



The American Society of Pharmacognosy

The ASP Newsletter
Volume 51, Issue 2



ASP 56th Annual Meeting: Natural Products Rising to the Top

By Dr. Amy Keller

This year's Annual Meeting will take place at the Copper Mountain Resort and Conference Center in Copper Mountain, Colorado, July 25-29, 2015. The meeting's theme, "Natural Products Rising to the Top," encompasses not only the ascending realm of natural products research, but the majestic setting of the meeting in Colorado's Rocky Mountains.

Symposium speakers include Drs. Jonathan Baell, Carole Bewley, Leslie Fischer, Paul Jensen, Will McClatchey, Daniel Romo, Derek Tan, John Tallarico, Peter Senter, Ben Shen, and Amy Wright. The diverse symposia represent a plethora of natural

products areas, from Recent Advances in Chemical Ecology to Natural Products and HIV.

The workshops being offered on Saturday, July 25, include "Peer Review at NIH: Grantsmanship and the Peer Review Process at NIH," presented by Dr. Dale Birkle Dreer, Chief of the Office of Scientific Review, National Center for Complementary and Integrative Health (NCCIH), "Advanced Analytical Technologies as Applied to Natural Products for Drug Discovery," presented by Mr. Mark O'Neil-Johnson, Vice

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Copper Mountain Resort and Conference Center in Copper Mountain, Colorado

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EDITOR'S CORNER



As the academic year has finished for many of us, summer is on our mind, and I hope many members will include the ASP Annual Meeting in Copper Mountain, Colorado, as part of their plans. Getting together to share scientific progress is one of the important functions of the Society, and Copper Mountain will offer an amazing array of speakers, poster sessions, workshops, and social events to enable us to learn more about the latest advances in natural products research, as well as interact more informally with our colleagues and friends. This issue of the *Newsletter* features a last article on the Annual Meeting, including important dates, and we are also including a list of local recommendations that you

may want to check out. I am looking forward to a great pharmacognosy meeting in the Rocky Mountains.

Also in this issue of the *Newsletter*, we continue our Fellows' series with ASP Fellow Dr. Bill Gerwick's take on the impact of limited federal funding on research in pharmacognosy in the United States. This thought-provoking article provides perspectives on the challenges for funding in our discipline at this time and notes that other countries are investing. ASP Tyler Prize recipient Dr. Ray Cooper writes about his perspectives on the future of pharmacognosy research and areas of potential growth for our society. Finally, ASP member Dr. Joe Chappell gives us an update on his attempts to create a white paper on natural products research in the United States, based on a meeting he and others initiated with NCCIH last month. These three articles together do a terrific job of helping us to consider how the future of pharmacognosy research could look in the United States in the next decade.

Like many of us, I was saddened by the death of past ASP President Dr. Lester Mitscher. Since we learned of his death just prior to going to press, we have included a brief notice in this issue of the *Newsletter* with comprehensive tribute planned for our Fall issue. We were also sorry to learn about the death of another pharmacognosist, Dr. Leonardus Kardono, who was a graduate student at the University of Illinois (UIC) at Chicago, Illinois. After returning to his home country of Indonesia, he continued a close collaboration with faculty at UIC.

Please be sure to look at our regular columns, including a fascinating look at the field work done in Panama by ASP member Dr. Kerry McPhail in "Pharmacognosy Field Notes." Dr. Dave Newman's "Hot Topics in Pharmacognosy" continues to make me think more expansively about natural products and even suggests that many so-called phytochemicals may be microbial in origin.

I hope you have a productive and restful summer. If you have suggestions for the *Newsletter*, please write or speak to me in person at the Annual Meeting in Colorado.

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

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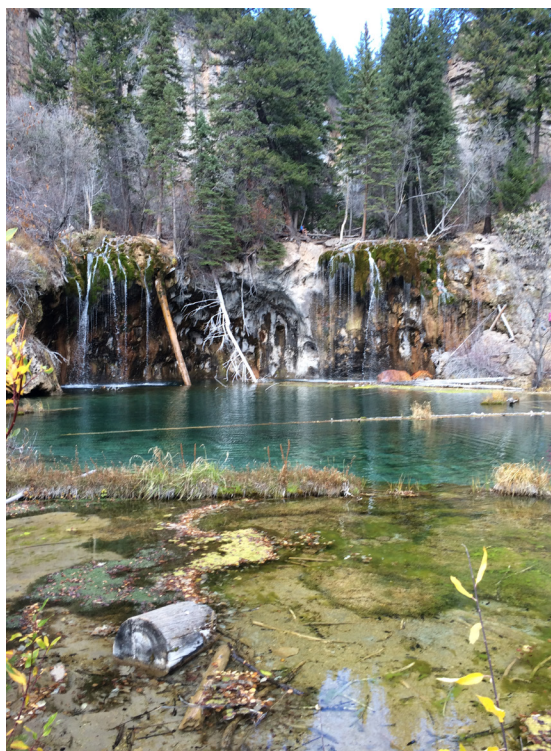
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President of Analytical Chemistry at Sequoia Sciences, Inc., "Entrepreneurship and Natural Products: Early Stage Opportunities for Your Discoveries," led by Dr. Cedric Pearce, Founder and CEO of Mycosynthetix and Dr. Nicholas Oberlies, Associate Professor at the University of North Carolina, Greensboro, North Carolina, "Bioassays and Pharmacology of Natural Products," presented by Dr. Babu Tekwani, Principal Scientist at the National Center for Natural Products Research at the School of Pharmacy, University of Mississippi, Oxford, Mississippi, and "Strategic Funding Priorities for Basic and Mechanistic Research," led by Dr. John Williamson, Branch Chief of Basic and Mechanistic Research in Complementary and Integrative Health Division of Extramural Research, NIH/NCCAM.

The excursion scheduled for Monday, July 27, will be an evening spent at the Soda Ridge Stables in Keystone, Colorado, 20 minutes by bus from the meeting venue, enjoying a barbeque dinner, music, a bonfire, and horseshoes and steer roping, among other ac-



Hanging Lake

MS. CHELSEA CONNON

tivities. On Tuesday, July 28, younger members are invited to ride a lift to Solitude Station at 11,375 feet above sea level, for lunch, views of the Gore and Ten Mile Mountain Ranges, and a guided hike along the Hallelujah Loop Trail. Following the hike, younger members will have the option of attending workshops focused on work-life balance, success in academia, industry, and entrepreneurship.

The Copper Mountain Resort and Conference Center is offering standard rooms to meeting attendees for \$125 per night plus tax, if reservations are made prior to July 2, 2015. This rate includes internet and use of the Copper Mountain Racquet and Athletic Club. Copper Mountain is 75 miles due west of Denver and accessed by Denver International Airport. Shuttle service (Summit Express) is available to conference attendees for \$54 one way. Parallel session speakers, award winners, speaker abstracts, logistical details, and other conference information are

available on the website: asp2015.org.

We look forward to seeing you in colorful Colorado! ■

THE SCIENTIFIC PROGRAM WILL INCLUDE THE FOLLOWING SYMPOSIA

- Natural Products and the Human Microbiota (July 27)
- Natural Products and HIV (July 26)
- Natural Products Total Synthesis (July 26)
- Natural Products in the Cosmetic Industry (July 27)
- Younger Members Research Spotlight (July 26)
- New Avenues in Botanical Research (July 27)
- Translational Studies of Natural Products (July 28)
- Microbial Metabolites and Bioactive Compounds From Plant Microbial Associates (July 29)
- Natural Products Anticancer Drug Lead Discovery (July 27)
- Beyond the Rule of 5 in the Design of Next-Generation Therapeutics (July 29)
- Enhancing Natural Product leads via Synthetic Manipulation (July 28)
- Natural Products in Neuroscience (July 26)
- Recent Advances in Marine Chemical Ecology (July 26)
- Novel Screening Strategies for the Identification of Therapeutic Lead Compounds (July 27)
- Chemical Transformations in the Biosynthesis of Natural Products (July 26)
- Microbial Interactions in Humans and Other Animals (July 27)
- Applications of Mass Spectrometry to Natural Products Drug Studies (July 28)

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ASP 56th Annual Meeting: Natural Products Rising to the Top

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Conference Center

WORKSHOP TOPICS AT THE YOUNGER MEMBER'S EVENT ON JULY 28

- “The Path to Becoming an Academic Professor,” led by Drs. Brian T. Murphy, University of Illinois at Chicago, Chicago, Illinois, and Sandra Loesgen, Oregon State University, Corvallis, Oregon
- “Getting the Most Out of What You Have: Funding and Running a Lab in Academia,” led by Dr. Kevin Tidgewell, Duquesne University, Pittsburgh, Pennsylvania
- “Triumphs and Challenges of Research at a Primarily Undergraduate Institution,” led by Dr. Amy Lane, University of North Florida, Jacksonville, Florida
- “Work-life Balance in Academia,” led by Dr. Marcy Balunas, University of Connecticut, Storrs, Connecticut
- “Managing a Full-time Career, Home, and Family,” led by Dr. Barbara Timmermann, University of Kansas, Lawrence, Kansas
- “From an Idea to a Start-up and Beyond,” led by Dr. Eduardo Esquenazi, Sirenas Marine Discovery, San Diego, California
- “Leading a Fulfilling Career and Balanced Life in Industry,” led by Dr. Jeremy Beau, Bayer CropScience, Research Triangle Park, North Carolina

IMPORTANT DATES

Hotel Reservation Deadline	July 2
Normal Registration Deadline	July 17
Workshops	July 25
Opening reception	July 25
Conference	July 26-29
Excursion to Keystone	July 26
Younger Members Social	July 27
Membership meeting	July 29
Closing banquet	July 29

Colorado Local Recommendations

By Dr. Amy Keller



Dr. Leah Villegas
Instructor, Pediatrics and Cardiovascular Pulmonary Research, University of Colorado Anschutz Medical Campus

What is your favorite summer activity in Denver or Boulder?

I enjoy going to concerts at Red Rocks.

What is your favorite summer activity in the mountains?

I highly recommend scenic drives, hiking trails, shopping and dining in Breckenridge.

Dr. Leah Villegas

DR. MYPHUONG LE

If you had one day free in Denver, Boulder and/or the regional mountain areas, how would you spend it?

If you can, try a picnic and hiking at Chautauqua Park in Boulder.

Can you recommend any fun places or activities in the Copper Mountain area (restaurants, hikes, etc.)?

I have never been to Copper Mountain, but I hear the Diggler (<http://www.visitcoppermountain.com/member-directory/resort-services/diggler>), scenic chairlift ride, and disc golf, are awesome.



Dr. Sylesh Venkataraman
Senior Director, Technology Development, Chromadex

What is your favorite summer activity in Denver or Boulder?

My favorite activities include hiking at Garden of the Gods and Pikes Peak (Colorado Springs area), and Rocky Mountain National Park (outside of Estes Park), and Chautauqua Park (Boulder).

Dr. Sylesh Venkataraman

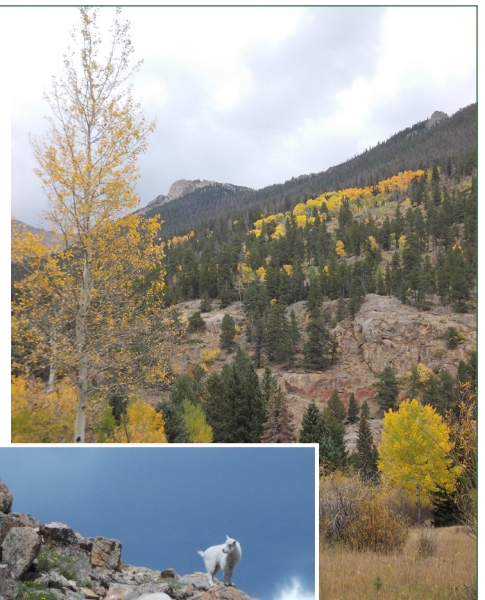
What is your favorite summer activity in the mountains?

I enjoy hiking and riding the Barr Train (Pikes Peak) and driving on the Trail Ridge Road in Rocky Mountain National Park.

If you had one day free in Denver, Boulder and/or the regional mountain areas, how would you spend it?

I would highly advise that you drive from Denver to Glenwood Springs and go on the Hanging Lake hike.

Editor's Note: Hanging Lake used to be the mountain area's best kept secret, but now has a designated exit and parking area off of eastbound I-70.



Clockwise: The view near the summit of Mt. Evans, Denver area; autumn in rocky Mountain National Park; Rocky Mountain bighorn sheep on Mt. Evans. PHOTOS: DR. AMY KELLER

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Colorado Local Recommendations

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Dr. Amy Keller

MS. LESLIE KNAUB

Dr. Amy Keller

Postdoctoral Fellow, Department of Endocrinology, Metabolism & Diabetes, University of Colorado Anschutz Medical Campus,

What is your favorite summer activity in Denver or Boulder?

I love attending summer music festivals downtown and the art walks in various locations throughout the city (Santa Fe and Tenynson are a few of the areas with art galleries and bustling culinary options, and the Larimer Square area hosts many outdoor music fests). I also love bike commuting on the Cherry Creek Bike Path. Start at Confluence Park, surrounded by ice cream, wine, coffee, and the REI flagship store, and make your way east into various Denver neighborhoods and sites. Also highly recommended is the Film On the Rocks series of movies at Red Rocks Amphitheater and the Sci-Fi Film series at the Denver Museum of Nature and Science.

What is your favorite summer activity in the mountains?

I really love hiking and mountain biking. During these activities, I enjoy aggravating my companions by taking photos and trying to identify every wildflower I see. There are lovely multi-use trails easily accessible all over the Rockies. The Summit County Recreational Pathway System (Recpath) connects several Summit County municipalities, and there is a lovely network of scenic single track trails around Aspen.”

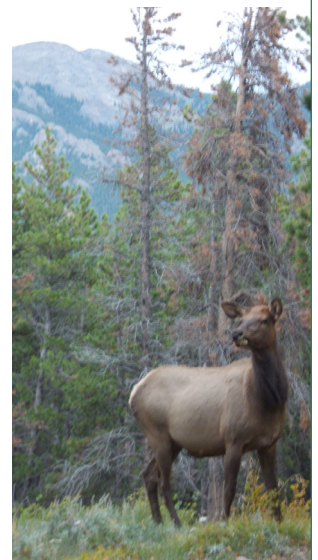
If you had one day free in Denver, Boulder and/or the regional mountain areas, how would you spend it?

Adventure 1: Summit Mount Evans, a Colorado Fourteener! Start at the parking lot at the beautiful Summit Lake and climb to the peak. Make sure to start early in the morning and be alert for thunderstorms and altitude sickness if coming from lower elevations (best to try this after acclimating to the area a few days). This hike offers unparalleled views of the Rockies and eastern plains and is a straightforward day trip from the Denver area.

Adventure 2: Rent a raft at Colorado River Rentals in Kremmling (\$40 or so, <http://coloradoriverrentals.com/>), near Winter Park, and paddle down the Colorado River. You will see gorgeous aquatic plants and wildlife, a bit of a riverside railroad, and have ample opportunity for cliff jumping off rocks and cliffs of various heights into the river.

Can you recommend any fun places or activities in the Copper Mountain area (restaurants, hikes, etc.)?

Why not try a local mountain brewery, such as Dillon Dam Brewery? It is located in the Dillon area about 10 miles east of Copper Mountain on I-70. ■



Clockwise: Summit Lake on Mt. Evans; View from Green Mountain (William F. Hayden) Park biking trails, Denver area; elk near Rocky Mountain National Park.

PHOTOS: DR. AMY KELLER

Journal of Natural Products Announces Schwarting and Beal Awards

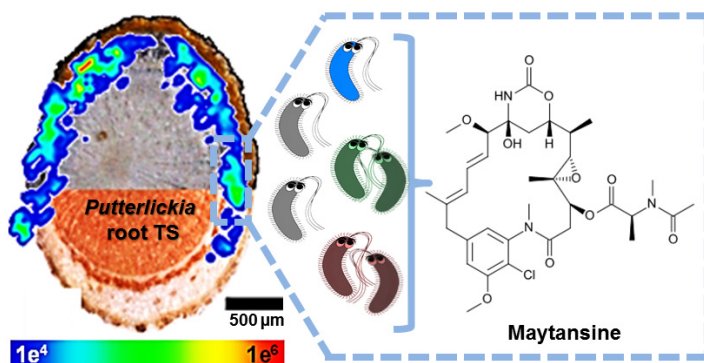
By Drs. Amy Keller and A. Douglas Kinghorn

The *Journal of Natural Products* announced the winners of the 2014 Arthur E. Schwarting Award and the 2014 Jack L. Beal Award. The 2014 Schwarting Award winning paper is "Endophytes are hidden producers of maytansine in *Putterlickia* roots," by authors Souvik Kusari, Marc Lamshöft, Parijat Kusari, Sebastian Gottfried, Sebastian Zühlke, Kathrin Louven, Ute Hentschel, Oliver Kayser, and Michael Spiteller (*J. Nat. Prod.* **2014**, *77*, 2577-2584). The 2014 Beal Award went to "Detailed analysis of (-)-palmyrolide A and some synthetic derivatives as voltage-gated sodium channel antagonists," from authors Suneet Mehrota, Brendan A. Duggan, Rodolfo Tello-Aburto, Tara D. Newar, William H. Gerwick, Thomas F. Murray, and William A. Maio (*J. Nat. Prod.* **2014**, *77*, 2553-2560).

Drs. Kusari and Spiteller, corresponding authors of the 2014 Schwarting Award publication, related, "We are deeply honored and thrilled to receive the coveted Arthur E. Schwarting Award 2014 for our work on the maytansine-producing endophytic communities of *Putterlickia* roots. In fact, we could hardly believe that out of all the excellent publications in the *Journal of Natural Products*, ours has been selected for this award. Microorganisms rarely exist in axenic forms in nature and endophytes are no exception. We started working on endophytic maytansine biosynthesis initially using axenic endophytic isolates, but it gradually became clear that maytansine biosynthesis is achieved by an endophytic microbial community. Our work is another example that exemplifies the fascinating network of chemical and molecular crosstalk between organisms coexisting symbiotically in nature. When working on endophytes, it is therefore useful to go beyond the "classic" microbiological approach of using only single organisms under monoculture conditions, and look for chemical communication strategies of endophytic "microbial consortia" harboring distinct ecological niches."

Corresponding author for the Beal Award publication, ASP member Dr. Maio, told the *Newsletter*, "I am deeply humbled by this national recognition of our work and thank the ASP award committee for honoring our manuscript with the Jack L. Beal Award. After synthesizing several stereoisomers of Palmyrolide A, we became interested in learning how the three dimensional shape of this molecule might affect its ability to regulate voltage-gated sodium channels. What resulted was truly a collaborative effort that integrated several disciplines, resulting in the prodigious amount of data seen in the publication. I want to especially thank all of my coauthors, notably the laboratories of my collaborators, Drs. William H. Gerwick and Thomas F. Murray. Without them, this manuscript could not have happened."

In 2001, the Foundation Board of the ASP



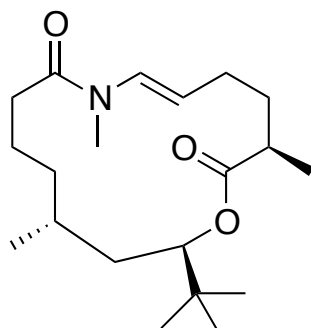
began a new initiative as a result of the Arthur E. Schwarting and Jack L. Beal Awards for best papers in the *Journal of Natural Products*. In this manner, two former distinguished editors of the journal are fondly remembered. The Schwarting Award is open to all papers published in the journal within a given year (either in print or electronically). In turn, the Beal Award is awarded to younger investigators, i.e., persons within 12 years of receiving their PhD degree or within 10 years of gaining their first professional appointment (e.g., Assistant Professor or an equivalent position in industry or government).

A two-tier process was used to determine the winners of the best papers published in the *Journal of Natural Products* in 2014, with Editors Daneel Ferreira, A. Douglas Kinghorn, Cedric J. Pearce, Philip J. Proteau, and Steven M. Swanson having nominated two papers each for the Schwarting Award and one each for the Beal Award. ASP President Phillip Crews then appointed an ad hoc committee [Drs. John Beutler, Chair, Shmuel Carmeli, and Mark Hamann] to make the final selections.

Drs. Kusari and Spiteller (joint corresponding authors) are housed in the Department of Chemistry and Chemical Biology, Technical University of Dortmund, Dortmund, Germany, and Dr. Maio is from the Department of Chemistry and Biochemistry,

New Mexico State University, Las Cruces, New Mexico. The corresponding authors of these papers will be invited to attend the Banquet at the 56th Annual Meeting American Society of Pharmacognosy to be held at Copper Mountain, Colorado, July 25-29, 2015, 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. Kusari, Spiteller, Maio and their co-authors! ■



Palmyrolide A

ASP Member Bachmann Featured on VICE

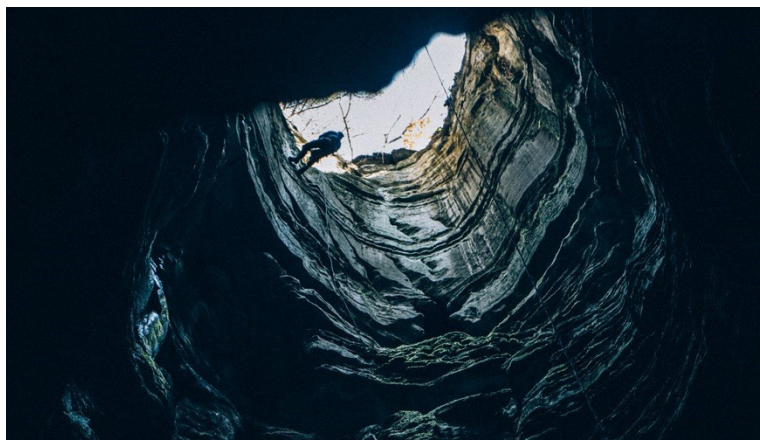
By Dr. Amy Keller

ASP member Dr. Brian Bachmann was featured on the investigative journalism television program VICE episode entitled “The Post Antibiotic World,” aired on April 17, 2015, on HBO. VICE presents newsworthy stories in a short, magazine format. Dr. Bachmann, Associate Professor of Chemistry at Vanderbilt University, Nashville, Tennessee, took a VICE reporter and camera crew into caves in search of novel antibiotics produced by bacteria.

Dr. Bachmann’s laboratory is centered on novel methods of detecting bioactive natural products from cave dwelling actinobacteria and myxobacteria. “Our current strategies are built upon the stimulation of secondary metabolism in producing organisms. The hypothesis behind this approach is that secondary metabolites exist to respond to environmental stimuli, be it competition, antibiosis, or nutrient availability, and that analysis of the corresponding change of metabolomic features in response to stimuli can be used to identify them within complex mixtures.”

One method prevalent in Dr. Bachmann’s laboratory is genome mining, or incorporating the knowledge of an organism’s genetic sequences for secondary compounds in natural product discovery. Dr. Bachmann explained, “We prioritize organisms for discovery based on their biosynthetic potential and isolate compounds inferred to have antibiotic activity and/or novel structures. Within the genome mining model, this is a ‘shoot first, ask questions later’ mode of discovery.” His laboratory is also interested in cave organisms’ chemical geomicrobiology, antibiotic resistance, and the chemical ecology of the bacteria in mixed culture.

Dr. Bachmann told the *Newsletter*, “It was a lot of fun to take the VICE team into a cave to share with them our program in drug discovery from cave microbes. Our brief segment involved two days of vertical caving, dropping four ropes into the 180 foot pit entrance on a freezing rainy day in November. It is always fun to take people into caves and talk about our research program. Talk about a captive audience! Shooting video in this environment is technically frightening, and sometimes I barely manage my panic on the way down. I find going up rope especially terrifying. But, it is also super fun, and for this reason, fortunately and unfortunately, one cave trip keeps us busy in the lab for at least a year. I tried to persuade the VICE folks that the really exciting trip was to the cave organism’s molecular scale, which is far more dramatic and challenging than the vertical work, but I had no luck with this. They did not bite.” ■



From the top down: Dr. Bachmann in the field; The view from below; Cave dwelling myxobacteria.

A Meeting of the Minds: Medicinal Plant Consortium Meets With NIH

By Dr. Joe Chappell

On May 19, 2015, the Medicinal Plant Consortium (MPC), a group representing a large array of academic, governmental, and private industry scientists across the globe, including ASP members, met with officials from the National Institutes of Health (NIH) at the Natcher Conference Center, NIH campus, in Bethesda, Maryland. The meeting served to better inform the National Center for Complementary and Integrative Health (NCCIH) and other NIH Centers and Institutes more fully about the emerging capabilities and research endeavors leading to new uses and applications of plants for human health now and in the future. The MPC presenters provided provocative windows into plants by elaborating on many of the outstanding questions, themes and opportunities currently being addressed in the plant science community.

For the MPC, Drs. Joe Noel, Salk Institute, La Jolla, California, Robin Buell, Michigan State University, East Lansing, Michigan, Basil Nikolau, Iowa State University, Ames, Iowa, and Dan Voytas, University of Minnesota, St. Paul, Minnesota, were the MPC presenters, while Drs. Toni Kutchan, Danforth Plant Science Center, St. Louis, Missouri, Elli Wurtzel, The City University of New York, New York, New York, Ed Eisenstein, University of Maryland, College Park, Maryland, and Joe Chappell, University of Kentucky, Lexington, Kentucky, served as MPC ambassadors. In attendance for NIH were Drs. Craig

Hopp, Program Director, Division of Extramural Research, NCCIH, John Williamson, Branch Chief, Basic and Mechanistic Research in Complementary and Integrative Health, Division of Extramural Research, NCCIH, Josephine P. Briggs, Director of NCCIH, and Barbara Gerratana, Program Director, Division of Pharmacology, Physiology, and Biological Chemistry, National Institute of General Medical Sciences (NIGMS), among others.

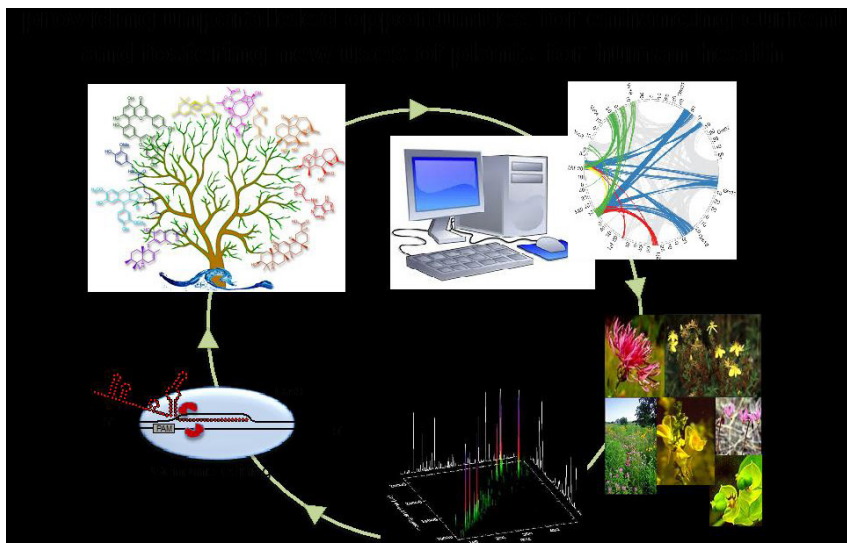
The Medicinal Plant Consortium (MPC) is a grassroots organization, spearheaded by many members of the ASP, associated with all facets of research concerning the advancement of plants and plant biology for human health. The initiative for the MPC was largely driven by requests from the NIH and especially the NCCIH for comments concerning the development of perspectives, aims and objects for their next 5-year strategic plan.

The MPC-NCCIH/NIH presentations were provided as a webinar with as many as 46 external participants logged in at any one time. The MPC has more than 90 signatures to its charter representing universities and research institutes, federal research facilities, and private research enterprises in 26 states supporting the development of emerging research capabilities and technologies for the utilization of plants for human health. Soon to be submitted to the NCCIH/NIH will be a follow-up white paper that highlights the opportunities and technologies discussed at the meeting on May 19, 2015. ■

The meeting can be viewed at:

<https://nih.webex.com/cmp0401isp13/webcomponents/docshow/docshow.do?isPluginInstalled=no&siteurl=nih&pluginDir=&nd=0.18173433291864283>

If you have questions, seek additional information or have comments about the MPC, please feel free to contact Dr. Chappell at the University of Kentucky (chappell@uky.edu) or Dr. Eisenstein at the University of Maryland (eisenste@umd.edu).



Reflections on Current Natural Products Issues

Natural products research in the United States of America is not as strong as it was 10 years ago. Pharma has moved away from natural product drug discovery. Scientists with skills in natural products are not finding many tenured faculty positions. Membership in ASP has decreased

By Dr. Ray Cooper

In the latter half of the 20th century, natural products research was reaching its zenith. The investigation of complex natural molecules from microbial, marine and terrestrial sources continued unabated. The pharmaceutical industry, in particular, had a “love fest” with natural products’ structures and sought chemical leads targeted as anti-microbials, anti-fungals, and anti-cancer drugs, leading to a long list of remarkable modern discoveries by academe and industry over many years.

However, as researchers in these drug discovery programs soon realized, eventually the leads dried up with the increased desire for receptor-based assays and the drive toward molecular biology. The research focus and direction changed from searching for leads towards *in silico* design and combinatorial chemistry. Natural products’ lead discovery programs in the pharmaceutical industry were disbanded. Furthermore, we are not funding training of researchers in academe to the same levels. Alas, the talent and expertise previously available to uncover remarkable structures, ‘mine’ the treasures of natural products isolation, and determine complex structures from complex mixtures, is dwindling.

However, natural products training and knowledge can be applied to many other scientific disciplines. Figure 1 shows many key areas populated by scientists

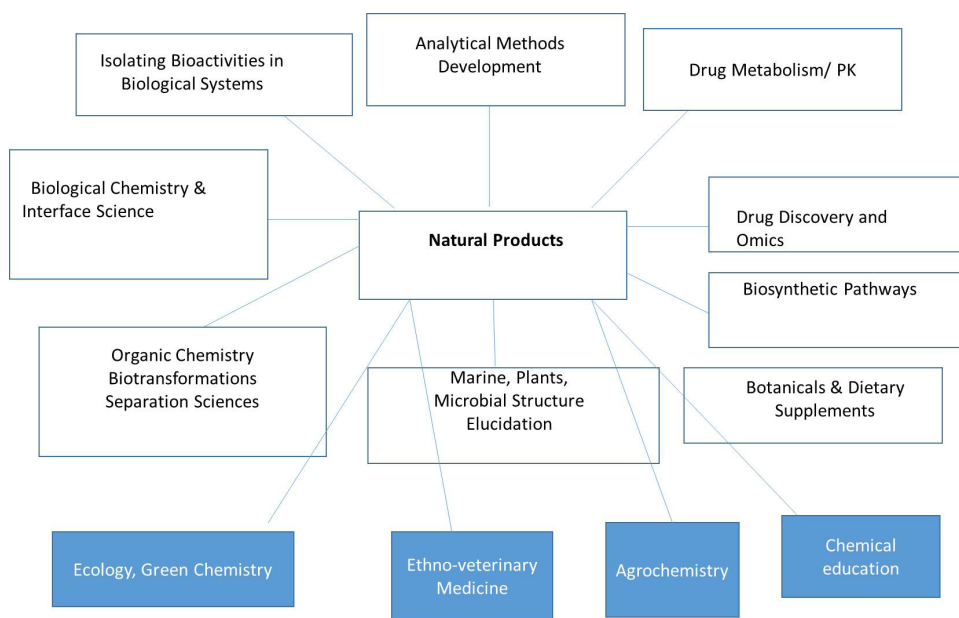


Figure 1: Examples of where the training and expertise in natural products chemistry can be successfully applied to other scientific disciplines.

DR. COOPER

originally trained in natural products and illustrates their impact on many other disciplines. There is a lot of interest, not only from the pharmaceutical industry, but also from the botanical supplement and bioalgal industry. Additionally, the technology taught for separation of natural products is applicable to analytical chemistry. Many students studying natural products will benefit if they apply for analytical, quality

assurance, metabolism, and pharmacokinetics work in the chemical, agrochemical and pharmaceutical industries. Surely, the ASP can be an umbrella organization to attract and retain these resources. Furthermore, we are witnessing some remarkable advances in genomic approaches (genomic mining, metagenomics, etc.), which may hold the key to future natural products and drug discovery research.

Resurgence of consumer interest requires a need for better science in botanical preparations.

A majority of the world still relies heavily on natural products, such as herbal remedies, for their primary health care. In fact, over the past several decades, literature (both scientific and popular) reflects an increased interest in natural products by the general public and has helped fuel a greater scientific awareness of drugs from nature and botanical medicine. The increasing movement of people across countries has

been accompanied by movement of their respective traditional medicines. There is the movement of Western medicine to developing countries and a flow of traditional medicines from China, among other examples.

This renewed interest in traditional herbal medicines has also contributed to a resurgence of interest in Western herbal medicine (and natural products), particularly in the United States and Europe, and

a desire for more chemical, safety, and efficacy information. There are the challenges of conducting sound scientific studies of botanicals, including sourcing and preparation of the products and understanding the types of scientific inquiry that will advance this field. Many challenges to the dietary supplement industry exist in order to improve the quality of botanical products

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Reflections on Current Natural Products Issues

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and to increase the industry's support of product safety and efficacy data. Thus, the role of trained natural products chemists, whether from marine or plant sciences, in

furthering the quality of botanical preparations and the quality of clinical research is evident throughout. Scientific leadership and high-quality scientific research are re-

quired to achieve higher-quality preclinical and clinical studies of herbal preparations and better-quality herbal products. The ASP can provide the platform for such activities.

Research in China is booming. Gesellschaft für Arzneipflanzen und Naturstoff Forschung (GA) is holding its first joint meeting in China in 2017. China is training large numbers of natural product chemists.

As Western drug companies eye traditional Chinese medicine for new products, China hopes to utilize its history of experimentation and rigorous documentation to compete in the global pharmaceuticals market.¹ China is spending billions to turn its traditional remedies into drugs and topple Big Pharma. For much of the past 300 years, China has never really cared whether Europeans or North Americans approved of its medical systems. China is now looking to take over an important and lucrative industry that has, to date, been centered in the West and supported by trained natural products' scientists. ASP Fellow Dr. William Gerwick recently wrote an informative article addressing the explosive growth of natural products in China and the potential for increasing the United States-China relationships.²

In China, The Dalian Institute of Chemical Physics (DICP) has initiated the 15-year Herbalome Project. This project aims to isolate every compound contained in all the medicinal herbs in the Chinese healing tradition and to utilize modern pharmaceutical practices to turn these plants into more efficient and marketable drugs. The Herbalome Project has a team of about 20 scientists investigating over 10,000

herbs in the traditional Chinese medicine (TCM) canon where the scientists analyze 500 samples every day. They have already started on almost 750,000 compounds.

China's interest in pharmaceutical R&D is part of a larger global movement where countries like India, Brazil and China, have significantly increased their production of vaccines and other medical therapeutics. A recent study in *The New England Journal of Medicine* estimated that China devoted \$160 billion to biomedical R&D in 2012 compared with \$131 billion that the United States spent the same year.³ From 2007 to 2012, China has increased spending in biomedicine research by about 33 percent every year.³

A reflection that the funding and training may be shifting to Asia is suggested by GA's joint international meeting in China in 2017. The ASP cannot stand idly by. We may want to consider reaching out to other Societies, particularly in the United States. We may wish to consider to broaden our base with those related to natural products, to be more inclusive of those working in less traditional areas of natural products, and also consider stronger ties and joint meetings with our global colleagues in South America (Brazil and Mexico), and Asia (e.g., China,

Korea and Japan), as well as maintaining strong ties with our friends in the GA.

Lastly, while globalization of medicine has typically been thought of as being the movement of Western medicine to developing countries, there is now a significant discussion of the "globalization of TCM" and how to improve the quality of Chinese medicine products as well as research their effectiveness. This is particularly relevant given the establishment of TCM programs and practitioners around the world. The challenges of conducting sound scientific studies of botanicals, from the sourcing of appropriate products to details on the preparation of the products, will require large numbers of trained natural products scientists.

In conclusion, as we consider a possible new name for the Society, perhaps it is time also to consider the need for strong education and an outreach campaign. Many are concerned that it is a complicated issue. Yet it may be time to reach out to a much broader canvas in three ways: to have a stronger presence in international meetings, to represent a broader base, and to have a stronger leading voice in the issues germane to our membership. ■

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ASP Fellows: Financial Support for the Natural Products Sciences

Dr. William Gerwick

Imagine that you have developed an incredible new strategy for discovering highly bioactive, structurally novel natural products. Now you have put it into practice, and it works! You have found the molecule of a lifetime! But then you have to tell your postdoctoral researcher to find another job, your student to spend their time as a teaching assistant (TA), and you pick up extra classes to cover your summer salary. Sadly, this has become the new reality for many in the natural products sciences. However, there is reason for fresh hope; a broad coalition is developing to reverse the downward trend in research funding, and the time is pivotal for all of us to contribute to this rising tide of support for research funding.

While there can be no argument of the enormous role science and technology has had in the development of the extraordinary economic engine we enjoy in the United States, it will be even more critical in the future, especially with the emergence of an increasingly technology and knowledge-driven world economy. Funding of scientific research in the US has trended steeply downward over the last 12 years, and this is especially true if one considers that research costs have inflated at almost double the general inflation rate over this period. Private sector funding of academic research in the US has declined as well (Figure 1).

A downward spiral in our treasured scientific community has both short and long-term consequences to our scientific infrastructure, our security as it relates to our capacity to respond to changing conditions and new needs, and our long-term economic prospects. And while there is a small uptick in federal budgets for research in 2015, and reason to hope for significantly increased funding in the future (see the final paragraph of this essay), it is nevertheless a critical moment in time that we, as a community, communicate broadly and persuasively the importance of public funding of research in the natural products sciences. Thus, as a member and Fellow of the American Society of Pharmacognosy, I urge each of you to take an active role in spreading this message.

As chronicled in typical scholarly fashion by National Institutes of Health (NIH) senior scientists and ASP mem-

bers, Drs. David Newman and Gordon Cragg, the value of natural products to our current spectrum of useful pharmaceuticals is undeniable.¹ Roughly 42% of all drugs are natural products themselves or derivatives that have improved pharmaceutical properties over the original natural product. Another 28% are drugs that imbed or derive inspiration from a structural feature first observed in a natural product, known as a 'pharmacophore.' Hence, in some sense, nearly 70% of all of our current medications derive or are inspired by natural products. Examples include Taxol®, a life-saving anticancer medication deriving from the Pacific yew tree which generates some \$3 billion a year in sales; the antibiotic daptomycin, one of the newest agents in our arsenal to combat skin infections, with sales over \$1 billion per year, and artemisinin, a new and highly effective anti-malarial drug deriving from a Chinese traditional medicine.

Our modern agriculture has also benefited enormously by pioneering natural products investigations and have given such useful molecules as the environmentally benign insecticides known as 'spinosads,' inspired herbicides based on the tripeptide bialaphos, and an anti-fungal.² These medications and agrochemicals improve human health, save lives, and contribute to the economic engine of our society; certainly, it would seem self-evident that it is in our best interest to continue to support the infrastructure that has spawned these important biomedical advances. Indeed, it is the expectation of the US populace that improved medications will be available and economically accessible to combat health conditions currently untreated, as well as to have answers for newly emergent diseases. Nevertheless, our society remains in great need of new and more effective treatments for diverse cognitive disorders, the neurosciences in general, inflammation in all its multiple outlets, drug resistance in general, obesity and metabolism, multiphasic botanical drugs, and the list continues.

Similar fundamental contributions of the basic sciences to diverse sectors of our society are abundant, from the buildings we occupy and the bridges we cross, the cell phones over which we talk and text, the foods we eat, and beverages we drink. We can all agree that we value these

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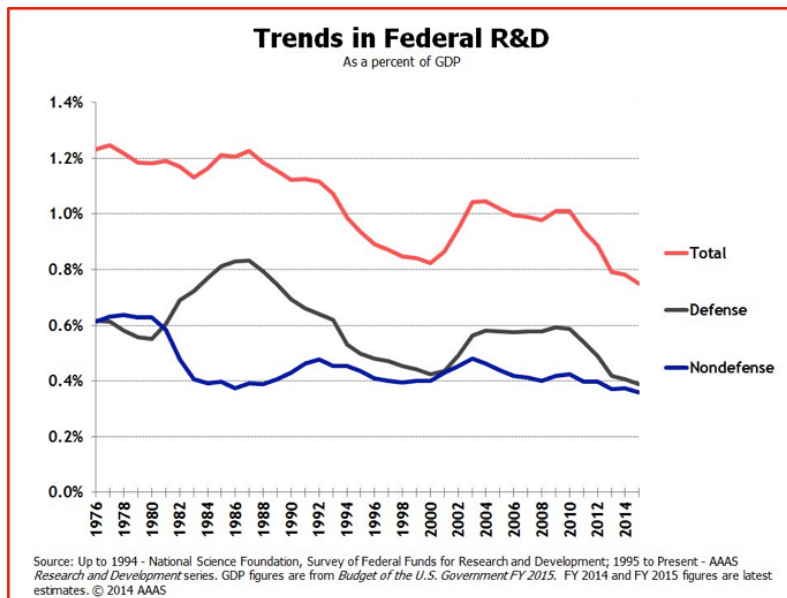
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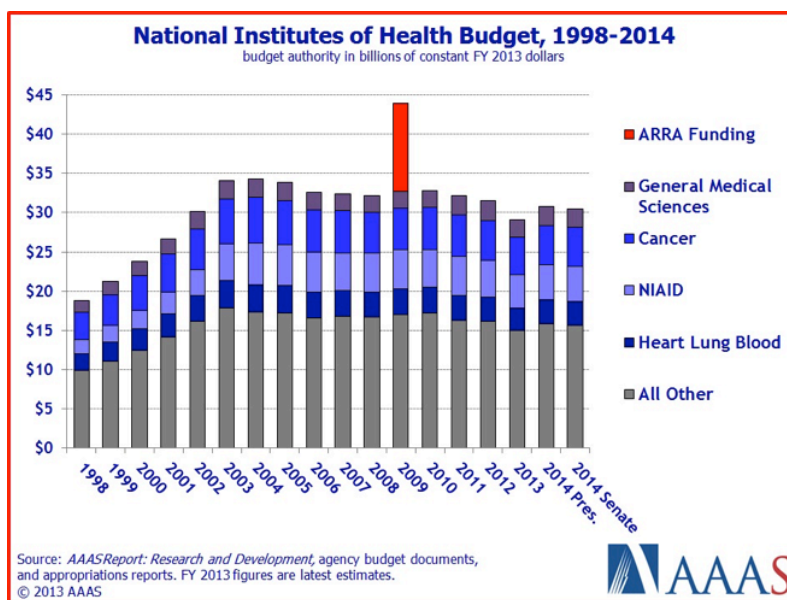
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advances in our daily lives, and that these are important to our country's economic vitality and political security. Science surrounds us and makes our lives better in so many ways; however, recognition of this in the US appears forgotten and is significantly underappreciated at the present time. Indeed, quoting Dr. Bruce Alberts (former Editor in Chief, *Science Magazine*) "... the United States is living off its past."³

Figure 1. (top) Historical data for Federal Research and Development spending as a percentage of GDP 1976-2015 (from <http://www.aaas.org>).



What made the second half of the 20th century so productive in the US in terms of scientific achievements, improvements to human life, and economic vitality? Of course this is a complex equation, but certainly the considerable investment of the US government and the private sector in developing a culture of science and the resulting innovation and entrepreneurship are an important part. For example, investment in science by government sources was over 1.2% of gross domestic product (GDP) in 1976, but has fallen to less than 0.8% today (Figure 1). The NIH, the major funding body of basic biomedical science in the US, funded 700 fewer research grants in 2013 than in 2012, and the National Science Foundation (NSF) funded around 1,000 fewer grants during this same period, due to the now infamous Sequestration. However, the broader trend is that research funding in general has been decreasing since 2003, with 12.5% fewer grants in 2014 than 2003 (Figure 2, 3). Paylines for 'likely' funding of a research grant is in the single digit percentage levels in some NIH institutes (published data for 2014 includes Fogarty 9.1%, National Center for Complementary and Integrative Health, [NCCIH] 8.7%, and the National Cancer Institute [NCI], 14.1%; in 1997, these funding rates were Fogarty 38.7%, NCCAM 56.5%, and NCI 32.1%). It is



untenable that only this small percentage of grants are of sufficient merit for funding, and reviewers and program officers alike are having to split hairs to decide between essentially equally worthy applications.

Figure 2. (lower) Historical data for the Budget of the National Institutes of Health spending by institute 1998-2015 (from <http://www.aaas.org>).

The consequences of this shortage of funding in the natural products sciences, and to science in general, are profound and enormously destructive to the discipline; they are also destructive, ultimately, to our society as we currently enjoy it. And unfortunately, the reduction of US funding of scientific research has negatively influenced private sector funding of US academics (with level private sector funding

worldwide, more has gone to other world regions such as Asia and Oceania). These features combine to further exacerbate the enormous difficulty that young and mid-career scientists face to acquire mainstream federal funding as well as private sector support. Consequently, they must cobble together the resources for operating their research programs from a diversity of smaller funding sources, each of which takes considerable time in the application process and resulting administration, leaving an ever smaller percentage of time for scholarly thought and research.

It has been estimated that government funded scientists currently spend close to 50% of their "research time" justifying their

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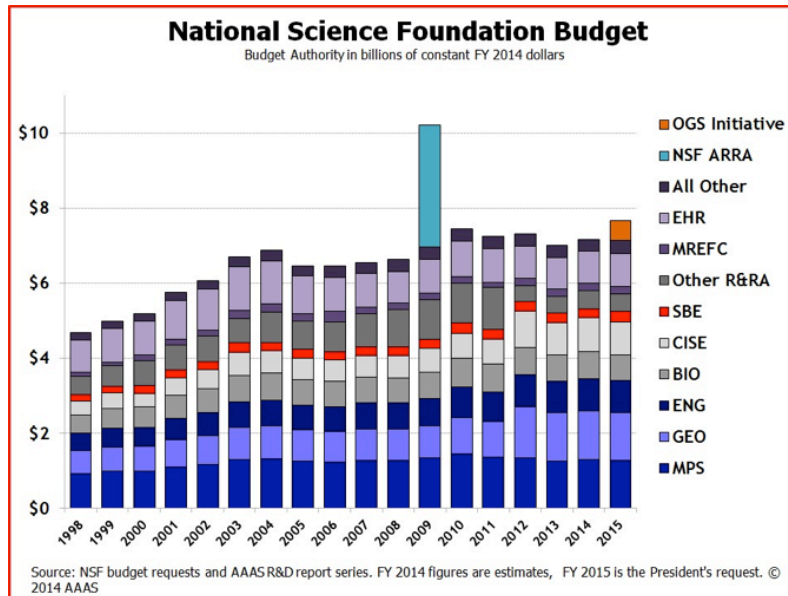
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research in terms of grant applications, reports and other grant administration. The impact of this on the success of early and mid-career faculty who are developing their programs under such constraints is unknown, but it can be reasonably predicted that it will become increasingly difficult to attract the best and the brightest to academic science careers under such conditions. Again, in the words of Dr. Alberts from 2014, “With the latest cuts created by the short-sighted political gridlock in Washington DC, are we headed to a future where the world’s most talented young scientists and engineers no longer want to pursue careers in the United States?”³

Figure 3. Historical data for the Budget of the National Science Foundation 1998-2015 (from <http://www.aaas.org>).

In a nutshell, we have some wonderfully talented young scientists who are working very hard and with great creativity and diligence, who deserve our support and could give incredible gifts in their lifetimes to science and society, but may not because they are so enormously underfunded and unappreciated. Extend this trajectory forward a few years, taking into account the enormous



perscholar.org/brain-trust/), and in my personal experience, I see these numbers as being accurate. Evidence of this is mounting in that several prominent junior and mid-career faculty have left the US for positions in other countries where research funding is more plentiful. Are we really willing to become second rate in terms of our scientific infrastructure and standing in the world? Do we really appreciate the impact this change would have

on the American psyche and way of life? As a society, we need to appreciate the long-term value that will result from support of these young and highly talented young and mid-career faculty to the future scientific workforce, and we need politicians and industry leaders to come together and powerfully champion this important cause. Inaction is not an option, as we are rapidly entering a downward spiral wherein we are systematically disassembling our scientific infrastructure.

So how we do correct this downward trajectory? First and foremost, we have to increase public funding of research in our universities and public institutions. A reasonable target would be to restore public funding of science to the equivalent level of over 1.2% of GDP as in 1976; this would essen-

Inaction is not an option, as we are rapidly entering a downward spiral wherein we are systematically disassembling our scientific infrastructure.

investment other countries such as Germany, Japan, China, Saudi Arabia, Brazil, and South Korea are making to grow and support a vigorous culture of science, and the future is not bright. Compare this with Sweden, Finland, and Israel, which lead the world with a combined public and private sector percentage of GDP funding of science (3.41, 3.55, 3.93, respectively), whereas the US aggregate lags behind at 2.79% (in 2012) (<http://data.worldbank.org/indicator/GB.XPD.RSDV.GD.ZS>).

What will the economic consequences be of a US that is no longer leading the world in science and technology, and thus is no longer the land of opportunity for the best and brightest? Indeed, it is reported that between 20-50% of American scientists are considering pursuing their research overseas ([tially be a doubling of the public science budget in the US. This needs to be distributed across the full range of academic types, from PhD granting research-intensive universities to 4-year colleges; all of these settings have talented and creative people that deserve support. The fundamental precept of “diversity” holds true in research as in biology: a diversity of research settings and approaches insures a resiliency and adaptability of the system to meet new challenges and opportunities as they develop. It is in the national interest; it is in our interest!](http://su-</p></div><div data-bbox=)

It has been presented in various venues that the current research enterprise in the US is unsustainable and needs a

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major overhaul in scope and structure. It is absolutely true that improvements can be made in how we use society's resources in the best ways possible, and that greater efficiencies in our scientific enterprise are conceivable, but let us not have that discussion overshadow the more substantial and significant one, namely, how has science benefitted the US in terms of our quality of life, economic strength, outlook for the future, and security? Does it then make sense to downsize that which has had so much impact? Is 'austerity' in funding science really a sound plan for stimulating the vitality of our economy and ensuring the longer term sustainability of our society?

In this light, it is reassuring to see recent recognition of these needs of the scientific communities, at least in part, by our political leaders on both sides of the aisle. Former Speaker of the US House of Representatives Newt Gingrich's call for a doubling of the

NIH budget, and former Connecticut Senator Joe Lieberman and former Utah Governor Jon Huntsman's call to galvanize efforts around grand challenges, like going to the moon in the 1960's, are breathing fresh air into this stagnant funding situation for scientific research. In this spirit, it becomes the task for each of us to communicate this message, in our daily contacts, our opportunities to speak to groups, and our ability to write and communicate our thoughts to a broader community.

So, let this short essay be a call to action; we cannot be silent on this issue for it is simply too important to our country and way of life. Let us carry this message forward, each in our own way, for our institutions, our academic children and grandchildren, and yes, for our own opportunities to give back to society that which we have been trained to do: to explore, be curious, innovate, and discover. ■

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ASP 2015 Election Results

By Dr. Amy Keller

Dr. Cindy Angerhofer has been elected ASP Vice President (2015-2016), and Dr. Joseph Betz has been elected Executive Committee Member (2015-2016), according to the ASP Tellers Committee, comprised of Drs. William Keller (Chair), Xiaolan Kou, and John Porter. Current ASP Vice President Dr. Edward Kennelly will serve as President (2015-2016), in accordance with the ASP Constitution. There were no constitution or by-laws amendments in this election.

The Tellers Committee was appointed by ASP President Dr. Phil Crews. In March of this year, 459 ballots were electronically sent to the ASP membership with 258 returned for a voter turnout of 56%.

Congratulations to Drs. Angerhofer and Betz!

Hot Topics in Pharmacognosy: Belated Recognition of Old Friends?

By Dr. David Newman

Is the “sourcing,” i.e. the identification of the plant organism(s) that actually produce the phytochemicals, now at the point that marine chemists were at approximately 25 to 30 years ago with respect to determining the actual source(s) of marine secondary metabolites? In the early 1980s, Dr. D. John Faulkner's group at the Scripps Institution of Oceanography reported the isolation and structure of renieramycin A (**1**) from a sponge collected in the Western Pacific.¹ What was unusual about this structure was that it very closely resembled a series of known antitumor agents, the saframycins A (**2**), B and C that had been reported² from the terrestrial microbe *Streptomyces lavendulae* and had gone into preclinical investigations in various countries using both naturally occurring and chemically modified variations.³ Saframycin A ultimately led to the semisynthetic production of Et743 (Yondelis[®]) many years later.

Over the next 20 years or so, it became obvious that in the marine environment, the majority of molecules found were the products of free-living microbes, with a relatively early example being the dolastatins from *Symploca* spp.⁴ and a more recent one involving the demonstration of the full biosynthetic pathway of didemnin B by Xu et al. in 2012.⁵ Perhaps the most telling example was the tour-de-force published by Piel's group⁶ demonstrating the biosynthetic potential of the

microbe *Candidatus Entotheonella* spp., as yet uncultivated, from the sponge *Theonella swinhoei* Y, where 31 of the 32 compounds reported from this sponge were genetically coded in the microbe.

In the plant arena, perhaps the most intriguing report in the early 1990s was the one from Stierle et al.⁷ reporting the isolation of a fungus from the Pacific yew tree that yielded very low levels of Taxol[®] upon fermentation. Over the last 20 years, there have been reports in the literature, with one as recently as 2013, that denied that this actually occurred.⁸ In this 2013 paper, the authors stated that their

culture (which they claimed was the same as Dr. Stierle's but from a culture collection) and two others did not produce any taxanes, nor did they contain the gene clusters necessary for production. In contrast, the following recent papers should be consulted for the results demonstrating production of Taxol[®] by a variety of endophytic fungi, including identification of the relevant genetic machinery in the fungi investigated.⁹⁻¹¹ These papers demonstrate this potential, and the Soliman and Raizada paper in 2013 is of significant interest because it points out that the experiments utilized in all previous work relied upon axenic culture methods, whereas in the plant there would be significant interaction and competition between different microbes. They demonstrated increased yields when competitive fungi and other agents were introduced into the cultures, a phenomenon known to “induce” expression of cryptic gene clusters.¹² One excellent example of this type of

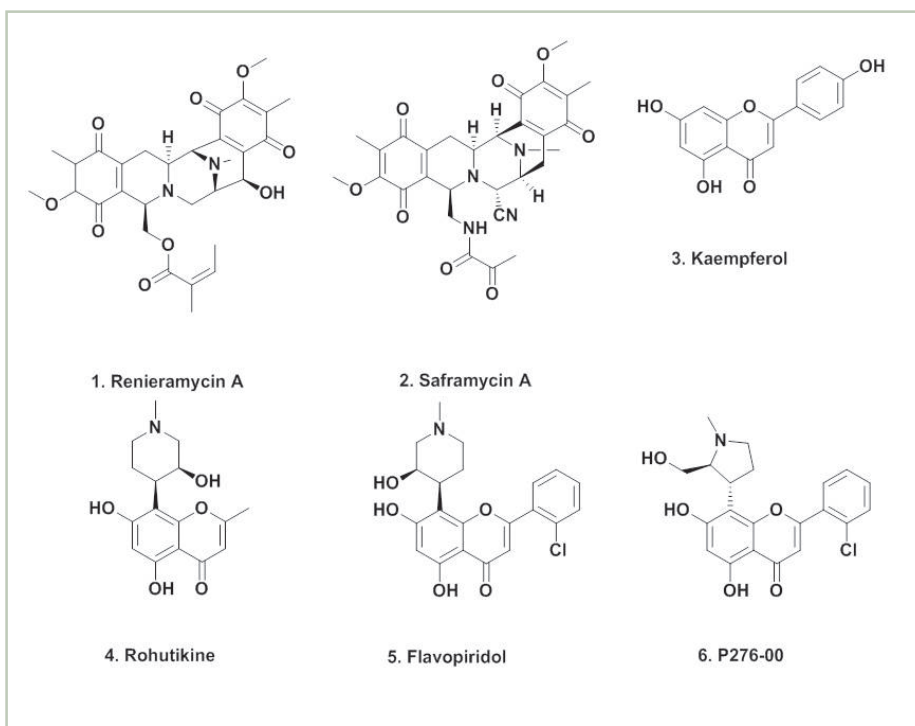
response is the report where suspension cells of *Taxus chinensis* var. *mairei* were co-cultured in a bioreactor with its endophytic microbe, *Fusarium mairei*; a doubling of the yield of Taxol[®] was observed.¹³

Perhaps the final comment on this particular agent would be the story around the production of Taxol[®] by the hazelnut tree, first reported in 2000.¹⁴ Quite recently, much more information plus transcriptome analyses were published by Ma et al. in 2013,¹⁵ demonstrating the

genes necessary for Taxol[®] biosynthesis. Yang et al. identified paclitaxel production in an endophyte, *Penicillium aurantiogriseum*, from hazel and identified the gene clusters involved, demonstrating evolution of the biosynthetic machinery in this *Penicillium* species independent of the plant host.¹⁶ In this case, there is little doubt that the fungus produces the compound.

Another very well-known “plant-sourced agent” is maytansine. The trials and tribulations relating to the source(s) of this agent

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Hot Topics in Pharmacognosy: Belated Recognition of Old Friends?

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have been well documented through late 2011 by Yu et al.¹⁷ and the consensus was that ansamitocin P3 was probably transformed within the plant to maytansine by transesterification. Recently however, Wings and coworkers reported growing axenic cultures of *P. verrucosa* but could not amplify genes involved in maytansine biosynthesis; a maytansine-producing eubacterium also could not be cultured outside of its natural habitat.¹⁸ By using molecular techniques such as rDNA sequencing and single strand conformation polymorphism, they identified that the *Actinosynnema pretiosum* ssp. *auranticum* eubacterium present in the rhizosphere of the plant is involved in maytansine biosynthesis. A later report in 2014 confirmed the rhizosphere site for maytansine production,¹⁹ but the exact microbe or microbial consortium was not yet identifiable. Whether the organisms are epiphytic or endophytic is not yet fully elucidated, but it does remove the “plant from contention.”

There is other recent work on other “plant-sourced compounds;” an interesting report details that kaempferol (**3**) was produced by fermentation of endophytic fungi isolated from sterilized rhizomes of the high altitude plant *Sinopodophyllum hexandrum* collected in the Taibai mountains of China.²⁰ These scientists isolated a fungus that only produced kaempferol and then another (identified as *Mucor fragilis*) that produced both podophyllotoxin and kaempferol. Whether the first fungus had a cryptic cluster associated with podophyllotoxin was not explored.

Another recent report demonstrated that the well-known compound rohitukine's (**4**) initial sources were *Amoora rohituka* and *Dysoxylum binectariferum*. Rohitukine was later reported from *Schumanniphyton magnificum* and *S. problematicum*. Due to the therapeutic potential observed for rohitukine derivatives, such as the clinical candidates flavopiridol (**5**) and the Piramal Healthcare Ltd. compound P276-00 (**6**), there was a search for other producers, including endophytes.

In 2012, Kumara et al. reported the production of rohitukine by fermentation of the endophytic fungus *Fusarium proliferatum* isolated from *D. binectariferum*.²¹ In 2014, the same group reported that four other fungal species, three *Fusarium* isolates from *D. binectariferum* and *Gibberella fujikuroi* isolated from *A. rohituka*, also produced the compound upon fermentation.²² They did make the point that the yield dropped during extended

cultivation, though this may be due to the loss of as yet unknown co-factors.

There are other recent reports of production of compounds such as huperzines, swainsonine, and older reports such as the ergot alkaloids, that are linked to microbes isolated from plants. However, the above recent examples should be enough to start people considering the possibility that in the next few years, using and learning from the techniques pioneered in genetic analyses of marine organisms and microbes with respect to secondary metabolites, might change ideas about the actual sources of “plant-derived secondary metabolites.”

To close this relatively short commentary, I will make three points that may give “food for further thought:”

- A frequent comment by phytochemical researchers is that terpene synthases are plant (sometimes fungal) biosynthetic processes. A very recent paper from the Kitasato Institute demonstrated that terpene synthases are well distributed in the actinobacteria, with over 260 being identified from total genomic analyses and some being expressed in heterologous hosts.²³
- Chalcone synthases (and chalcones are usually considered to be plant metabolites) were identified in *Streptomyces maritimus* by Moore et al. back in 2002, as a new Type III PKS system.²⁴
- In Traditional Chinese Medicine (TCM) there are very specific instructions if one goes into the literature (1,500 years plus ago), that specify site, meteorological conditions, time of year, and specific parts of a plant for collection and medicinal use.

In addition, it has often been observed and reported that general plant collections in Africa and Asia do not always yield the same active agents when recollected at or very close to the original site, but little emphasis was placed upon specific timing of recollections.

Thus, might these requirements in TCM, and recollections with observed differences, be due to the possibility that under different conditions, the microbial flora in, on, and around the plant (thinking of the plant as a host in this instance), may alter and influence the production of the desired compound(s)? Certainly a topic for continued debate. ■

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Behind the Scenes in Pharmacognosy: Fun with Aeroponics!

Last summer, the *Journal of Natural Products* published “*Thielavialides A–E*, *nor-spiro-azaphilones*, and a *bis-spiroazaphilone* from *Thielavia* sp. PA0001, an endophytic fungus isolated from aeroponically grown *Physalis alkekengi*,” work from the laboratory of ASP member Dr. Leslie Gunatilaka, Director and Professor, Southwest Center for Natural Products Research and Commercialization at the University of Arizona Cancer Center, Tucson, Arizona. Dr. Gunatilaka’s laboratory pursues innovative techniques in understanding the relationship between plants and endophytic fungi in environmental stress. We are grateful to Dr. Gunatilaka for sharing his work in more detail, including the group’s emphasis on local and international collaborations. Please read the article, *J. Nat. Prod.*, 2014, 77 (6), pp 1467-1472. doi: 10.1021/np500237h.

By Dr. Amy Keller

How did you become interested in endophytic fungi and compounds therein?

My interests in natural products date back to my undergraduate research project on the investigation of medicinal plants of Sri Lanka. During my graduate studies with Dr. D. H. R. Barton and postdoctoral studies with Drs. Barton, Carl Djerassi, and David Kingston, I gained experience in studying natural product biosynthesis, isolation, identification, synthesis, and their evaluation for potential biological activity. When I moved to the University of Arizona, Tucson, Arizona, to take up my first independent position in the United States, I was fascinated to see how some plants without xerophytic adaptations survive in the harsh environment of the Sonoran desert. This observation led me to hypothesize that some microorganisms living in symbiotic association with these plants, such as endophytic and rhizosphere fungi, may produce small-molecule natural products capable of modulating stress (heat-shock) response in plants.

Thus, I became interested in plant-associated fungi. Our work on secondary metabolites of endophytic and rhizosphere fungi of Sonoran desert plants resulted in a number of natural products capable of modulating heat-shock response in a heat-shock induction assay routinely used in our laboratory. To our pleasant surprise, one of these compounds, monocillin I, was found to confer thermotolerance to the model plant, *Arabidopsis thaliana*, by interacting with the plant heat-shock protein, HSP100. Subsequently, we showed that co-culturing of *A. thaliana* seedlings with the fungus



From left to right: Mr. Brandon Freidhof, Mr. Felipe Hilario, Mr. Thiago Porto, Dr. Leslie Gunatilaka, Dr. Kithsiri Wijeratne, Ms. Patricia Espinosa-Artiles, Dr. Yaming Xu.

APRIL BAGLEY

producing monocillin I resulted in survival up to 45° C for 75 minutes, whereas *A. thaliana* in the absence of the fungus did not survive at this high temperature. We have thus far investigated over 500 endophytic fungi and have isolated numerous natural products, some bearing unprecedented carbon skeletons or with potential anticancer, anti-HIV, and anti-tuberculosis activities.



Who in your laboratory carried out the research?

Although the work described in this paper was carried out by Dr. Kithsiri Wijeratne, Dr. Raphael Gruener, and Ms. Patricia Espinosa-Artiles, our project on investigation of endophytic fungi for bioactive and/or novel small-molecule natural products is a large collaborative effort between my group (Drs. Bharat Bashyal, Kamal Gunaherath, Angela Hoffman, Kithsiri Wijeratne, Jianguang Luo, Jair Mafezoli, Maria

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Aeroponic chambers used for cultivation of plants under a controlled environment (in a greenhouse)

DANIEL BUNTING

Behind the Scenes in Pharmacognosy: Fun with Aeroionics!

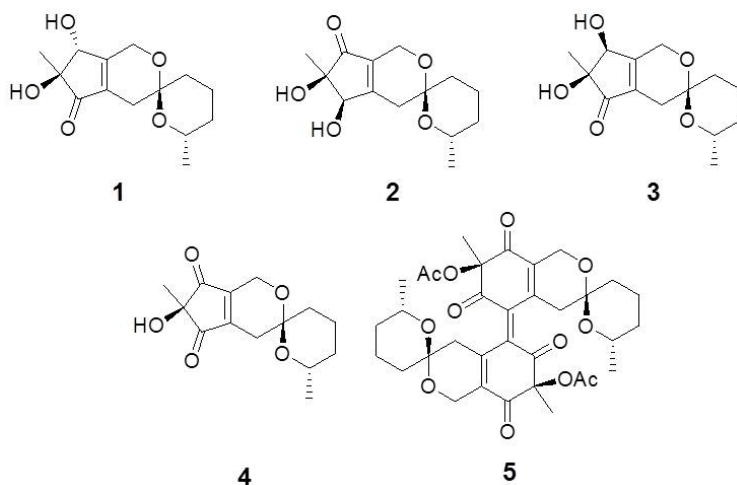
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Oliveira, Priyani Paranagama, Jacqueline Takahashi, Yaming Xu and Jixun Zhan, and Ms. Patricia Espinosa-Artiles and Manping Liu), and the groups led by Drs. Nafees Ahmad, Elizabeth Arnold, Eli Chapman, Istvan Molnar and Donna Zhang (all from University of Arizona), Stan Faeth (Arizona State University, Tempe, Arizona), Scott Franzblau (University of Illinois at Chicago, Chicago, Illinois), and Luke Whitesell (Whitehead Institute, Cambridge, Massachusetts).

Could you provide a brief explanation of the work and results in your own words?

We have recently developed an innovative soil-free aeroponic technique for the cultivation of plants under environmentally-controlled conditions. This facilitates the efficient production and structural diversification of their bioactive metabolites. As high-lighted by Dr. David Newman in his series on "Hot Topics in Pharmacognosy," published in the 50th Anniversary Issue of the *ASP Newsletter* (Vol. 50, Issue 4, pp 18-19), successful application of this technology to *Withania somnifera* (ashwagandha) resulted in efficient production of the commercially available, but expensive, plant natural product withaferin A (current Sigma-Aldrich price for 5.0 mg is \$352).

Prior to our work reported in our publication, we and others have investigated endophytic fungal strains inhabiting plants and mosses found in their natural environments. We thought that it would be interesting to see if plants grown under environmentally controlled conditions would also harbor endophytic fungi, and if so, would these produce metabolites with biological activity? To this end, we sampled live tissues of several medicinal and related plants, including *Withania somnifera* and several *Physalis* sp., and cultivated them using our environmentally controlled aeroponic technique for their endophytic fungi. We were



Chemical structures of thielavialides A (1) – E (5)

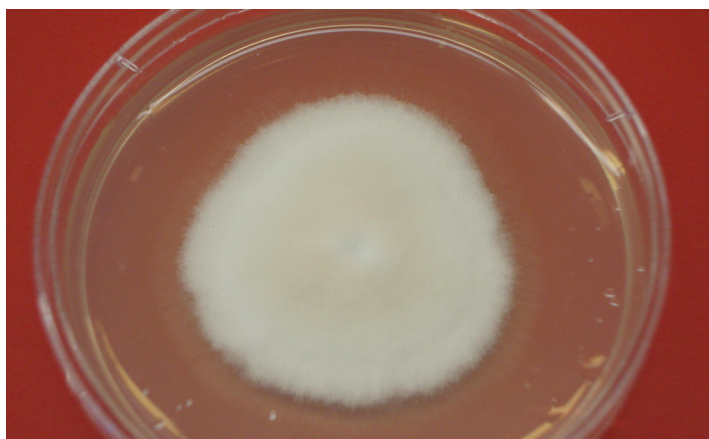
intrigued by the fact that in contrast to plants growing under natural conditions that harbor numerous endophytic fungi, these plants cultivated under a controlled environment were found to host only a few culturable endophytic fungi. This observation may support the hypothesis that plants harbor symbiotic endophytic fungi for ecological interactions with their environment; under controlled environmental conditions this symbiotic association may not be essential for their survival.

Of those investigated, only the leaf tissue of *Physalis alkekengi* (bladder cherry) contained a culturable endophytic fungal strain, identified as a *Thielavia* sp. Investigation of the ethyl acetate extract derived from a culture of this fungus resulted in the isolation and characterization of five new metabolites consisting of four nor-spiro-azaphilones and a bis-spiro-azaphilone together with the known spiro-azaphilone, pestafolide. Although none of the compounds encountered showed any activity in our cell and mechanism-based anticancer bioassays, pestafolide has been reported to have mild antifungal activity. Co-occurrence of these metabolites in this endophytic fungus led us to postulate biosynthetic pathways to all new metabolites starting from pestafolide.

You successfully isolate compounds from endophytic fungi in a plant grown aeroponically. Do you think this method of growth had any influence on the compounds you discovered?

There is evidence that the prevalence of endophytic fungi in a given plant species may be influenced by the environment (ecological factors) in which it grows. We believe that under environmentally controlled greenhouse conditions used for growing plants aeroponically, it may not be essential for plants to harbor many endophytic fungi which may produce metabolites required for their survival in their native environ-

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A petri dish with the endophytic fungus, *Thielavia* sp. PA0001

PATRICIA ESPINOSA-ARTILES

Behind the Scenes in Pharmacognosy: Fun with Aeroponics!

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ments. Although the compounds we discovered in *Thielavia* sp. PA0001 had no activity in biological assays available to us, it is possible that they serve some useful functional role in the host plant.

What is a favorite nonscientific activity of your lab?

We receive many foreign visiting scholars who bring cultural diversity and new ideas to the group. When they leave, all of us get together with food and drinks to bid farewell to them. In addition, we organize an annual Halloween lunch party with international cuisine. We invite interested family members and university administrative staff.

What is your laboratory's motto or slogan?

Our laboratory's motto is "work diligently with colleagues and other scientists from academia and industry worldwide involved in areas related to natural products discovery and development in a mutually beneficial manner," as everything we do with isolation and medicinal chemistry of natural products is focused on our intended common goal of discovery and development of new and effective therapeutic agents for cancer, neurological disorders, and HIV.

What is your greatest extravagance in the laboratory?

We provide our group with whatever resources they need to



Physalis alkekengi plant growing under aeroponic conditions

DR. RAPHAEL GRUENER

work efficiently to keep up with our above "motto." The greatest extravagance in our lab is the recent acquisition of a 400 MHz NMR spectrometer which has accelerated our work and collaboration with scientists from developing countries. ■

Former ASP President Mitscher Dies

by Dr. Thomas Prisinzano

Former ASP President and Professor Emeritus, Dr. Lester A. Mitscher, died May 8, 2015, at the age of 83. The research of Dr. Mitscher, former Department of Medicinal Chemistry Chair and University Distinguished Professor at the University of Kansas, ranged from the development and popularization of the use of circular dichroism for structural elucidation to the isolation of novel entities using bioassay-guided fractionation. He specialized in the search for new antimicrobial agents and was a key player in the development of both tetracycline- and quinolone-based agents.

Throughout his highly decorated career, he earned numerous awards and honors, including the Research Achievement Award in Natural Products Chemistry from the American Pharmaceutical Association in 1980, the Ernest H. Volwiler Award for Research Achievement from the American Association of Colleges of Pharmacy in 1985, the Higuchi-Simons Award in Biomedical Sciences at Kansas University in 1986, the Bristol-Myers Squibb Edward E. Smissman Award in Medicinal Chemistry from the American Chemical Society in 1989, fellow of the American Association for the Advancement of Science in 1995, the Division of Medicinal Chemistry Award from the American Chemical Society in 2000, and the Norman R. Farnsworth Research Achievement Award from the American Society for Pharmacognosy in 2007. ■

Editor's Note: In light of Dr. Mitscher's immense contributions to ASP and natural products as a whole, Dr. Prisinzano will contribute a comprehensive obituary for our Fall issue.



Pharmacognosy Field Notes: Rain, Cyanobacteria, and Giant Spiders

By Dr. Kerry McPhail

I recently paged through two very small (4.5 x 3.25 inch) field collection notebooks, a green one labeled “Panama, Santa Fe, 02/2010,” and a blue one labeled “Panama, Volcán (Chiriquí), 06/2010.” When I got to the back of the green Santa Fe book, there was a brief day-by-day log of six days in Santa Fe National Park, situated in the Veraguas mountain range, that brought back a flood of memories. In the then “new iteration” of the Panama International Cooperative Biodiversity Groups program (ICBG) with Dr. William Gerwick as Principal Investigator, my interests were the diversity of aquatic and terrestrial cyanobacteria for their natural product chemistry. Hence, I went on two expeditions in 2010 to the interior highlands of Panama in collaboration with ICBG colleague Dr. Alicia Ibáñez, a botanist, conservationist, and author of “Guía Botánica del Parque Nacional Coiba.”

As far ahead as possible, ICBG participants planned collaborative expeditions for maximal cost efficiency and productivity. Therefore, at the same time, graduate student Mr. Chris Thornburg from my laboratory was to join Drs. Roger Linington, Marcy Balunas, and Kevin Tidgewell, past and current Panama-based ICBG post-doctoral researchers at the time, on a marine collection expedition to the Gulf of Chiriquí and Coiba National Park, off the Pacific coast of Panama. Chris’ primary directive was to make focused collections of the coibamide A-producing cyanobacterial assemblage for laboratory culture.

All parties met in Panama City at the Hostal Amador Familiar for the night, not far from the Bridge of the Americas. The next morning, we set off on our separate ways, although all driving west on the Pan-American Highway to Santiago de Veraguas, Panama. The marine expedition continued further west to David, from where they would dive daily in the Gulf of Chiriquí and then Coiba National Park, as arranged by Panama-based professional diver Mr. Kevan Mantell. Assisting me as part of the terrestrial contingent were Alicia and Rodolfo, a student field assistant who I quickly learned was also a professional dancer. In Santiago, we turned north to start the winding drive up to Santa Fe village in the Smithsonian Tropical Research Institute (STRI) Toyota truck.

When we stopped for a large meal along the way, Rodolfo and I had no idea that it would be the last time we felt satisfied of hunger for over a week. We arrived at Santa Fe village around



Victor, Alicia, Manuel and Rodolfo (L to R) modeling the trashbag raincoats.

DR. KERRY MCPHAIL

3 pm, stopping at a beautiful bamboo house, which turned out to be a shop selling beads and beaded ornaments. The owner greeted Alicia warmly, and shortly afterwards two men arrived (Victor and Manuel) who would be our guides and porters of the botanical specimens that Alicia and Rodolfo would collect. From there we continued north as far as we could drive on the steep rocky road leading towards the National Park, finally parking near someone’s farmhouse. As I lifted my backpack out of the back of the truck I looked towards the mountains, which rose steeply on the other side of the Santa Maria River, and wondered how it would be to walk down from an elevation of over 1,300 m (4,300 ft) back to our current 430 m (1,400 ft) with a backpack full of samples. We set off and walked for an hour, reaching a palapa (thatched, unsided shelter) where we rigged our hammocks for the night, of course with the expert help of guide Victor.

The next morning we set out at 8 am to cross the Santa Maria River. I had no idea that we would have to wade cross this broad, winding river five times before starting the steep climb into the cloud forest, nor that I would very shortly be gulping that river

continued on page 23

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Pharmacognosy Field Notes: Rain, Cyanobacteria, and Giant Spiders

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Victor, Manuel and Rodolfo crossing the Santa Maria River on Day 2.

DR. KERRY MCPHAIL

water untreated, all health concerns gone in the dripping humidity. After a strenuous day of walking, wading, and climbing with an unwieldy backpack it was a relief to arrive at a shack where we could sleep again under cover. For the first time that day though, water was not close at hand and we had an agonizing climb down a steep slope to wash under a small waterfall and get water for cooking. During the night it rained hard, the start of near constant rain for the next week. Our destination the next day was the high cloud forest where we would find a place to set up a base camp out of which to operate for the duration of our collection days. There ensued the most strenuous hiking up and down four very steep, rocky slopes in sometimes driving rain. Where our path did level out we found ourselves wading through muddy swamp, boots and shins submerged. My logbook notes: "trousers kept falling down because of heavy wet mud – remember belt next time!"

After reaching the high plateau we finally settled on a place to set up camp. Our guides expertly wielded their machetes to clear a living area and construct support frames for the five hammocks, each set up with a flysheet to escape the constant rain, as well as a log seat and footrest to elevate our feet out of the mud. Despite our hard work, we were now very wet and cold, and after a warm dinner it was heaven to be snug and dry, suspended in our hammocks.

I had no idea that we would have to wade cross this broad, winding river five times before starting the steep climb into the cloud forest, nor that I would very shortly be gulping that river water untreated, all health concerns gone in the dripping humidity.

As our first day of collecting dawned, Alicia produced very heavy-duty black trash bags and duct tape, and expertly directed me in making a raincoat with sleeves and a hood. We wore these raincoats continually for the next five days, and subsequently used them whenever I returned to Panama for the next three years. What a relief to head out then to collect samples along the trail without our heavy backpacks. We walked at a relatively fast pace for about an hour before turning around to start sampling as we made our way slowly back towards the camp. Alicia and Rodolfo spent a lot of their time in the lush "garden forest," while I found more cyanobacteria on the exposed sections of the high plateau where the vegetation was low and there was a lot of standing water.

Thus, I spent the rest of the day on my own collecting a range of unfamiliar cyanobacterial assemblages from exposed rocks, small caves and shallow small pools along what seemed to be the most picturesque of garden paths. I had to marvel that this single trail through the Sante Fe National Park, on which one could walk between the Pacific and Caribbean coasts, was a very old (gold) mining trail built hundreds of years ago by early Spanish explorers. Lunch consisted of a tiny can of tuna with two saltine crackers, supplemented in no small measure by the majestic views over the seemingly endless forest that expanded to the horizon in a gently breathing silence. As the afternoon wore on, hunger and the driving rain made for slower and slower sample collection, also hampered by a constantly fogging camera. I was very glad to meet up with Alicia and Rodolfo for the descent back to camp and warm soup dinner, after processing samples under a suspended flysheet that provided a comfortable communal shelter.

Over the next three days, we followed a similar routine, punctuated with an occasional meeting of native peoples passing us by on the trail. In each case, we asked in what month it did NOT rain, and mostly received a different answer every time much to our growing hilarity. Since February was one of the driest months in the rest of Panama, we could only conclude that it never stopped raining in Sante Fe National Park!

By the time we broke camp and headed back to the truck, it was slow going. Wet gear is heavy gear, and taking off one's backpack to sample became harder and harder, no doubt also because we had not eaten more than half our regular diets for

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Pharmacognosy Field Notes: Rain, Cyanobacteria, and Giant Spiders



Dr. McPhail collecting cyanobacteria from the high plateau trail.

DR. ALICIA IBÁÑEZ

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six days. Nevertheless, on the last full day's hike, the thought of reaching Sante Fe village, rather than staying one last night out in the palapa near the river, spurred us on to keep going to the truck. In admiration, I watched the guides balancing heavy loads down the steep slopes with graceful speed as they rapidly disappeared ahead of us. Since I was no longer stopping to collect samples I also ended up ahead of Alicia and Rodolfo once more, this time missing the turning down to the Santa Maria River where the guides waited. It did not take me too long to realize my mistake as I turned around and started calling out, although I was upset with myself nevertheless that it was getting late and we still needed to cross the river before dark with what little energy we had left. A few minutes later I could only watch in envy as Manuel came running towards me, taking my backpack and slinging it easily over his shoulder as we set off at a jog back to the others. When we reached Santa Fe village an hour or two later and said good-bye to Victor and Manuel, I had to smile at how they had tried to teach me "Panamanian" Spanish, correcting the vocabulary I had gleaned from Alicia, whose "Spanish" Spanish was surprisingly incompatible with rural Panama at times.

After a lucky last minute meal of chicken and rice at a local restaurant in Santa Fe village just past closing time, the rustic luxury of Hostal La Qhia, with hot showers and beds, was bliss. How funny that after all those days in the forest, my first experience of a large spider was sitting outside our room pulling apart

our backpacks to air the soggy, smelly contents, and to take off our socks. My exclamation at the very large spider skittering across the paved walkway near me brought a response from Alicia that there was no need to worry if it was so large. "Only the small ones are a problem," she said as she slowly made her way over to take a look. There followed the casual observation that in fact this was one of those small problematic spiders! Later that evening, it was a surprise to find how alien the English conversation of young backpackers sounded as they relaxed under the central palapa. We sat nearby silently processing collections from that last long day, dripping with exhaustion, Alicia clearly unwilling to even try to understand their English chatter as we just looked at each other uncomprehendingly.

The five or so hours driving back to Panama City went by in a blur, although undoubtedly we stopped to eat and upon arriving in Panama City, we must have delivered samples to STRI. Ironically, the STRI truck then had a flat tire when Alicia dropped me back at the Hostal Amador Familiar where I was meeting up with the marine expedition party again. Thank goodness the flat tire happened where there was help in the form of Roger! Shortly afterwards, Chris brought me up to date with the diving expedition over dinner. As he described his 11 dives on reefs with names like "The Fridge," "Twin Peaks," and "Montaña Rusa" ("Roller Coaster"), images of the pumping current and unsettling surge in the crystal cool water of Coiba National Park in February were all too vivid. I had to laugh at his anecdotes of shooing away sharks that were "guarding" a ledge where a large patch of the precious coibamide-producing cyanobacterium was growing, and of stealing Marcy's patch of cyanobacteria when she was distracted by Kevan momentarily and subsequently mystified over the disappearance of the sample.

I could only exclaim enviously as he described snorkeling in a deep cove where filter-feeding whale sharks would glide up from the deep with their mouths open, turning away just before they reached the snorkelers. By the time I had finished the family size pizza in front of me I could appreciate that Chris's formidable efforts to assemble live samples of the coibamide-producing cyanobacterium were well beyond what we had accomplished on any previous collection trip, thanks in no small part to his diving buddies - Kevan Mantell, Kevin Tidgewell, Marcy Balunas, Kelly Peach, and Roger Linington.

Thus ended a tremendously productive trip in all aspects; the division of labor for marine and terrestrial expeditions was enabled by the synergistic collaborations envisioned in our pre-trip planning. Once again, we left in awe of the uplifting and often surreal experiences that we have come to associate with Panama. ■

Thus ended a tremendously productive trip in all aspects; the division of labor for marine and terrestrial expeditions was enabled by the synergistic collaborations envisioned in our pre-trip planning. Once again, we left in awe of the uplifting and often surreal experiences that we have come to associate with Panama.

Meet a New ASP Member

New ASP Member Dr. Stephen Polyak is an Associate Professor in the Department of Global Health, at the University of Washington, Seattle, Washington. Dr. Polyak holds numerous other positions, including Member of the Center for AIDS Research at the University of Washington/ Fred Hutchinson Cancer Research Center and Affiliate Investigator in the Vaccine and Infectious Disease Division, also at the Fred Hutchinson Cancer Research Center. Dr. Polyak is a virologist and cell biologist interested in the impact of natural products on these organisms. He shares his interest in collaborating with other ASP members as well as his enthusiasm for music. We are excited to welcome Dr. Polyak to the ASP and look forward to meeting him at this year's Annual Meeting.

By Dr. Dan Kulakowski

How did you hear about the ASP?

I have been aware of ASP for several years, largely through my collaborations on silymarin with Dr. Nicholas Oberlies at the University of North Carolina at Greensboro, Greensboro, North Carolina. I have been thinking about going to the ASP meeting for the past couple of years. Now that our research project has matured, I think it is time to get our work in front of natural product researchers.

Why did you join ASP?

I joined ASP because I believe our work is ready for the ASP audience, and I think my research needs input from this field. As a virologist and cell biologist, I think the work we have been doing on how natural products like silymarin engage mammalian cells to provide cytoprotection might be well received. I also think we have applied novel biological and “omics” tools to understand the interaction between natural products and cells. As a highly collaborative scientist, I also think ASP membership might lead to new and exciting interactions.

Do you belong to any other scientific societies?

I am a lifetime member of the American Society for Virology. I am also a long-standing member of the American Association for the Study of Liver Diseases (AASLD) and the International Society of Interferon and Cytokine Research.

What are your current research interests in pharmacognosy?

My interests are to unravel the complexity by which natural products interact with mammalian cells to protect them from damage from viruses and chronic inflammation (among other causes). I am interested in applying systems biology to study cellular responses to natural products, defining the cellular targets to which natural products bind, and how binding confers biological activity. I would love to expand our studies that have been focused on silymarin and silymarin flavonolignans to other novel, bioactive compounds.

What is your scientific background?

I received my BS in Biology and PhD in Molecular Virology (both from McMaster University, Hamilton, Ontario, Canada), and have done post-doctoral training in the interferon (IFN) and hepatitis C



Dr. Polyak at the International Symposium on Hepatitis C Virus and Related Viruses, in Banff, Alberta, Canada, 2014. (Yes, there are two HCV virologists playing with the banquet band.)

virus (HCV) fields. Thus, my expertise is largely on virus-cell interactions. I have been studying HCV-host interactions for over 20 years with an emphasis on how this virus induces inflammation (pro-inflammatory cytokines and chemokines) and, for over 8 years, how natural products target cells to limit virus infection and inflammation. Our work on silymarin has been applied to human immunodeficiency virus (HIV), where we are studying how silymarin inhibits T cell activation, which is central to the inflammatory diseases that many HIV positive patients experience despite a viral load controlled by anti-retroviral therapy. The ways in which silymarin inhibits cellular inflammation are also applicable to other inflammatory diseases.

What would you like to achieve through your membership?

I would like critical feedback from the ASP membership. I would like to explore opportunities for new collaborations directed at defining universal biological mechanisms of action of

natural products.

What do you like doing in your spare time?

Born and raised in Canada, I played competitive hockey while growing up. As an aging athlete, I still play in a couple of men's beer leagues in the Seattle, Washington, area, and I am known as a solid defenseman. To keep up with the younger players and surpass my peers, I also train a couple of times per week at a friend's gym, where I partake in crossfit-like workouts. I have been bike commuting several times per week for four years. I also enjoy playing guitar, singing, and writing songs (see photo). I like to communicate and visit with my college-aged daughters, travel, attend theater, cook, and consume the end products of fermented botanicals.

What are you currently reading?

I am presently reading “The Drunken Botanist” by Amy Stewart. I am not kidding. This was a 50th birthday gift from a friend. I am sure most ASP members know this, but the book is an interesting collection of facts and vignettes about the many, many botanicals that are fermented.

What is your favorite organism to study, or for general interest?

Viruses and mammalian cells are my favorite organisms. Do I have to pick one? ■

New Members of ASP 2014



Welcome to ASP!

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 21 domestic full members, 9 international members, and 11 associate members. We look forward to meeting you and learning more about you and your work.

ACTIVE MEMBERS

Dr. Mohamed Abou Donia
Princeton, New Jersey

Dr. Matthew Bertin
La Jolla, California

Dr. Judy Bolton
Chicago, Illinois

William Bornmann
Missouri City, Texas

Dr. Jason Chen
Ames, Iowa

Dr. Jason Crawford
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Dr. Alessandra Eustaquio
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Mr. Theodore Weyna
Madison, Wisconsin

Mr. Jiaxuan Yan
Madison, Wisconsin

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. 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.

The Chemistry and Biology of Natural Products Symposium IX

June 25-26, 2015

**University of Warwick, Coventry,
United Kingdom**

www2.warwick.ac.uk/fac/sci/wcibb/meetings/chemistryandbiologysymposium/

Gordon Research Conference: Natural Products

July 26-31, 2015

Proctor Academy

Andover, New Hampshire

www.grc.org/programs.aspx?id=11732

Joint Meeting of the Society for Economic Botany (SEB) and the Indigenous Plant Use Forum (IPUF)

June 28-July 2, 2015

Clanwilliam, Western Cape, South Africa

www.econbot.org/

63rd International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA)

August 23-27, 2015

Budapest Congress Center

Budapest, Hungary

ga2015.hu/

ASP Annual Meeting

July 25-29, 2015

**Copper Mountain
Resort & Conference Center
Copper Mountain, Colorado**

asp2015.org/

2nd International Conference on Natural Products Utilization

October 14-17, 2015

Novotel Plovdiv Hotel

Plovdiv, Bulgaria

icnpu2015.cim.bg/



In Memoriam: Leonardus B. S. Kardono (1955-2015)

By Drs. Harry H. S. Fong, A. Douglas Kinghorn,
and Djaja Djendoel Soejarto

On April 1, 2015, former graduate student and valued colleague Dr. Leonardus B. S. Kardono, of Jakarta, Indonesia, passed away due to a traffic accident. At the time of his death, at the age of 59, Dr. Kardono held the position of Assistant Minister for Health and Medicine, in the Ministry of Research and Technology, in the Indonesian government. He had a distinguished scientific and administrative career as a Professor in Pharmacy and Organic Chemistry, and had held the prior senior positions of Director, Research Center for Chemistry, Indonesian Institute of Sciences (2005-2010) and Program Director of Food Health and Medical Sciences, International Center for Interdisciplinary and Advanced Research, Indonesian Institute of Sciences (2011-2015). He served as Vice President of the Indonesian Chemical Society (2005-2010) and of the Indonesian Natural Products Chemistry Association (2004-2008), and was a Visiting Professor at Kobe Pharmaceutical University, Kobe, Japan (2000), and Ehime University, Matsuyama, Japan (2001). In August, 2014, he received an Innovator Award from the Indonesian Institute of Sciences.

Dr. Kardono was a graduate student of the Pharmacognosy Graduate Program of the University of Illinois at Chicago, Chicago, Illinois (UIC), and received a PhD degree in 1992, with his dissertation topic devoted to the phytochemical study of two Indonesian plants with cytotoxic and antimalarial activities. One of us (A.D.K) served as his Major and Thesis Advisor. Earlier, he trained in Pharmacy at Bandung Institute of Technology (ITB) [BS, 1980; registered pharmacist (apothecary) diploma, 1981],



Dr. Leonardus B. S. Kardono

DR. NINA ARTANTI

The career ascent of Dr. Kardono on his return to Indonesia after he graduated in 1992 was nothing short of spectacular, and, as three of his former professors while he was in graduate school, we are very proud of all he accomplished.

where he met his future wife, Efi, whom he married in 1988. As a graduate student, Dr. Kardono presented his research work at the Annual Meetings of ASP held in Park City, Utah (1988), San Juan, Puerto Rico (1989), and Chicago, Illinois (1991).

While in Chicago, he proved to be an extremely friendly and highly energetic person, and was very well liked by all who met him. In the years after his graduation, Dr. Kardono remained a very good friend of the pharmacognosy group at UIC, and facilitated the development of agreements that led to the collection and investigation of the potential anticancer and chemopreventive principles of many Indonesian plants. He hosted visits of the UIC pharmacognosy faculty to Jakarta, Indonesia, on a number of occasions, and last visited Chicago in 2010 for the symposium held in honor of the 80th birthday of the late Dr. Norman R. Farnsworth.

The career ascent of Dr. Kardono on his return to Indonesia after he graduated in 1992 was nothing short of spectacular, and, as three of his former professors while he was in graduate school, we are very proud of all he accomplished. He was a superb ambassador for UIC and for the PhD Program in Pharmacog-

nosy and must have served as a very positive role model for numerous younger scientists in his home country.

In addition to his wife, Efi, Dr. Kardono leaves three children, Ancilla, Cornelia, and Teresa. For them, this untimely loss of such a warm and inspiring person due to a tragic accident must be unbearable. We extend to them our deepest condolences. ■



Brief News From Washington

By Dr. Georgia Perdue

- **In a letter to Congress, 14 state attorneys general asked for an investigation of the herbal supplements industry and for the Food and Drug Administration (FDA) to have stronger oversight over the industry.** The main complaint is that the herbal supplements on the market do not contain the ingredients listed on the labels. Herbal industry groups and some consumer advocates have, as expected, criticized the effort. **The Council for Responsible Nutrition said, “concerns raised in the letter about alleged widespread safety issues are not true.”** A *Washington Examiner* headline: “Regulate herbals now, states ask Congress.” (Stay tuned)!
- The cries for greater regulation of herbal supplements seem to have been heard by the FDA, which has not reviewed these products since 1988. It held a two-day “hearing” in April to obtain “information and comments from stakeholders about the current use of human drug and biological products labeled homeopathic.” The 38 invited participants, representing consumers, patients, caregivers, healthcare and lawyers and industry, provided answers and information on a num-

ber of specific questions from the FDA, received in advance. Each participant was rigidly held to five minutes of presentation and five minutes of questions from an FDA panel. A brief flavor: **Dr. Adriane Fugh-Berman**, Georgetown University Medical Center, Department of Pharmacology and Physiology, instructor of a course on medicinal plants, and former employee of the National Center of Complementary and Integrative Health (NCCIH), noted that most consumers do not know what homeopathic drugs, on the shelves alongside other over-the-counter (OTC) drugs, are. They believe homeopathic drugs are completely safe because they are diluted; “They are not diluted.” **“It is misleading to have homeopathic medicines next to FDA approved OTCs.”** **“Homeopathic medicines are not regulated as are dietary supplements. [They] should be segregated and defined as to what they really are. There is no reliable information regarding homeopathic medicines to suggest they are effective.”** “In 1922 ... it was recommended that the active ingredients be listed according to FDA rules, including the full name of the plant [etc.]. It is not safe to have misleading products on the shelves. Consumers do not understand what homeopathy is.” **Dr. Michael De Dora, Center for Inquiry**, noted “... homeopathic drugs have no effect in treating medical problems. They can cause harm.... [B]illions are spent every year on these products.... **The FDA should take action.**” **He recommended three steps: test homeopathic drugs; look into the labeling; evaluate [the efficacy] of the active ingredients.**” **Then he loudly said “regulate.”** Dr. Wayne Jonas, former director of the National Institutes of Health (NIH) Office of Alternative Medicine, now with Samueli Institute, which focuses on homeopathic medicine research, said top journals do not publish papers dealing with homeop-

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athy because reproducibility is a problem. **Naturopathic physicians said France, Germany, and Britain use homeopathy; “...there is no need to change the guidelines. Current labeling is detailed and adequate.”** **Ms. Jeannine Ritchot, Health Canada, Ottawa, Canada, noted “Canada regulates natural health products including homeopathic products, traditional medicines, plant and herbal medicines and probiotics.”** Other proponents said the vast majority of homeopathic products are appropriately labeled and comply with FDA and the HPUS* requirements. Other comments: **Dr. Paul Mittman, Southwest College of Naturopathic Medicine and Health**

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Brief News From Washington

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- Sciences, strongly advocated for schools of pharmacy to include classes on homeopathic medicine and for the FDA to equip itself with staff knowledgeable about homeopathy.** As expected, there were several lawyers representing clients dealing in homeopathic medicine; one welcomed interaction with FDA. *HPUS-Homeopathic Pharmacopoeia United States. (See the NCCIH website for a great article on homeopathy.)
- **On March 3, 2015, Dr. Harold Varmus, National Cancer Institute (NCI) Director, dropped a BOMB, stunning everyone not only at NCI, but throughout all of NIH and the scientific community. Since his position is a presidential appointment, he sent his letter of resignation to the President announcing he was stepping down on March 31, 2015. On April 1, 2015, Dr. Douglas Lowy, NCI Deputy Director since July 2010, assumed the role of Acting Director.** Dr. Lowy has been a cancer researcher for more than 40 years. He and his close collaborator, Dr. John T. Schiller, recently received the **National Medal of Technology and Innovation.**
 - At Dr. Varmus' last NCI Board of Scientific Advisors (BSA) meeting, he said his preference is that Dr. Lowy be made permanent Director of NCI. **Highlights of his valedictory comments:**
 - He pointed out the great effort he made for the **Frederick National Laboratory** to be more obvious to others and more exciting in developing new therapeutic studies. He encouraged the laboratory to take on more projects involving the University of Maryland, College Park, Maryland, and Johns Hopkins University, Baltimore, Maryland, and to consider various ways to engage them.
 - Keeping cancer centers "in a healthy state is important." He proposed an increase of \$10-15 million per year for the centers, a plan to be vetted at the June meeting of the National Cancer Advisory Board/BSA.
 - **He helped create the Center for Global Health**, "... having a major effect in world health." "If we do nothing, the toll in many countries will be astonishing. There is interest and eagerness ... in India, China, Turkey, Indonesia, Mexico, all of which are building cancer centers."
 - "...the future of the country depends very heavily on **basic medical research, which is being done at universities** [which need to be a productive community]... otherwise we are in trouble. **Support outstanding people with stable funding**, e.g., Outstanding Investigator Award..."
 - **"...postdoc training is too long and investigators start too late; we are trying to accelerate this. It is important to change the graduate training ... the Master's Degree is important; raising salaries for postdocs and using PhDs in biological sciences is important. TEAM science is very popular on university campuses."**
 - Every grant holder is being asked to serve as a reviewer in study sections—"everyone who is asked to serve will serve."
 - Review existing programs structurally... in these times of financial distress. "the ... budget will be pretty flat for the next five years."
 - On April 6, **Dr. Margaret Hamburg**, the former FDA Commissioner, was appointed to a four-year, part-time position as **Foreign Secretary of the Institute of Medicine**. Dr. Hamburg is the second woman to hold this position. She will serve as a **senior adviser on international matters to the Institute of Medicine (IOM) President and Council and will also be a liaison to foreign academies of medicine and science.** Her father, Dr. David A. Hamburg, was President of IOM from 1975 to 1980.
 - **"Algae as a mini-factory" can be used to produce a malaria parasite protein ... for a vaccine to prevent transmission of the malaria parasite from host to mosquito.** This, according to a statement from researchers at the University of California School of Medicine, San Diego, California. The idea is to prevent transmission of the malaria parasite from infected humans to mosquitoes, similar to how the measles vaccine works. The research team produced a large quantity of Pfs25, "a protein found on the surface of the malaria parasite's reproductive cells ... in the mosquito's gut after it feeds on a malaria infected blood meal." The gene is introduced into the algae after the protein is formed. The team has enough Pfs25 for laboratory testing. (See February 17, 2015, *Infection and Immunity*).
 - **This coming fall, Rockville, Maryland, will be home to a new GlaxoSmithKline vaccine center.** The British company says it will focus on "key late stage development programs, vaccine discovery, and new platform technology development." Glaxo's research facilities in Philadelphia, Pennsylvania, and Cambridge, Massachusetts, will be incorporated in the Rockville research center.
 - **A natural product, cytisine, helps people stop smoking.** Sopharma AD, a Bulgarian company, has been marketing cytisine as Tabex®, in Central and Eastern Europe for many years. **The compound is isolated from the seed of *Laburnum anagyroides* Medik. (Fabaceae), with the common name of golden-chain (flowers are yellow).** [It grows in Austria, Czech Republic, France, Germany, Hungary, Italy, Romania, Serbia, and Switzerland]. Bulgaria has cultivated 100,000 trees. Recent clinical trials in Britain and New Zealand showed better results than Chantix®. A small United Kingdom company, Ricanto, with funding from NCCIH, has begun preclinical trials of their newly named Extab, in California. Success in trials could mean worldwide marketing and the cultivation of at least 300,000 trees in the United States (from an article by Mr. Todd Frankel, *Washington Post* 5/17/15). Stay tuned!
 - The National Science Foundation reported that researchers have found that about 5% of phosphate in shallow waters samples are taken up by microbes and changed to phosphonates. "[F]or the first time microbes are producing phosphonates in the ocean ...very quickly." "This is important as it affects the marine food web...." ■

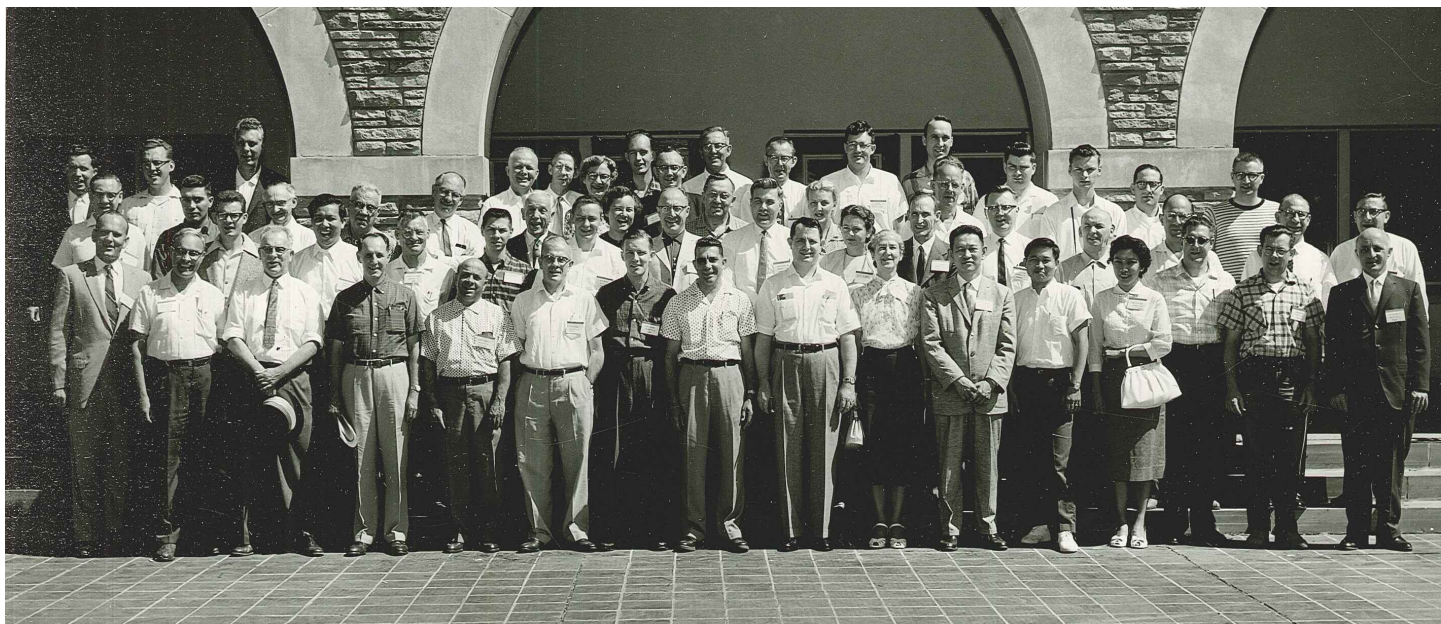
From the Archives: A Window Into Today's Dynamic ASP

By Ms. Devhra BennettJones

When the Society's members travel to Copper Mountain, Colorado, for the ASP Annual Meeting this July, they will navigate the path of the men and women that built the ASP from 36 years of annual Plant Science Seminar meetings. The first ASP Annual Meeting was held 65 years ago at the University of Colorado at Boulder, Boulder, Colorado (CU). The 1960 meeting was held June 30 – July 2 in the Colorado University Memorial Center on the campus. The scientists and their families were lodged in the Libby Hall dormitory. Both of these buildings continue to serve the campus today. A reflection on that first ASP Annual Meeting is a window into the genesis and growth of today's dynamic Society.

Elodea canadensis, Menthap piperita, Atropa belladonna, Datura stramonium, and Lychnis alba.

Entertainment and socializing with colleagues, as well as making new friends, were considerable inspirations to attend the Plant Science Seminar Annual Meetings and ASP Annual Meetings. At the 1960 Annual Meeting, the Society ate together, took breaks together, and enjoyed sight-seeing on their caravan journey through the beautiful Rocky Mountain National Park, outside the town of Estes Park, Colorado. (In 1960, Estes Park was a popular hunting area and summer home destination.) From there, the ASP members ventured on to Horseshoe Park, enjoying the spectacular views of the continental divide and glacially-



The meeting schedule preceded the annual conference of the American Association of Colleges of Pharmacy, allowing members to attend both scientific assemblies. Notable scientists such as Drs. Maurice C. Andries, L. David Hiner, Curtis H. Waldon, Varro E. "Tip" Tyler, W. Paul Briggs, and Charles Bliven opened the first session. The scientists covered subjects still relevant today such as: pharmaceutical education; pharmacognosy textbooks; the importance of plant research in medicine; ecological issues; and, genetic research. In 1960 the Society's members were interested in the study of specific plants that continue to be important to pharmacognosists, such as *Vinca major*,

sculpted valleys. They traveled onward, enjoying a break at Hidden Valley Lodge, and driving on through Rainbow Curve, taking pleasure in views of numerous beaver dams and the resulting ecosystems. From Rainbow Curve they proceeded to the Forest Canyon Overlook, marveling at numerous cirques carved by the Big Thompson Glacier. Next was Iceberg Lake, offering views of Sundance Mountain and the rock streams, stone circles, and stone polygons formed by the freezing and thawing of glacial ice. They traveled through Fall River Pass, treasuring the vistas of how water and ice carved the Colorado landscape. The *continued on page 32*

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From the Archives: A Window Into Today's Dynamic ASP

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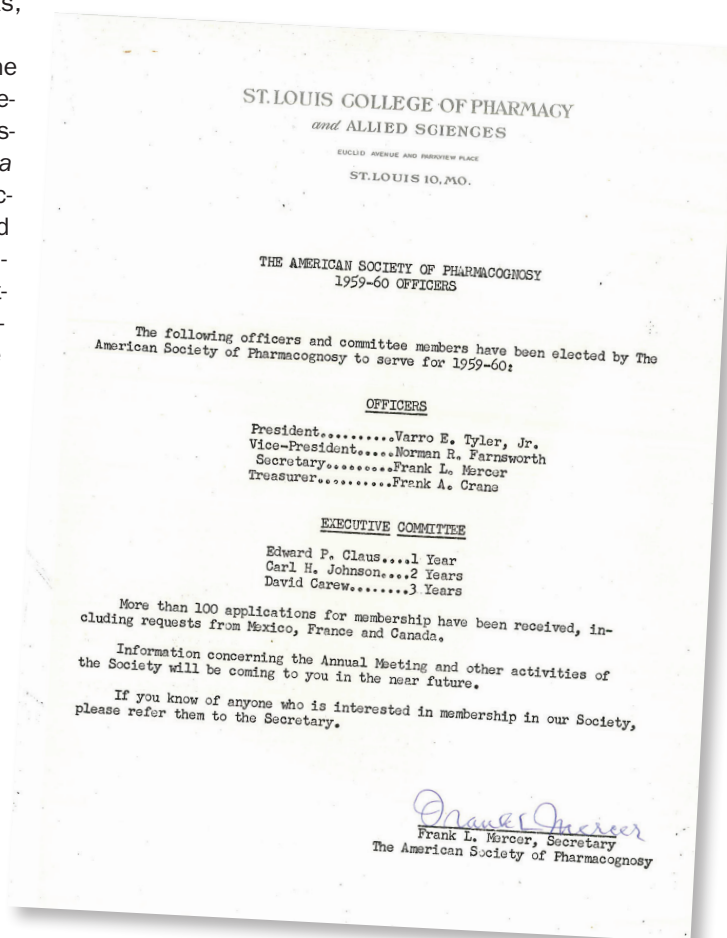
voy proceeded on through Milner Pass to the Continental Divide where they could enjoy the dichotomy between the geography of the eastern and western slopes. From this peak, the Society members relished the patterns of reseeding and re-vegetation from area fires. The return trip to Boulder offered the opportunity to see the panoramas in reverse order, culminating with the sunset at Rainbow Curve.

The 1960 ASP Annual Business Meeting followed the format similar to the agenda today, minus the option of receiving the minutes and reports on a USB drive. It began with an assessment of the first year of activities by President Varro E. "Tip" Tyler, followed by the ASP Committee Reports, and concluded with the nominations for officer elections, closing remarks, and adjournment.

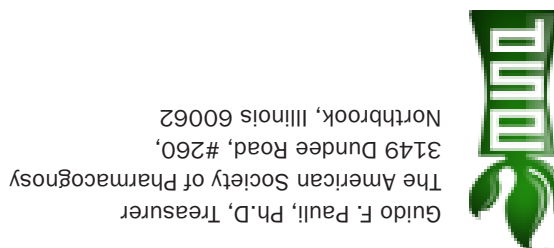
One of the most significant and enduring legacies of the 1960 ASP Annual Meeting was the quest for, and endorsement of, the Society's publication of *Lloydia*, now the esteemed *Journal of Natural Products*. The pursuit of *Lloydia* was initiated by President Tyler, advanced in the official recommendations from the ASP Publications Committee, and made a part of the ASP Constitution and By-laws. The committee asked for permission for the ASP Executive Committee to finalize negotiations with the Lloyd Library and Museum to co-publish and co-fund *Lloydia*. They suggested the following amendments:

- A. Article VI (5), A Publications Committee shall be appointed by the Executive Committee to be composed of an Editor, who will serve as chairman, and ten additional members who shall be known as the Editorial Advisory Board. The Editor and Editorial Advisory Board shall serve for five-year terms and may be re-appointed.
- B. By-Laws – Section IV (a), Annual membership dues of eight dollars (\$8.00) are payable during the last quarter of the fiscal year for membership in the Society for the following year and shall include a subscription to the official journal of the Society.

The wisdom of the Society's establishment of a scientific publication cannot be understated. In 2013, *The Journal of Natural Products* had an impact factor of 3.947 and 20,791 total citations. The *J. Nat. Prod.* has brought worldwide respect to the Society and broadened the scope of the ASP's membership. The Society's members can take pride in the distinguished history of their organization as they return to Colorado to learn, teach, and unite together along with the 2015 Annual Meeting theme, *Exploring the Fundamental Science and Applications of Natural Products in the Modern World*. ■



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Guido F. Pauli, Ph.D., Treasurer
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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.

Associate Membership

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

Current membership dues and Journal of Natural Products subscription rates can be found at www.pharmacognosy.us.

Emeritus Membership

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

Current membership dues and Journal of Natural Products subscription rates can be found at www.pharmacognosy.us.

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

Dr. Robert J. Krueger, Ferris State University · Dr. Roy Okuda, San Jose State University

Dr. James E. Robbers, Purdue University · Dr. Yuzuru Shimizu, University of Rhode Island

Dr. David J. Slatkin, Chicago State University · Dr. E. John Staba, University of Minnesota

Dr. Otto Sticher, Swiss Federal Institute of Technology

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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3149 Dundee Road, #260, Northbrook, Illinois 60062. Email: gfp4asp@gmail.com