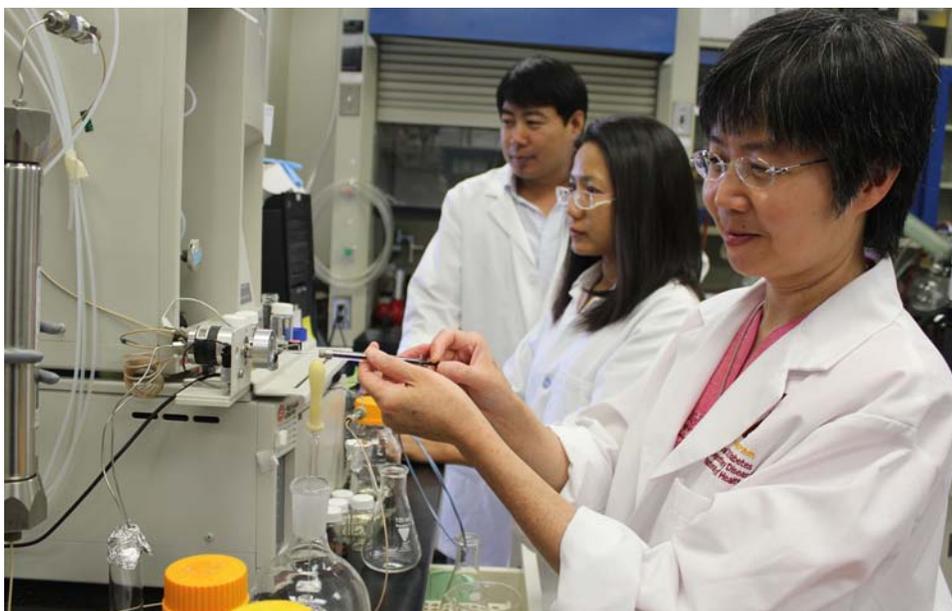
My research interest is focused on naturally occurring cancer chemoprevention and anticancer agents with low toxicity. Therefore, I usually work with edible species. As a part of the exploration of important medicinal plants of Pakistan for cancer treatment, initially six Pakistan plants were chosen for the study based on ethnopharmacological data. Among these plants, *Withania coagulans* showed the highest biological potential. Interestingly, this plant, popularly known as vegetable rennet, is also a highly valued medicinal plant.

## Who in your laboratory carried out the research?

The research was made feasible with the arrival of Dr. Ihsan-ul-Haq, a visiting scholar who worked in Dean John Pezzuto's laboratory at The Daniel K. Inouye College of Pharmacy, University of Hawai'i at Hilo, Hawai'i (DKICP-UH Hilo.) Sponsored by the Higher Education Commission Pakistan, Dr. ul-Haq conducted most of the experimental work, along with my postdoctoral associate, Dr. Ui Joung Youn. In addition, our collaborators from Dean Pezzuto's laboratory performed the cancer chemopreventive bioassay testing. The X-ray crystal structure was done by Dr. Charles Simmons, from the Department of Chemistry at UH Hilo.

## Could you provide a brief explanation of the work and results in your own words? In what way are the data in your paper new?

The overall aims of this study were to evaluate the cancer chemopreventive potential of withanolides from *W. coagulans* as nuclear factor kappa B (NF-κB) and inducible nitric oxide synthase



MS. MAGGIE MORRIS

(From right to left) Dr. Leng Chee Chang works in her laboratory at The Daniel K. Inouye College of Pharmacy at the University of Hawai'i at Hilo with Ms. Mayuramas "Jan" Sang-Ngern, a Ph.D student and Dr. Ui Joung Youn, a postdoctoral associate. Dr. Chang is the principal investigator on a project that aims to find a natural product treatment for cancers with fewer side effects and lower toxicity than current therapies.

(iNOS) inhibitors. NF-κB is an important transcriptional factor that regulates numerous physiological processes including cellular proliferation, development, differentiation, immunity, apoptosis, inflammation, and metabolism. The critical role for persistently-active NF-κB is evident in many cancers. Aberrant NF-κB activity dysregulates growth and survival, promotes angiogenesis, migration and invasion of tumor cells, and induces tumor immune tolerance. The structure and absolute stereochemistry of new withanolides (1-3) were determined by NMR, NOESY, CD and X-ray diffraction methods. This is the first report of structure-activity relationship of stereo structures of *W. coagulans* withanolides with inhibition of nitric oxide and NF-κB activities. They inhibited nitric oxide production in LPS murine macrophage RAW

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## Behind the Scenes in Pharmacognosy: Team Spirit Leads the Way

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264.7 cells, and inhibited tumor necrosis factor-alpha induced NF-kB activation, with  $IC_{50}$  values in the range of 1.6-38.5  $\mu$ M.

### What impact does this research have on natural product science and health research in general?

Plants with ethnopharmacological uses have been a primary source for early drug discovery and chronological experiences with these plants as curative tools have helped to isolate and develop single chemical entities in modern medicine. In the present study, six medicinally-important plants selected from different areas of Pakistan and based on extensive information from local healers, were investigated for biological activities to evaluate their cancer chemopreventive and cytotoxic potential. Seven different bioassays were used: inhibition of TNF- $\alpha$  activated NFkB, aromatase inhibition, inhibition of NO production in lipopolysaccharide activated macrophage RAW cells (iNOp), interaction with RXRE, induction of QR1, DPPH free radical scavenging and inhibition of LU-1 lung cancer cell and MDA-MB-231 breast cancer cell proliferation. This investigation established the isolation of biologically active entities from *W. coagulans* that had been used extensively in the folk medicine to treat cancer. The exploration of the cancer chemopreventive and anticancer potential of the plant and the compounds isolated therefore provides a new addition to natural products science and health research. The purified compounds can serve as a promising source for new drug development to combat cancer. Proposed future prospects of the research include:

The isolation of more withanolides from the plants containing them for the establishment of a broader structure-activity relationship (SAR); this will be followed by the development of synthetic approaches for the most active analogues. Also, studies for preclinical trials could be carried out to evaluate the in vivo activity and toxicity of the isolated compounds. The identification of bioactive and less cytotoxic natural products in *W. coagulans* that are edible should promote the use of *W. coagulans* as herbal remedies for anticancer regimens. The low cost of *W. coagulans* should increase access to their use as an alternative treatment for cancer in Pakistan and in United States.

### What is a favorite nonscientific activity of your lab?

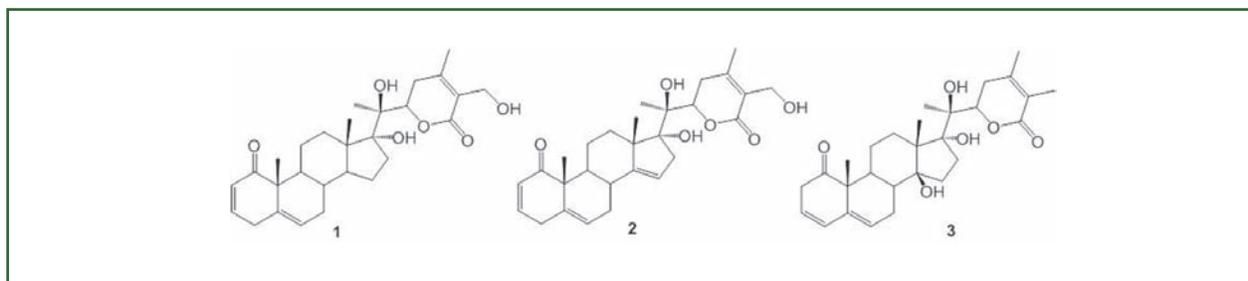
It ranges from exploring the beauty of Hawaii to practicing meditation for inner peace.

### What is your lab's motto?

Practice the discipline of perseverance, promote an effective-team spirit with consensus and cooperation; be passionate in what we do, and compassionate in helping others.

### What is your greatest extravagance in the laboratory?

Shimadzu high performance liquid chromatography (HPLC) includes evaporate light scattering detector (ELSD) and photo diode array (PDA) detectors. ■



(From left to right) Three new steroidal lactones, withacoagulin G (**1**), withacoagulin H (**2**), and withacoagulin I (**3**)

**Practice the discipline of perseverance, promote an effective team spirit with consensus and cooperation; be passionate in what we do, and compassionate in helping others.**

# ASP Fellows Series: Collaboration, The Key to Exploring Nature's Treasure Trove

By Dr. Gordon Cragg

For some 20 years, I served in the Natural Products Branch of the National Cancer Institute (NCI); since my retirement in late 2004, I have continued to participate in National Institutes of Health (NIH) natural products programs as an NIH Special Volunteer. For me, this has been tremendous honor and privilege, and I have had the pleasure of collaborating with many outstanding researchers in the discovery and development of novel drugs from the boundless resources of Nature's treasure trove. What has impressed me most is that natural products drug discovery and development is truly an international collaborative effort, encompassing the exploration of global genetic resources by teams comprising talented scientists from many disciplines, working in academia, research institutes, government and companies, large and small, and in countries worldwide.

A taste of the international, multidisciplinary and multi-institutional flavor of natural products research may be obtained by perusing some of the chapters in the *History of the ASP* published in 2009 in celebration of the 50<sup>th</sup> Anniversary of the Society.<sup>1</sup> Chapters 4-8 give brief accounts of "Pharmacognosy in Action" over the past 50 years at United States academic institutions, ASP partners in countries abroad, United States government organizations, the pharmaceutical and United States herbal industries, and United States research institutions. The diversity of international investigators, source organisms and countries of origin is highlighted in Chapter 9 which briefly reviews some major milestones achieved in natural products drug discovery in the past 50 years



by ASP members and their colleagues.

Summaries of the discovery of 20 important naturally-derived classes of bioactive compounds are presented; the vital role of multidisciplinary research, including semi- and total synthesis and medicinal chemistry, in addressing supply problems and optimizing promising lead structures is clear. Also included in Chapter 9 is a fascinating account by ASP member Dr. Bill Fenical of the evolution of his program studying marine microbes as sources of novel bioactive metabolites, referred to by Dr. Bill Gerwick in his first ASP Fellows Series article.<sup>2</sup> Illustrating the need for risk-taking and persistence emphasized by Dr. Gerwick, Dr. Fenical and his team have achieved outstanding success in the isolation of novel, potent agents, such as salinosporamide from *Salinispora tropica*, a major new marine actinomycete taxon isolated from marine sediments.

Finally, Chapter 10 highlights exciting developments in genomics and combinatorial biosynthesis, plant endophytes and other microbial symbionts, the identification of cryptic (silent) gene clusters in microbes, biopharmaceuticals, and the power of total synthesis and combinatorial chemistry.

Recent reviews have elaborated on how these developments play key roles in the discovery and development of novel anticancer agents.<sup>3,4</sup>

The history of the discovery and development of Taxol<sup>®</sup> vividly illustrates the essential need for long-term commitment, patience, persistence, and optimism as emphasized by Dr. Gerwick,<sup>2</sup> combined with the power of multidisciplinary collaboration on an international scale. Isolated in 0.01% yield by the late Dr. Wall and ASP member Dr. Wani from the bark of *Taxus brevifolia* first collected in Washington State in 1962, Taxol was not considered any better than many other cytotoxic compounds available at the time, and it was only advanced to preclinical development 15 years later after showing superior activity in some human solid tumor xenograft models. The crowning moment, however, was the seminal discovery in 1979 by ASP member Dr. Susan Horwitz that Taxol possessed a unique mechanism of action which spurred intense interest in its further development. Poor water solubility made formulation extremely difficult and required the addition of substantial amounts of the emulsifying agent, Cremophor EL, which later was thought to be the culprit causing severe anaphylaxis which resulted in the deaths of several patients in Phase I clinical trials.

Needless to say, the enthusiasm of clinicians and NCI waned considerably and nearly terminated further development, but fortunately some clinicians, having seen some tumor regressions, persisted and developed a slow infusion which, combined

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**What has impressed me most is that natural products drug discovery and development is truly an international collaborative effort, encompassing the exploration of global genetic resources by teams comprising talented scientists from many disciplines working in academia, research institutes, government and companies, large and small, and in countries worldwide.**

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with premedication, overcame the allergic reactions. The setbacks experienced in the early trials had led to reduced production of the drug (an expensive and environmentally unfriendly process) which restricted the progression of Phase II trials, but the observation of significant activity against refractory ovarian cancer in 1989, and metastatic breast cancer a short while later, caused a resurgence of interest, and highlighted the urgent need to develop more abundant and reliable sources of the drug.

In 1991, Bristol-Myers Squibb (BMS) was selected by NCI as a Cooperative Research and Development Agreement (CRADA) partner, and working with the United States Department of Agriculture (USDA) Forest Service and Bureau of Land Management, and Hauser Chemical Research based in Boulder, Colorado, 1.6 million pounds of bark were harvested and 130 kg of Taxol produced. Meanwhile, in an effort to find better and more sustainable sources, NCI sponsored worldwide surveys and assessments of alternative *Taxus* species, as well as research into cultivation, hydroponics, plant tissue culture, biosynthesis and total synthesis, but it was the pioneering development of a semi-synthetic conversion of a precursor, 10-deacetylbaccatin III (10-DAB), to Taxol and other active analogs by the French chemist, Dr. Pierre Potier and his group which provided the key breakthrough. 10-DAB and other baccatins are isolated in good yields from the leaves of the European Yew, *T. baccata*, a sustainable source, in contrast to the bark of the Pacific Yew, *T. brevifolia*.

The Italian company, Indena SpA, worked with BMS in producing relatively large quantities of 10-DAB from cultivated *T. baccata*, and this was efficiently converted to Taxol using a semi-synthetic method developed by Dr. Robert Holton of Florida State University. Taxol is now also produced on a commercial scale using plant tissue culture. Thus, after overcoming many, apparently insurmountable challenges, Taxol was finally approved by the FDA for use in the treatment of refrac-

tory ovarian cancer in 1992, some 30 years after the first Pacific Yew bark collection! Since then it has been approved for the treatment of refractory breast cancer and several other cancers. The saga of the Taxol supply crisis, including the signing of the Pacific Yew Act into law by the President in August, 1992, has been documented,<sup>5</sup> and the success story of Taxol and related analogs in the treatment of countless patients worldwide, as well as continuing research into the development of more effective derivatives, is discussed by ASP member Dr. David Kingston in chapter 6 of reference 4.

Semi- and total synthesis have continued to play critical roles in solving natural supply problems, and have provided adequate quantities of several marine-derived anticancer agents which have advanced into clinical use or trials, such as ecteinascidin 743 (Yondelis), Eribulin (Halaven®), discodermolide, and analogs of dolastatin and hemiasterlin.<sup>3,4</sup> Combinatorial biosynthetic techniques have been applied to the production of novel analogs of microbe-derived anticancer agents, such as the anthracyclines, ansamitocins, epothilones, and enediynes.<sup>3,4</sup>

International collaboration continues to be an essential factor in the drug discovery process, and many natural product research groups have established close and productive collaborations with scientists and communities in biodiversity-rich countries. Support for such programs, which generally include research groups from United States and host country institutions, as well as industry, has been provided through government grant mechanisms, such as the International Cooperative Biodiversity Group (ICBG) program coordinated by the NIH Fogarty International Center (<http://www.icbg.org/>). Through contracts with botanical and marine biological organizations, NCI has performed extensive collections of plants and marine invertebrates in over 30 countries, and has established a repository of extracts (<http://dtp.nci.nih.gov/branches/>

[npb/repository.html](http://dtp.nci.nih.gov/branches/npb/repository.html)) which are available to research groups worldwide for studies related to any human disease.

All these programs are subject to agreements with organizations in host countries ensuring equitable collaboration and benefit-sharing, in line with the principles of the United Nations Convention on Biological Diversity (CBD). The impressive progress that has been made in drug discovery and the conservation of host country natural resources, as well as the promotion of drug discovery initiatives and infrastructure development in host countries, and some of the problems encountered in establishing collaborative agreements, are discussed in reference 6.

Natural products drug discovery and development is very much alive and well, and with the creative exploration of new frontiers and the application of new technologies in collaboration with our colleagues nationally and internationally, we can confidently expect a bright and productive future. ■

1-<http://www.pharmacognosy.us/what-is-pharmacognosy/the-history-of-the-asp/>.

2-Gerwick, B. *ASP Newsletter*, **2012**, 48 (4), 9-10; **2013**, 49 (1), 9-10.

3-Cragg, G.M., Grothaus, P.G. and Newman, D.J., Impact of Natural Products on Developing New Anti-Cancer Agents, *Chem. Rev.* **2009**, 109, 3012-3043.

4-Anticancer Agents from Natural Products, 2<sup>nd</sup> Edition, Eds: Cragg, G. M., Kingston, D. G. I. and Newman, D. J., CRC Press/Taylor and Francis, Boca Raton, 2012.

5-Cragg, G. M., Schepartz, S. A., Suffness, M., and Grever, M. R.: The taxol supply crisis. New NCI policies for handling the large-scale production of novel natural product anticancer and anti-HIV agents. *J. Nat. Prod.* **1993**, 56, 1657-1668.

6-Cragg, G. M., Katz, F., Newman, D. J. and Rosenthal, J. The Impact of the United Nations Convention on Biological Diversity on Natural Products Research. *Nat. Prod. Rep.*

**Natural products drug discovery and development is very much alive and well...**

# Pharmacognosy Field Notes: From the Tropics to the Poles

Dr. Marcy J. Balunas



MARCY BALUNAS



KIM DIVER

Left: Cyanobacteria on a reef in Bastimentos National Park, Panama.  
Right: Dr. Balunas collecting in Coiba National Park, Panama.

**M**y research group at the University of Connecticut (UConn), Storrs-Mansfield, Connecticut, studies marine microorganisms with a focus on microbiology, natural products chemistry of tunicate-associated bacteria, and psychrophilic marine and glacial bacteria. We travel near and far, from Long Island Sound, to Alaska, and even Panama, to collect a diverse range of organisms.

Last August we began collections in sub-Arctic Alaska, where part of our work involves the collection of marine tunicates and their associated bacteria from Kachemak Bay along the southern coast of Alaska. These tunicate-associated bacteria are likely used by the host organism for chemical defense and may thus have interesting biological properties against human pathogens. We stayed at the University of Alaska Fairbanks/National Oceanic and Atmospheric Association field station in Kasistna Bay, accessible only by boat near a town whose population includes 259 residents.

Last year, we decided not to dive in the frigid waters but to collect tunicates during extreme low tides, which sometimes required us to hike to marine field sites, a strange concept when you think about how most marine field collections are done! During one of those hikes we heard some rustling and saw a black bear; fortunately, he was up a hill but it is definitely not something you expect to see while collecting marine tunicates! In addition, we visited the Seldovia and Homer marinas while we were there and found some great specimens. We also went tide pooling and found some very interesting tunicate species that are exposed during the extreme tidal changes.

Probably one of our most memorable collection experiences to date has been to Matanuska Glacier in Alaska where we spent an amazing day collecting glacial bacterial samples. We teamed up with two professional ice-climbing guides from Mica Guides.

The guides scouted out four locations: one where a very old portion of the glacier is exposed; one at the very top of the glacier that experiences high levels of solar heat; one where glacial moraine has been deposited over glacial ice; and one that experiences a fair amount of human disturbance from tourists. From each of these sites we collected several ice cores using a custom-made drill bit capable of obtaining foot long cores. We also collected glacial till as well as glacial meltwater, which at one location was thought to be percolating from beneath the glacier. Because Alaska has such a strong tourist fishing industry we were able to easily ship our samples back to the lab where we have been busy isolating cold-obligate bacteria.

My choice to study cold-obligate organisms lies in their unique biological characteristics, including their ability to regulate mem-

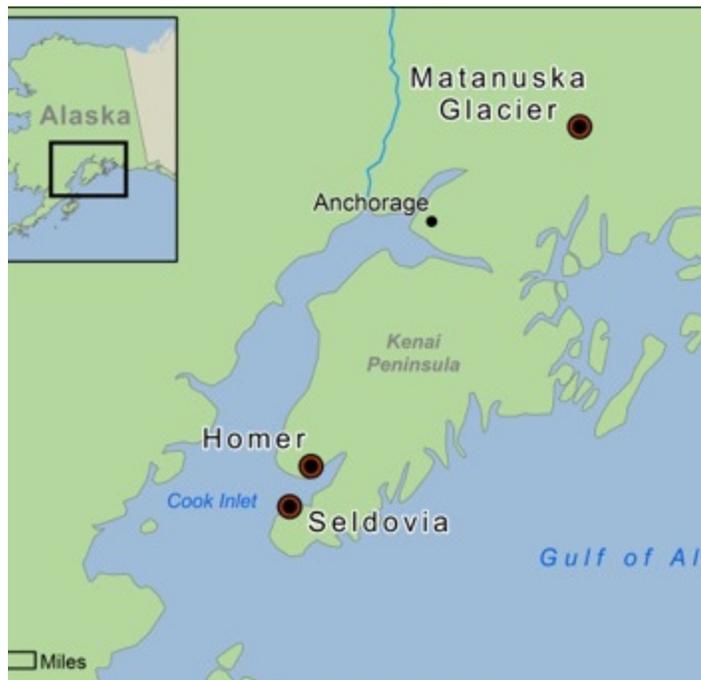
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## Pharmacognosy Field Notes: From the Tropics to the Poles

continued from page 18



KIM DIVER



Left: Sorting collections in Panama. Right: The collection sites of Alaskan tunicates.

brane fluidity, continue transcription and translation, adapt to sudden temperature changes, inhibit intracellular ice crystal formation, continue enzymatic processes using cold-adapted enzymes, and maintain nutrient and waste transport. With our focus on tunicate-associated and psychrophilic bacteria, we conduct selectivity-based drug discovery from marine microorganisms, including synthetically modifying our natural product isolates.

For one of our most promising natural product leads collected in the Republic of Panama, we have continued with preclinical development of a marine cyanobacterial natural product, santacruzamate A, which we found to be a remarkably potent and isozyme-selective histone deacetylase inhibitor. In addition, we have begun collections of tunicates from both the Pacific Ocean and Caribbean Sea off the coast of Panama. We also work on the development of fundamentally novel methodology for discovery of cytotoxic payloads for antibody-drug conjugates for which we collect organisms, from Panama, the Long Island

Sound, and Alaska. And finally, we have begun investigation of bioactive secondary metabolite production from glacial and periglacial bacteria collected in Alaska. These collection locations have allowed for several exciting research trips from the tropics to the “poles”.

The tropical adventures began during my postdoctoral training when I lived and worked in Panama, and the adventures continue as part of the Panama International Cooperative Biodiversity Group. Panama is an amazing place to study marine organisms with a distance of only about 50 miles between two very different bodies of water. In Panama, the Caribbean is typically warmer and contains a higher diversity of coral reef environments than the Pacific, which is home to much larger marine animals and some extraordinary dive locations. Panama also has several fantastic scientific facilities including the Smithsonian Tropical Research Institute, the Institute of Scientific Investigations and High Technology Services, and the University of Panama.

*continued on page 20*

**My choice to study cold-obligate organisms lies in their unique biological characteristics, including their ability to regulate membrane fluidity, continue transcription and translation, adapt to sudden temperature changes, inhibit intracellular ice crystal formation, continue enzymatic processes using cold-adapted enzymes, and maintain nutrient and waste transport.**

## Pharmacognosy Field Notes: From the Tropics to the Poles



KIM DIVER

Celebrating another year during the Balunas Laboratory Avery Point BBQ.

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In comparison, Long Island Sound might seem a bit less exotic but UConn is only an hour away from Long Island Sound and boasts a state-of-the-art marine campus at Avery Point with several ocean-going vessels, a high-flow seawater laboratory, full scientific diving operations, and faculty, staff, and students committed to advancing marine sciences. We are fortunate to have these facilities at such close proximity, which has enabled several exciting lines of research and allows for all members of

my lab to experience on-site collection trips even if they do not dive. We are even able to collect right off the dock during the cold winter months in Connecticut. And, we celebrate the end of each year at Avery Point with a collection trip and lab barbeque!

We are hopeful that our diversity of collection locations will lead to both biological and chemical diversity and eventually to some exciting medicinally relevant discoveries. Check out our current progress at <http://homepages.uconn.edu/~mjb10021/>. ■



PHOTOS BY KIM DIVER AND A MICA GUIDE

Left: Coring a glacier. Right: Field sterilization of ice cores.

**Some dive locations are so astonishingly beautiful – carpets and shelves of living coral growing to the edge of a fathomless abyss – they impart breath-taking memories that last a lifetime.**

# Meet a New ASP Member

ASP is pleased to welcome many new members to the society this year. One of our new members for the summer of 2013 is Dr. Huzefa Raja, a postdoctoral researcher at the University of North Carolina (UNCG), Greensboro, North Carolina. Dr. Raja took the time to share his interests in fungi natural products and golf with us. We are pleased to become more acquainted with him.

By Mr. Dan Kulakowski

## How did you hear about the ASP?

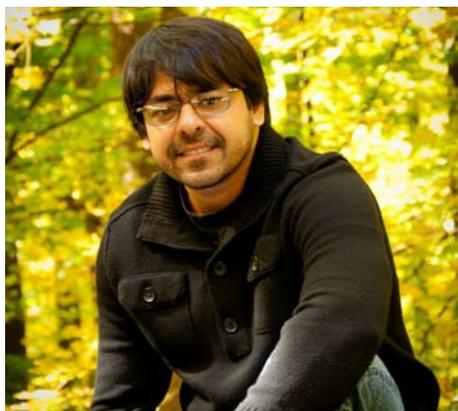
I first heard about ASP while I was working with ASP member Dr. Jim Gloer at the University of Iowa, Iowa City, Iowa, on a project focused on isolation of natural products from freshwater ascomycetes, a group of fungi that live and reproduce in freshwater habitats. At that time, I was a graduate student at the University of Illinois Urbana-Champaign (UIUC), Urbana, Illinois, working on my Ph.D. with Drs. Carol Shearer and Andrew Miller.

## Why did you join ASP?

I joined ASP after I attended a couple of ASP meetings (San Diego, 2011 and New York, 2012). In the past 2 years, I have been a postdoc with ASP member Dr. Nicholas Oberlies who works with natural products from fungi at the University of North Carolina at Greensboro, North Carolina (UNCG). It was this collaboration that continued to foster my interests in the potential that fungi have in the field of natural products. To learn more about the chemistry research carried out with fungi and make new contacts in this area of research, I decided to join the ASP. Not to mention getting discounted rates during meetings.

## Do you belong to any other scientific societies?

Since 2001, I have been a member of the Mycological Society of America (MSA), which is a society that is dedicated to advancing the science of mycology; this is the study of fungi of all kinds including mushrooms, molds, truffles, yeasts, lichens, plant pathogens, and medically important fungi. I would strongly encourage ASP members working with fungi to consider joining the MSA. It will help them learn about fungi and network with mycologists.



Dr. Raja

SID VERMA

## What are your current research interests in pharmacognosy?

My main interests are in isolating novel strains of fungi for extraction and isolation of bioactive compounds. I am continuing work on bioactive compounds from freshwater fungi, as there is great potential for finding new and interesting chemistry from this poorly studied ecological group of fungi. I am currently focusing on isolating fungi from different habitats (aquatic versus terrestrial) and ecological groups (saprobes versus endosymbionts) and describing novel taxa using molecular phylogenetic tools in order to enrich the search for novel bioactive molecules and to better understand the chemical mycology of fungi.

## What is your scientific background?

I earned my bachelors and masters degrees in Plant Biology (Botany) from the University of Madras in Chennai, Tami Nadu, India. Since my masters degree was mainly focused on course work, I wanted to gain research experience working in the laboratory. In order to do that, I joined the M.Phil. program at Vivekananda College, University of Madras. During my M.Phil., I worked on fungal endophytes with Dr. T.S. Sury, who was instrumental in introducing me to the fascinating world of fungi. After my M.Phil., I decided to apply to graduate school in

the United States and was accepted in the laboratory of Dr. Carol A. Shearer, where I worked on freshwater ascomycetes. For my Ph.D., I developed and addressed questions concerning the taxonomy, habitat and substrate distribution patterns of freshwater fungi along a latitudinal gradient in the Florida peninsula. After my Ph.D., I continued to work at UIUC for about 3 years as a postdoc with both Dr. Shearer and Dr. Andrew Miller (Illinois Natural History Survey). This was my first postdoc and it was focused on collecting and describing freshwater fungi along an altitudinal gradient from the Peruvian Amazon to the Andes.

## What would you like to achieve through your membership?

I am interested in learning about the state of the art research in natural products with fungi; networking for future research positions and opportunities; meeting and making new colleagues and, of course, sharing fungal natural product discoveries with fellow members. I hope that someday in the future there can be a joint meeting of the MSA and the ASP. I think there is a lot the mycologist can learn from the natural products chemists and vice versa.

## What do you like doing in your spare time?

I used to watch and play cricket back in India. More, recently, a good friend Scott Jarmusch (an aspiring analytical chemist) introduced me to the game of golf and I am hooked on to it. So, I like to play golf when I get a chance. I also like watching movies and hanging out with friends.

## What are you currently reading?

Nothing currently, but I am thinking about reading *The Hobbit* by J.R.R. Tolkien. I love the song, "Far Over the Misty Mountains Cold," from the movie.



# New Members of ASP 2013

ASP would like to welcome new members. The Society's main objectives are to provide the opportunity for association among the workers in pharmacognosy and related sciences, to provide opportunities for presentation of research achievements, and to promote the publication of meritorious research. New members include 14 domestic full members, 7 international members, and 15 associate members. We look forward to meeting you and learning more about you and your work.

## ACTIVE MEMBERS

Professor William  
Gerard Bornmann  
Houston, Texas

Dr. Brian Carroll  
Gig Harbor, Washington

Dr. Chia-Chuan Chang  
Taipei, Taiwan

Dr. Gregory A. Ellis  
Madison, Wisconsin

Mrs. Laila S. Espindola  
Brasília, Brazil

Dr. Eduardo Esquenazi  
San Diego, California

Dr. Joseph L. Evans  
Saint Louis, Missouri

Dr. Jose Antonio  
Guerrero-Analco  
Ottawa, Ontario, Canada

Dr. Jon C. Henrikson  
Minneapolis, Minnesota

Amninder Kaur  
Greensboro, North Carolina

Professor Sami Khalid  
Omdurman, Sudan

Dr. Takaaki Kubota  
Sapporo, Japan

Dr. Jong Hwan Kwak  
Gyeonggi-do, Republic of Korea

Dr. Hsiao-Ching Lin  
Los Angeles, California

Wendy Luo  
Deerfield, Illinois

Dr. Venkat R. Macherla  
San Diego, California

Dr. Joe-Ann H. McCoy  
Asheville, North Carolina

Susan J. Murch  
Kelowna, British Columbia,  
Canada

Dr. Huzefa A. Raja  
Greensboro, North Carolina

Mr. Arun Rajgopal  
Ada, Michigan

Dr. Amira S. Wanas  
University, Mississippi

## ASSOCIATE MEMBERS

Adedoyin D. Abraham  
Aurora, Colorado

Ms. Aline Isis Porto Ventura  
Armelini  
Jundiá, Brazil

Ms. Tamam M. El-Elimat  
Greensboro, North Carolina

Maryam Elfeki  
Chicago, Illinois

Ms. Hailey A. Houson  
Valley Center, California

Mr. Seong-Hwan Kim  
Seoul, Republic of Korea

Ms. Omodeboyin  
Ayodamope Lawal  
Ibadan, Nigeria

Mr. Jie Li  
Columbus, Ohio

Mr. Joonseok Oh  
University, Mississippi

Ms. Noemi Daquioag Paguigan  
Greensboro, North Carolina

Miss Mayuramas Sang-ngern  
Hilo, Hawaii

Ms. Karina M. Szymulanska-  
Ramamurthy  
Chicago, Illinois

Ms. Christina E. Turi  
Kelowna, British Columbia,  
Canada

Mrs. Fidelia Ijeoma Uche  
Stoke-on-Trent, United Kingdom

Matthew Wright  
Lebanon, Tennessee

# In Memoriam: Dr. Andrew Marston



Dr. Kurt Hostettmann

**A**SP member, Dr. Andrew Marston, died on March 26, 2013 at the age of 59. It is very sad for a retired professor to write an obituary for a younger colleague and friend.

Andrew studied chemistry at the University College, London University, and obtained his B.S. degree in 1975. I met him for the first time that same year when he joined the University of Neuchâtel, Switzerland, as a British Council Award recipient. He was involved in the phytochemistry of gentians and published his first paper with me on flavonoids of *Gentiana pyrenaica*. After Neuchâtel, Andrew went back to England to conduct his doctoral studies at Liverpool University in the field of peptide synthesis where he received his Ph.D., followed by a postdoctoral work at the German Cancer Research Centre, Heidelberg, Germany, from 1979 to 1983.

ASP President Dr. David Newman told the *Newsletter*, "Dr. Andrew Marston will definitely be missed both as a chemist and as a gentleman. I met him quite a few years ago, as we graduated from the same university chemistry department, though in my case, quite a few years earlier, and agree



Dr. Marston in Botswana, 2008 and, while fishing there in the same year.

with everything that Dr. Hostettmann has so eloquently expressed."

In October of 1983, he joined the Institute of Pharmacognosy and Phytochemistry, University of Lausanne, Switzerland, to work with me on a Swiss National Science Foundation research project for one year. Dr. Marston was just a brilliant young scientist, and the initially planned one year stay became a stay of 26 years!

Andrew was involved in the isolation of biologically active compounds from plants used in traditional medicine and in the application of new chromatographic techniques for the separation and isolation of plant constituents. He has done pioneering work in the field of centrifugal partition chromatography which resulted in the publication of nice research papers and a couple of review articles.

He also achieved original work in the development of enzyme inhibition tests on thin layer chromatography (TLC) plates (TLC bioautography) which are useful for the search of acetylcholinesterase inhibitors from plants (treatment of Alzheimer's disease). For his important contribution in various fields of phytochemistry, Andrew received prestigious Rhône – Poulenc Rorer Award of the Phytochemical Society of Europe (PSE) in 1994. He was a member of the ASP Committee from 1996 to 2000. Together, Andrew and I published a book on preparative chromatography techniques

which was translated in Japanese, Chinese, Indonesian, Farsi, and Spanish. In 1994, my Institute was transferred from Lausanne to Geneva University, where Andrew held the position of *Maître d'enseignement et de recherche* (which corresponds to Senior Lecturer) until my retirement in 2009. When I retired, Andrew decided to leave Geneva University and became Professor of Chemistry at the University of the Free State, Bloemfontein, South Africa. In his new job, he was conducting phytochemical investigation on indigenous plants and was teaching organic chemistry and natural product chemistry.

Andrew was an outstanding phytochemist, and his work resulted in the publication of more than 150 research papers and 35 review articles and chapters in books. Some of his papers were published in *Journal of Natural Products*. He was also a referee for this journal. He attended a couple of ASP Annual Meetings and presented lectures and oral communications in numerous other international symposia. He was teaching in workshops held in Uruguay, Panama, Mexico, Peru, Brazil, Thailand, China, Indonesia, Zimbabwe, Botswana and Mali. We visited all these countries and many other more together. This created strong ties and friendship. Andrew was, without any doubts, my closest friend as we worked together for a total of 27 years and shared many beautiful things together. Life can be cruel; around two years ago, Andrew lost his mother, his father, and his wife within four months. He passed away on March 26, 2013, in Bloemfontein, after a surgery of the brain to control his Parkinson's disease resulted in cerebral bleedings. He was born in Africa (Northern Rhodesia which became Zambia after independence in 1964) and died in Africa. He had always special links to this continent and was a friend of Africa. The scientific community is losing a great phytochemist. Everybody will miss Andrew because he was always modest, friendly and helpful – a real British gentleman! I shall miss a friend whom I considered my younger brother. My thoughts go to his two sons Mark and Jonathan, and to his brother Keith. ■

# Conference Calendar

The *Newsletter* is pleased to announce the following upcoming conferences and meetings. The events portrayed here reflect what listings and notices the *Newsletter* has specifically received. For a more extensive calendar, please visit the ASP website at [www.phcog.org](http://www.phcog.org). If you have a conference or event you would like mentioned, please send us relevant information, including any graphics or appropriate fliers, at [asp.newsletter@lehman.cuny.edu](mailto:asp.newsletter@lehman.cuny.edu).

## **ASP 54<sup>th</sup> Annual Meeting**

St. Louis, Missouri

**July 13-18, 2013**

[www.pharmacognosy.us/calendar-of-events/future-asp-meetings/](http://www.pharmacognosy.us/calendar-of-events/future-asp-meetings/)

## **Association of Official Analytical Chemists: 127<sup>th</sup> Annual Meeting & Exposition**

Chicago, Illinois

**August 25-28, 2013**

<http://www.aoac.org/>

## **Gordon Research Conference: Natural Products**

Andover, New Hampshire

**July 28-August 2, 2013**

<http://www.grc.org/programs.aspx?year=2013&program=natprod>

## **61<sup>st</sup> International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA)**

Muenster, Germany

**September 1-5, 2013**

[www.ga2013.org/](http://www.ga2013.org/)

## **52<sup>nd</sup> Annual Meeting of the Phytochemical Society of North America**

Corvallis, Oregon

**August 3-7, 2013**

<http://psna2013.com/>

## **1<sup>st</sup> European Conference on Natural Products**

Frankfurt, Germany

**September 22-25, 2013**

<http://events.dechema.de/events/en/Events/1st+European+Conference+on+Natural+Products.html>





## Brief News From Washington

By Dr. Georgia Perdue

- Most of you already know that **cuts due to the “sequester” are in place for National Institutes of Health (NIH). It took a 5% cut, “\$1.5 billion cut per year as long as sequestration lasts,”** a Hill staffer told me. According to a not too happy National Cancer Institute (NCI) director Dr. Harold Varmus, speaking at the March Board of Scientific Advisors (BSA) meeting, “...each institute has been given latitude how to handle these cuts. Aims include: minimize the damage and **keep the numbers for grants...share the pain across everything ... protect our critical investment – new investigators, as much as possible.** The success rate for grants is 14% and **we will try to maintain as high a success rate as possible....**Sequester slows our work across a wide variety of work and affects our integrity and the successful careers of scientists. It discourages talented students, undercuts investments, and undermines leadership in science.... **Over the next couple of years we will focus to maintain opportunities for those we have trained to succeed....**We are being very careful how we spend the money; we will defer travel, conferences, and anything else [that can be deferred]....”
- In early June, NIH issued a statement with **additional information about the impact of the “sequester:”** 700 fewer grants overall will awarded compared to FY 2012; a 4.7% decrease, generally, in non-competing grants; all areas of science will be affected.
- Key **changes for SBIR/STTR** have been issued by NIH (see [www.sbir@od.nih.gov](http://www.sbir@od.nih.gov) )
- **Funding Opportunity: The National Center for Complementary and Alternative Medicine (NCCAM) and the National Institute of General Medical Sciences (NIGMS) have issued an RFA, Genomes to Natural Products.** (RFA-GM-14-002). The RFA was posted on March 1, 2013, and the earliest submission date is June 17, 2013. The application due date is July 17, 2013.
- It seems that **natural products research is very popular in Europe.** An exciting new cooperative research effort, **BioXplore**, was awarded a \$2 million euro grant from the European Union. Other partners include the **Hadassah Academic College in Jerusalem, Israel, the Biodiversity and Environmental Research Center in Nablus, Israel, the Leitat Technology Center in Barcelona, Spain, and the Hellenic Regional Development Center, Athens, Greece.** Consultants from **Rutgers University, New Brunswick, New Jersey, and North Carolina State University, Raleigh, North Carolina,** have agreed to participate, as have Israeli botanists. Many of you may know the president of Hadassah Academic College, **Dr. Bertold Fridlender**, who received his Ph.D. in medical microbiology from the University of California (UCLA), Los Angeles, California, and carried out botanical research at Rutgers University.
- At the June **NCCAM Advisory Council Meeting, a new concept for Botanical Research Centers was approved.** The concept is the combined effort of the Office of Dietary Supplements (ODS) and NCCAM, based on input from an “Expert Panel” which provided ideas to **strengthen ongoing botanical research.** Collaborative efforts and coordination with government agencies, academia and the private sector will be required. ODS and NCCAM hope to support “cutting-edge, interdisciplinary and multi-component research efforts.” Stay tuned.
- Last February, a NCCAM Council member raised the possibility of coming up with a **better defined name for NCCAM.** A small working group was put together and discussed the challenge by teleconference. While nothing was decided, the challenge remains.  
*continued on page 26*

**Over the next couple of years we will focus to maintain opportunities for those we’ve trained to succeed**

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ing definitive has been decided, some of the concerns about the name include: its divisive nature as it implies an opposing view to conventional medicine; implications that it advocates CAM rather than the research the center conducts regarding the usefulness and safety of CAM products, and that NCCAM's research should be emphasized more. This discussion has just begun.\* Stay tuned.

- April 25, World Malaria Day, the National Institute of Allergy and Infectious Diseases (NIAID) provided an update of **exciting research results: the discovery of ELQ-300, a quinoline derivative which kills the malaria parasite in each of its three lifecycle stages. ELQ-300 is now proceeding to preclinical trials.** The drug was discovered collaboratively by researchers from three institutions: Oregon Health and Science University, Portland, Oregon, Drexel University, Philadelphia, Pennsylvania, University of South Florida, Tampa, Florida, and Monash University, Clayton, Australia. Funding was provided by Medicines for Malaria Venture, a drug discovery venture group, and NIAID, NIGMS, and the Wellcome Trust. Detailed research results were published in *Science Translational Medicine*, March 20, 2013. Another quinolone derivative, the NITD609 antimalarial drug, is in Phase II clinical trials (see December 2010 column). **NIAID director Dr. Anthony Fauci described all findings as “terrific stuff coming out of malaria research,”** at his early June Advisory Council meeting.
- **A breakthrough for the anti-malarial drug artemisinin: Dr. Jay Keasling**, University of California, Berkeley, California, succeeded in producing a **semi-synthetic version of artemisinin.** The French pharmaceutical company Sanofi will produce this new compound. Dr. Keasling's funding was provided by the Bill and Melinda Gates Foundation, the international nonprofit organization PATH and One World Health.
- **NIAID scientists reported in early May that they have “identified a gene that helps malaria-causing parasites to elude the mosquito immune system, allowing the microbes to transmit efficiently to people [when they are bitten].”** The scientists are looking into whether **“antibodies against the gene can block its function and allow the mosquito immune system to recognize and eliminate malaria-causing parasites.”** (see *Science* May 9, 2013 online issue). Stay tuned.
- A report released in April by the Infectious Diseases Society of America (IDSA), highlights a serious problem—**“antibiotic shortage.”** Only four “big pharma” companies are still working on antibiotics. While many scientists have commented on this recently, according to this report, **this shortage of antibiotics is very**

**“worrisome” because treatments for gram-negative bacteria and gram-negative “superbugs” are lacking.** Since 1998, only four antibiotics have been discovered by the world's “biggest drug companies.” The IDSA report attributes this problem to the near insurmountable “regulatory hurdles” imposed by FDA and the fact that companies do not make nearly the profits on antibiotics as they do with other drugs. Stay tuned.

- **The reliability of published results of NIH-funded research is still plaguing NIH** (see September 2012 column). **NIH Director Dr. Francis Collins has formed a trans-NIH committee because NIH is very serious about this matter and wants to raise awareness of the problem.** At the March NCI BSA meeting, Dr. Harold Varmus noted that this has even reached the Hill: **Senator Richard Shelby (R-AL) wants to know from Dr. Collins why it is difficult to replicate published research.** Dr. Varmus once again summarized the results of a September 2012 workshop at which there was **“unanimous agreement that there is a problem.”** **“Many published results are misleading or wrong.”** A sample of the remedies discussed at the workshop include, “first, do no harm; mentorship and training needed; improve practice and ethical standards.” Questions asked include, is this a new problem? **Is the incidence rising?** Are there **different criteria for academia and industry?** Are the “phenomena real”? “[is it] intentional or sloppy work due to inadequate research training?” Who is responsible, investigators... institutions... grantees... funders...? Some of the common characteristics of non-replicable data include: “inadequate numbers of samples of subjects; failure to validate reagents; substandard number of experiments....” There will be more workshops. Stay tuned. ■

*\*(Personal note. When I was publishing *Washington Insight*, a newsletter for natural products scientists, I was faced with similar questions by people on the Hill. At that time CAM was heavily in the spotlight as Senator Tom Harkin (D-IA) was pushing NIH to establish a CAM office. (The Senator has announced he will not seek re-election. Perhaps this will make a name change easier). It was assumed that my newsletter was related to CAM. It reached the point where I had to remove, “a newsletter for natural products scientists,” from the masthead. I did, however, succeed, in promoting pharmacognosy among members of Congress who actually used the term at some of the hearings!)*

# From the Archives: A Night at the Missouri Botanical Gardens

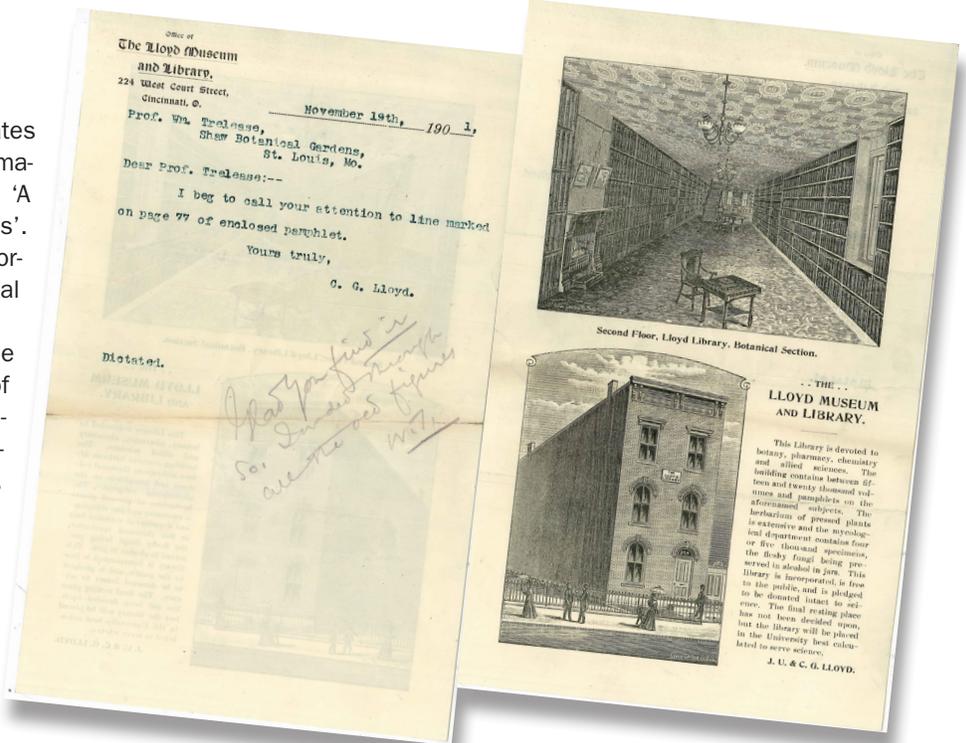
By Ms. Devhra BennettJones

**O**n Monday, July 15, 2013, the delegates of the 54<sup>th</sup> American Society of Pharmacognosy Annual Meeting are invited to 'A Night at the Missouri Botanical Gardens'. The gathering will offer ASP members the opportunity to appreciate a world renowned botanical research center.

When asked about the significance of the event, Dr. Peter Raven, President Emeritus of the Missouri Botanical Garden and George Engelmann Professor of Botany Emeritus at Washington University in St. Louis, Missouri, stated, "In an age of rapid extinction it is extremely important for pharmacognosists to integrate their efforts with institutions and individuals that are involved in plant research. The Missouri Botanical Garden is such an institution that values integrated research. Scientific research coordination is crucial as we are losing the plants and indigenous knowledge at a rapid pace."

In the spirit of Dr. Raven's advocacy, ASP, Missouri Botanical Garden, and the Lloyd Library, have a history of integrated teamwork in their devotion to botanical sciences. This is marked by the correspondence between the originator of the ASP's *Journal of Natural Products* (previously *Lloydia*) and one of the Lloyd Library founders, Mr. Curtis Gates Lloyd, and the Garden Director, (1889-1912), Dr. William Trelease. The Lloyd Library Archives document their correspondence over a 24-year period, beginning in 1896. Mr. Lloyd was an esteemed mycologist, a collector of mycological specimens, and authored numerous works on the subject. He and Dr. Trelease exchanged letters about various botanical topics. In 1896, Dr. Trelease conferred with Mr. Lloyd about his published notes on the 'West Indies'. Throughout the 1890s, Dr. Trelease kept Mr. Lloyd informed about the Garden's fungi resource acquisitions, such as their accession of the *Journal of Botany*, Volume 5, published in 1846, and his efforts to acquire a copy of the first edition of *Genera Plantarum*, published in 1737.

The botanical research cooperation between the Lloyd and the Garden was reciprocal. In 1899, Dr. Trelease requested photographs of Mr. Lloyd's illustrations from his *Mycological Notes*. Dr. Trelease assured him that the invoice for the photographs would be paid in a timely manner. The two scholars assisted each other with unique research resources prior to the conception of inter-library-loan. The Lloyd Library Archives holds records demonstrating that Dr. Trelease sent Mr. Lloyd journals which were punctually re-



turned to the Garden library. Since both men were responsible for the acquisitions of a botanical library, they conferred about how to classify such publications. In the age of the card catalog, they believed that it was important to insure that both botanists and biologists could find pertinent library resources. Their collaborative scholarly association continued into the 1920s when Mr. Trelease was a faculty member at the University of Illinois, Chicago, Illinois.

The integrative dimensions of the 54<sup>th</sup> ASP Annual Meeting is reflected in the conference program and the mission of the Missouri Botanical Garden. Dr. Mark O'Neil-Johnson, Vice President of Analytical Chemistry at Sequoia Sciences in St. Louis, Missouri, and Dr. Ray Cooper, Chief Science Officer of Phytoscience, Inc., serve as the Organizing Committee leaders.

O'Neil-Johnson remarked, "The garden is world renowned. It is among the top three in the world, in the same league as the Kew Botanical Garden and the New York Botanical Garden, in that they all engage in applied research. Their dedication to applied research is one of the many reasons for us to go there during the conference. We will have Dr. Peter Raven speak to us, too. He is a champion of applied research. We have a stellar line-up of speakers and we have a program that advances implementation. It is our goal to make it a natural-products-at-the-crossroads and looking-to-the future-market-of-botanicals program. *Planta Medica* is publishing the abstracts for us; this is one of the leading in-

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**The Missouri Botanical Garden is such an institution that values integrated research.**

## From the Archives: A Night at the Missouri Botanical Gardens

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ternational journals in the field of medicinal plants and natural products with a worldwide audience. “

The conference leaders are of the same mind in their quest to provide a comprehensively integrated program. Cooper noted, “With this conference we really are covering all of our bases and giving prominence to science, sustainability, and aspects of botanical taxonomy for the ASP members. We are hosting about 400 delegates and hope to have as many of them as possible join us for the evening at the garden. The evening at the garden is for all delegates to enjoy the exhibits and the garden. We also have the Missouri Botanical Garden’s President, Dr. Peter Wyse Jackson addressing the attendees. In addition to these notable scientists from the garden, Dr. Rainer Bussmann and Dr. Wendy Applequist of the garden’s William L. Brown Center will be chairing a session on botanical research with guests from the Royal Kew Botanical Gardens and the New York Botanical Gardens.”

The representation of the William L. Brown Center at the

54<sup>th</sup> Annual ASP Meeting symbolizes Dr. Raven’s call for an integrated approach to botanical research. Dr. Bussmann, Director and William L. Brown Curator for Economic Botany of the Center stated, “At the William L. Brown Center we have an institute for economic botany. There are only two of them in the western world. When the ASP members come to the Missouri Botanical Garden they will already have had the opportunity to hear Dr. Raven’s plenary talk. They can stroll through the gardens and see the plants that are of interest. The ASP is the largest professional organization related to the discovery of drugs from botanical compounds. Having the conference here is an opportunity to get the professional community to St. Louis to share the resources that we have.”

The night at the Missouri Botanical Garden will offer the ASP members not only the opportunity to see an exemplary and unique integrated botanical research operation, but also the pleasure of communing with colleagues in a scenic venue. ■

## UIC to Host Garden Walk and Memorial Lecture

*By Mr. Chris Shoemaker*

**T**he University of Illinois (UIC) at Chicago College of Pharmacy will host the 2013 Garden Walk and annual Alan Lesniewicz Memorial Lecture on Friday, August 23, 2013, to celebrate the first and only urban medicinal plant garden in the city of Chicago, Illinois.

The day will include a Garden Walk with information about medicinal plants and feature ASP Past President Dr. Barbara Timmermann delivering the Alan Lesniewicz Memorial Lecture entitled, “In Quest of Tomorrow’s Medicines from Native Plants of the Prairie.”

Named in memory of Dorothy Bradley Atkins, BS 1945, the medicinal plant garden was created in 1999 with a \$1 million gift from her husband, Dr. Robert Atkins. As the daughter of a pharmacist and a graduate of the UIC College of Pharmacy herself, Dorothy Bradley Atkins had a lifetime interest in pharmacognosy. Today, the garden serves as a resource for education and research at the UIC College of Pharmacy, as well as providing a quiet escape from the hustle and bustle of urban life.

Alan Lesniewicz, who suffered an untimely death in the early spring of 2008, was employed by the University of Illinois at Chicago for more than 16 years. His wife, Cherise A. Greski-Lesniewicz, worked for the University for more than 25 years. Both Alan and Cherise believed firmly in the power of medicinals and in the importance of educating the public about the benefits of taking natural approaches to solving medical problems. Mrs.



Atkins Medicinal Plant Garden, UIC.

Greski-Lesniewicz wanted to recognize Alan by a gift to the College in his name. ■

Those with questions can contact Mr. Shoemaker at: [cjshoema@uic.edu](mailto:cjshoema@uic.edu).

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## ASP Membership

### Full Membership

Full membership is open to any scientist interested in the study of natural products.

Current membership dues and Journal of Natural Products subscription rates can be found at [www.pharmacognosy.us](http://www.pharmacognosy.us).

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Associate membership is open to students of pharmacognosy and allied fields only. These members are not accorded voting privileges.

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Emeritus membership is open to retired members of the Society who maintained membership in the Society for at least five years.

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### Honorary Membership

Honorary members are selected by the Executive Committee of the American Society of Pharmacognosy on the basis of meritorious service to pharmacognosy.

### Present Honorary Members are:

Dr. David P. Carew, University of Iowa · Dr. John M. Cassidy, Oregon State University

Dr. Geoffrey A. Cordell, University of Illinois at Chicago

Dr. Gordon C. Cragg, National Institutes of Health · Dr. Harry H.S. Fong, University of Illinois at Chicago

Dr. William Keller, Nature's Sunshine Products, Inc. · Dr. A. Douglas Kinghorn, Ohio State University

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Dr. Hildebert Wagner, University of Munich · Dr. Mansukh Wani, Research Triangle Institute

Additional information about membership may be obtained by writing to the Treasurer of the Society:

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