ASP President Pearce Addresses Members

By Dr. Cedric Pearce

am grateful to the membership of the Society for giving me the chance to be President of The American Society of Pharmacognosy for the next year, and I thank you for trusting me with the position. I would also like to thank all of the committees and their members for their hard work that has resulted in the current position of the Society.

From our recent experience at the Annual Meeting in Portland, which included a lot of quality science, interesting talks, fun social events, and a beautiful location, we should conclude that the Society is sound with a strong body of fine accomplishments and members. The Foundation is strong under the continued leadership of Drs. Bob Krueger and John Cardellina, and we can

maintain funding student travel awards, Society prizes, and research support awards. There are many future opportunities as we continue to investigate the world of biologically active natural products, and a few challenges that we need to start to address with strategic input from our committee members.



1. The inclusion policy that was discussed at both the Executive Committee meeting, and then again from the floor during the business meeting is a key issue. Dr. Gil Belofsky and his



Dr. Cedric Pearce

- committee members have been charged with drafting a more comprehensive and explicit addition for the Society constitution to replace the current statement.
- 2. The finances of the *Journal of Natural Products*, profits from which have supported the Society for a number of years, were discussed by ASP Treasurer Dr. Jim McAlpine. The current strategy of our publishing partner, the ACS, is to expand the marketing presence of the publishing group into China and India, and this, initially, will be at a cost. The goal is to improve revenues through this expanded market, and subsequently improve profits to be shared with ASP. We need to continue to support *J. Nat. Prod.* with good manuscripts disclosing our best data so that the journal will prosper.
- **3.** We continue to make progress on the new website and will have this functioning as soon as we can. I have full confidence in Mr. Jason Evans, our new webmaster, and others involved, and expect good progress to be made. Many thanks to Drs. Barry O'Keefe and Ed Kennelly for pushing this item.

ASP Membership is strong. The enthusiastic Younger Members group is very active, and this year had a dedicated conference session as well as the traditional party. The ASP Fellows group is productive. I attended the ASP Fellows lunch and heard continued on page 3

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EDITOR'S CORNER



n this issue of the *Newsletter*, we welcome incoming ASP President, Dr. Cedric Pearce. His front-page story summarizes the many issues that ASP has been engaged in, and his vision for the future of the Society. I hope you will take some time to read this detailed analysis, and provide him with any feedback.

The ASP is saddened to report the loss of former ASP President Dr. Charles Hufford. Dr. Hufford passed away as we were going to press for the summer *Newsletter*, and I wanted to be sure to run a remembrance of him that did justice to all of his contributions to the field of pharmacognosy, as well as to the American Society of Pharmacognosy over

his many years as a key member of this Society. I think the comprehensive tribute by his former student, Dr. John Williamson, is a very fitting homage indeed. I last saw Dr. Hufford and his wife, ASP member and former President Dr. Alice Clark, at the 16th annual International Conference on the Science of Botanicals in the spring of 2016. Although Dr. Hufford had recently retired, I was struck by his continued interest and commitment to pharmacognosy research at the University of Mississippi.

Another milestone of a different sort has occurred at the ASP *Newsletter*. Dr. Amy Keller, who served for 11 years as the Assistant Editor of this publication, has decided to resign to spend more time on research. She was recently awarded a grant from the Veterans Administration, and I am very happy she will be able to focus more time on her research. However, I will miss working with Amy very much, and from the reactions I have heard from a number of ASP members who contribute to the *Newsletter*, they will miss her as well. Many noted her pleasant and professional way of interacting with *Newsletter* authors. We will advertise for a new Assistant Editor, and if you have any suggestions, please e-mail me at edward.kennelly@lehman.cuny.edu

The 2017 ASP Annual Meeting in Portland, Oregon was a huge success, and the highlights can be reviewed in Dr. Kerry McPhail's wrap-up article. She and the entire Organizing Committee are thanked for their considerable efforts to make this meeting so memorable. I also encourage you to read about the major award winners, including Dr. Guy Carter (Norman R. Farnsworth Research Award), Dr. Richard van Breemen (Varro Tyler Award), and Dr. Katherine Ryan (Matt Suffness Award). The significant contributions each of these scientists has made in the field of natural products is truly inspirational.

Our regular columns continue to provide the main framework for the *Newsletter*. Dr. Dave Newman's "Hot Topics in Pharmacognosy" covers in detail vancomycin that was introduced by Eli Lilly Company in the mid-1950s, and continues to be an important skeleton for new drug development. Dr. Georgia Perdue keeps us abreast of news from Washington, even as she has just gotten married. Georgia, congratulations! Thanks for always getting your article submitted on time, even when your life is extraordinarily busy. In "Meet a New ASP Member," we get to know better one of the invited speakers to the 2017 ASP Annual Meeting, Dr. Kenji Kurita. Dr. Kurita is a former student of ASP member Dr. Roger Linington, and we are very glad he decided to join the ASP. In "From the Archives," we learn more about Dr. George Pettit's groundbreaking trip in the early 1970s to the People's Republic of China. Dr. Pettit, an avid photographer, even managed to dig up some vintage photos from this trip.

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/jobs/

NEWSLETTER STAFF

Edward J. Kennelly, Ph.D. *Editor-In-Chief*

Nancy Novick
Design & Production

Devhra BennettJones Gordon Cragg, Ph.D. Kevin Tidgewell, Ph.D. ASP Newsletter Committee

The contribution deadlines are: Spring Issue Feb. 15 Summer Issue May 15 Fall Issue Aug. 15 Winter Issue Nov. 15

Please send information to: Edward J. Kennelly, Ph.D.

Edward J. Kermeny, Ph.D.
Editor In Chief, ASP Newsletter
Department of Biological Sciences
Lehman College, CUNY
250 Bedford Park Blvd. West
Bronx, NY 10468
718-960-1105

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ASP President Pearce Addresses Members

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first hand about their commitment to sharing their experience. In particular they are aware of the challenges faced by the Society's younger members in the process of establishing themselves and their careers. Having Fellows write articles for the *Newsletter* was discussed at length; the article that Dr. Jon Clardy wrote about the history of the ICBG program and the subsequent effect at an international level on natural products research was very interesting; it was also distressing to learn of its demise. We should expect to see more from Fellow's essays in future *Newsletters*.

It was pointed out by one of our distinguished members that as a group we are great at the discovery of new biologically-active products with the potential to address unmet needs, but have not always been successful in moving these forward. We have exceptions and some members have managed to have their discoveries commercialized. Exactly how this is done is not science. It usually involves resources that we are less familiar with. Howev-

of a strong Society; I would like to thank everyone again for inviting me to these functions.

What about the future of pharmacognosy—politician's understanding of science is not to be relied upon—members need to be vigilant about protecting the data that we generate, in the past, now, and from research in the future—and how this will be of value to society, whether it is a new medicine, a novel agrochemical, or a better understanding at the molecular level of how organisms interact? In order to communicate to the general public we need to be familiar with simplified descriptions of what we do. If you have ever pitched an idea to a group of potential investors then you will be familiar with the format; it is called "The Elevator Pitch," and typically lasts a couple of minutes. Describing how the structure of a new natural product is elucidated within a 2 minute framework is very difficult and involves a lot of short cuts, similarly with the mechanism of action of a new medicine. Tales about traditional medicine are conceptu-

We should conclude that the Society is sound with a strong body of fine accomplishments and members.

er with input from the more experienced members, which possibly could be shared through the *Newsletter*, we can become more entrepreneurial. ASP Secretary Dr. Nick Oberlies and I have been giving workshops on science entrepreneurship to natural products groups for the past few years, including at the ASP annual meeting at Copper Mountain. We have also organized a symposium, "Natural Products and Entrepreneurship," for the ACS regional conference in Charlotte this November. Our main goal with these workshops/symposia is to raise the awareness, especially of younger scientists, to non-traditional career opportunities.

As you all know, in spite of the Society being called The American Society of Pharmacognosy, we are and always have been an international group. There were scientists from 28 countries at the conference this year, emphasizing the international flavor of the ASP. We have well over 100 members from the Brazilian Society of Pharmacognosy as members of ASP. A lot of us travel to other pharmacognosy society's conferences, and many of us collaborate internationally. I plan to attend the Korean Society's annual meeting in November. We should make sure that we maximize the opportunity to collaborate with our international members, and I plan to establish an ad hoc committee including international members to look into ways that we can do this.

On the last day of the conference Dr. Ed Kennelly invited me to the *Newsletter* Committee lunch with Drs. Gordon Cragg and Kevin Tidgwell at the excellent Mother's Bistro. Outgoing Assistant Editor Dr. Amy Keller called in; she will be continuing to write articles for the *Newsletter*, and Ms. Devhra BennettJones called in to briefly discuss such topics as shelf space for ASP archives at the Lloyd Library. We also went through the outline of articles for the next edition. It was a noisy meeting, but very productive (and delicious).

All of the above helped me understand the significance of what is going on as well as how it integrates into the functioning

ally easier for the average person to grasp than a description of how a particular medicine was discovered and how it works. Some ideas about how to approach this could be the subject of a future article.

Biodiversity and environmental issues are tied up with the future of what we do. Coral reefs, where a number of our members search for new chemistry, are at serious risk. One reason I recently learned SCUBA was to see these marine wonders before they all disappear. The plants in tropical rain forests are continually being cut down, and the land used for farming. We need to explore these environments while they are still available to be explored. Again, we need to work with our international members.

And this brings to mind the ninth and final point that I wanted to cover during the business meeting. In many ways it is the biological activity inherent in many natural products that makes pharmacognosy so exciting to study. This is too important an issue to gloss over here and I intend to write further about this for a future edition of the *Newsletter*.

I consider us a fearless group of scientists and explorers. Recall the talk from Dr. Bill Baker, and others who have searched the world for new medicines, exposing themselves to obvious risks, e.g., large predators, and hidden risks, e.g., microscopic parasites. For many of us, the more toxic the venom, the more attractive the organism. The adventures are endless and many good stories have been told. Former ASP Honorary Member Dr. Albert Hofmann accidentally discovered the biological activity of LSD, a compound that he had synthesized, and then repeated the experiment on himself to be sure of the results. He then repeated this on volunteers from his lab—in the 1940s these were true pioneers who could only be incredulous about the potency of this derivative.

The world is lucky to have us. Keep up the good work! ■

I consider us a fearless group of scientists and explorers.

In Memoriam: Charles D. Hufford

By Dr. John Williamson

long-time member and past President of ASP and champion of pharmacognosy and natural products chemistry, Dr. Charles D. Hufford died May 15, 2017 at the age of 72. He is survived by his wife, ASP member and past President. Dr. Alice Clark.

A friend and colleague of both Drs. Hufford and Clark for many years, ASP President Dr. Cedric Pearce wrote, "I was greatly saddened when I learned of Charlie's passing, as were many others. Professor Hufford, Charlie, was such a great supporter of the Society and served as President in 1996-1997. He made many significant contributions to both pharmacognosy and the ASP, touching many of us with his cheerful but businesslike approach. I enjoyed interacting with him when visiting Ole Miss, attending ASP conferences, and other natural products and infectious diseases meetings. I know that we'll all miss him, but especially Alice, who has my deepest sympathy."

Born in Sycamore, Ohio, Dr. Hufford earned both his pharmacy degree (1967) and Ph.D. (1972) from The Ohio State University and served as a pharmacist in the Air Force Reserve. At the time of his death, Dr. Hufford was an associate dean emeritus for research and graduate programs and professor emeritus of pharmacognosy at the University of Mississippi School of Pharmacy. His career as a researcher officially spanned 1972 to 2015, but Dr. Hufford never really retired and was commonly seen checking in on the School's exceptional NMR facility, which he had created four and a half decades earlier.

Dr. Hufford was a fixture in ASP serving in virtually every leadership position in the Society at one time or the other, including President. Known as a gentle giant among his peers and students, he was well respected as a researcher and as a leader in the field of pharmacognosy.

Dr. Hufford's research was varied-beginning with his time as a student working



Professor Charles Hufford and his wife, Profesor Alice Clark, in their laboratory at the University of Mississippi.

COURTESY OF THE UNIVERSITY OF MISSISSIPPI SCHOOL OF PHARMACY

with the southwestern ragweed plant Ambrosia ambrosioides and discovering the sesquiterpene, damsinic acid with Dr. Ray Doskotch at The Ohio State University College of Pharmacy—to the antileishmanial activity of manzamine alkaloids from the marine sponge Acanthostrongylophora ingens. His interests also included the use of herbal remedies long before the surge of their use leading to the Dietary Supplement Health and Education Act of 1994.

During his career he concentrated on

and postdocs and was the consummate teacher, from his undergraduate courses in dietary supplements and antibiotics to his graduate courses in advanced NMR strategies. Although his students were always keenly aware of his expectations of excellence, they knew he would always be around to provide guidance for achieving it. During my days as a pharmacy student, Dr. Hufford was respected as being stern but fair as a professor, a rare distinction among the students. Former graduate students can

Known as a gentle giant among his peers and students, he was well respected as a researcher, and as a leader in the field of pharmacognosy.

isolating compounds with antibiotic activities from compounds found in higher plants, using fungi as predictors of mammalian drug metabolism, isolating and characterizing antifungal compounds effective against opportunistic infections, and discovering new agents for systemic Candida and Cryptococcus infections. Dr. Hufford was also one of the principal investigators of the National Institutes of Health's New Drugs for Opportunistic Infections grant that was funded for 25 years at the University of Mississippi.

Dr. Hufford loved working with students

expound on many nightmarish tales of his cumulative exams with arrays of complex spectral data from which one was required to derive a chemical structure. Mr. Frank Wiggers, his friend and colleague for many years at the University of Mississippi, said it best, "He was an accomplished and admired professor and administrator who had a knack for making those under him better employees and colleagues."

Dr. Hufford was both clever and practical when it came to the lab. As Dr. Dave Rotella, a young assistant professor at the continued on page 5

Dr. Hufford was not just dedicated to the field of pharmacognosy but also to making the University of Mississippi a national hub for natural products research.

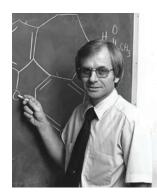
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time pointed out about one of their joint projects: "We were using a natural product as a starting point for structure-activity studies as a calmodulin antagonist, instead of buying the material from Sigma (\$400/100 mg). Charlie worked with a student to cultivate and optimize the organism that produced it so that soon we had grams of material."

Although Dr. Hufford rarely showed emotions as a researcher he did have one trait that would have made him a poor poker player, as former faculty colleague Dr. Mark Hamann recalled: "I first noticed one of his signature traits, his expression of emotion by ringing his hands together." Dr. Mitch Avery, another colleague, once noted that it was easy to tell when Dr. Hufford had just met with a dean based on his hand gestures alone.

pi faced in regard to budgets, the State's health disparities, controversial academic standards, the athletic program's issues and controversy, the pharmacognosy program served as an oasis that seemed as if it would endure forever. Indeed the dissolution of the Pharmacognosy Department

and Charlie's passing seem one and the same. Charlie's commitment to Pharmacognosy, NMR spectroscopy, and high academic standards were clearly a cornerstone and enduring strength of research and graduate education programs at the University of Mississippi. The strength and endurance of pharmacognosy at Ole Miss can clearly be attributed to Charlie's com-



sociation, logged more than 30 perfect games, and was a member of both the Senior All Star Bowling Association Hall of Fame and the Mississippi State Bowling Association Hall of Fame. In his and Alice's zeal for softball, he once coached a team during which she fractured her arm early in a game but stayed in to finish

the game with a win.

Over the years, I have personally heard many wonderful stories filled with respect, humor, and admiration of the Alice and Charlie team from so many well-known ASP members including Drs. Jack Rosazza (my own Ph.D. advisor), Norm Farnsworth, Dave Slatkin, Lynn Brady, Doug Kinghorn, Jon Clardy, Jim McChesney, John Beutler,

During his career he concentrated on isolating compounds with antibiotic activities from compounds found in higher plants, using fungi as predictors of mammalian drug metabolism, isolating and characterizing antifungal compounds effective against opportunistic infections, and discovering new agents for systemic Candida and Cryptococcus infections.

Dr. Hufford was not just dedicated to the field of pharmacognosy but also to making the University of Mississippi a national hub for natural products research. As Dr. Hamann puts it. "Charlie's most unique feature was his undaunted and tireless support for pharmacognosy at Ole Miss." Until very recently his efforts and commitment led to perhaps one of the longestrunning and independent departments dedicated to pharmacognosy. During Charlie's leadership as Chair and later as Associate Dean, the department reached the remarkable achievement of full retention of 100% of its faculty during a two-decade stretch. During this period countless students joined the program wide-eyed and highly enthusiastic about the promise of great discoveries to be made by traveling to exotic locations and curing human disease with natural products. Despite the many challenges that the University of Mississip-

mitment to his students, faculty and pharmacognosy colleagues."

No one in the field of natural products can think of Dr. Hufford without his research partner and spouse of 32 years, Dr. Clark. They were a formable team in the advancement and recognition of pharmacognosy. In 1980 I was a student worker in their lab, and it didn't take me long to see that these two were a unique pair in their love for each other and the science they were so very dedicated to.

Outside of the lab it was hard to know Dr. Hufford without knowing his infatuation with sports, especially softball and bowling. He was a competitive bowler who approached the sport as he did everything else: with commitment to constant improvement. In the University of Mississippi's remembrance, it was pointed out that Charlie actually held 10 championship tournament titles with the Senior All Star Bowling As-

Geoff Cordell, Mark Hamann, Dave Rotella, Heinz Floss, Dave Carew, Jack Beale, Farouk El-Feraly, Pat Davis, and Larry Robinson, to name only a few. Dr. Hufford, with his calm rational ways, was an easy man to like and remember.

For me, not only do I owe my introduction to pharmacognosy to Alice, Charlie, and Jim McChesney, I am indebted to the encouragement they have given me for the past 37 years. My own words echo those spoken in Dr. Hufford's eulogy given by Mr. Wiggers: "The ripples Charlie Hufford cast upon this earth will go on for a very long time."

Alice, our thoughts and prayers are with you. ■

Memorial contributions in Dr. Hufford's memory may be made to Charles D. Hufford Graduate Student Fellowship Endowment, The University of Mississippi Foundation, 401 University Ave., Oxford, MS 38655.

2017 ASP Annual Meeting Wrap-up

By Dr. Kerry McPhail

memorable 58th ASP Annual Meeting was had by all accounts from those who ventured west to join the "Natural Product Corps of Discovery" in Portland, Oregon. The Organizing and Scientific Committee members thank the 529 attendees representing 28 countries, sponsors and exhibitors, as well as presenters, who collectively made for such a successful and inspiring meeting at the Hilton Downtown Portland.

There were five well-attended pre-meeting Saturday workshops that comprised two consecutive half-morning sessions (scientific writing and anticancer mechanisms of action), two parallel afternoon sessions (grant writing and natural product extraction to elucidation), and one all-day session (applications of NMR).

The first three days of meetings from Sunday to Tuesday featured invited symposium speakers each morning from Belgium, Hong Kong, and Japan, and all across the United States, who expertly represented the conference theme of "Venturing into the Unknown," both in terms of technological and geographical/ecological frontiers. Contributed and invited presentations in two parallel afternoon symposia were engagingly delivered by a broad and diverse natural products community from academia, education, government, and industry, and the lively discussions elicited continued on in the two dynamic poster sessions.

The Awards Symposium on Wednesday morning comprised six lectures. The Norman R. Farnsworth ASP Research Achievement Award was given this year to Dr. Guy Carter, currently of Biosortia Pharmaceuticals, who shared with us thirty years of perspective on natural products in big pharma. Dr. Richard Van Breemen received the Varro Tyler Prize for his extensive work on standardization, safety and efficacy of botanicals at University of Illinois, Chicago. A special mention must be made of the exceptional poise and focus of this year's recipicontinued on page 7







2017 ASP Annual Meeting Wrap-up



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ent of the Matt Suffness Award: amidst repeated fire alarms and ensuing announcements due to a technical fault in the hotel system, Dr. Katherine Ryan (University of British Columbia) gave a superb lecture on her work on cofactors in natural products biosynthesis.

After Dr. Ryan's eventful lecture, the remaining award presentations proceeded smoothly with Fatma Alawadhi (Kilmer Prize), Samantha Gromek (Student Research Award), and Siddharth Tripathi (John Faulkner Travel Award).

The social program included an outing to the Oregon Museum of Science and Industry on Monday evening, where great company and conversation was augmented for many by experiencing Pompeii: The Exhibition. On Tuesday evening, 160 attendees gathered at the Punch Bowl Social for the Younger Members' event. This appears to be the largest younger member event at any ASP meeting, with many reports of an excellent career guidance panel discussion accompanied by great food and atmosphere.

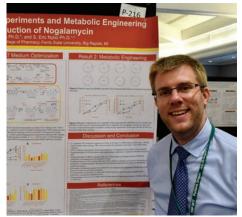
The meeting closed with the final banquet on Wednesday evening, at which Drs. Barry O'Keefe and Nick Oberlies surely outdid themselves in the witty



roasting of two (one past, one outgoing) ASP presidents: Drs. Edward Kennelly (2015-16) and Cindy Angerhofer (2016-17). Incoming ASP President Dr. Cedric Pearce has much to look forward to at the upcoming ASP 2018 meeting in Lexington, Kentucky, where we hope to see you all again. ■















ASP Award Winners 2017

The Newsletter wishes to recognize and congratulate all ASP award winners. Best wishes and congratulations to all.

Norman R. Farnsworth Research Achievement Award

Guy Carter

Biosortia Pharmaceuticals

Varro E. Tyler Prize

Richard van Breemen

University of Illinois at Chicago

Matt Suffness Young Investigator Award

Katherine Ryan

University of British Columbia

D. John Faulkner Travel Award

Tripathi Siddhartha

University of Mississippi

Travel Grant for Active Members

Jana Braesel

University of Illinois at Chicago

Skylar Carlson

University of Wisconsin Madison

Jie Li

Scripps Institute of Oceanography

Erin McCauley

University of California Santa Cruz

Charles Naman

Scripps Institute of Oceanography

Jerry McLaughlin Student Travel Award

Laura Bocanegra

National Auto. University Mexico

Lynn Brady Student Travel Award

Emily Britton

University of North Carolina Greensboro

Zhibin Liang

University of Hawaii, Manoa

Logan MacIntyre

University of Prince Edward Island

Nathan Moss

Scripps Institute of Oceanography

David Carew Student Travel Award

Manuel Rangel-Grimaldo

National Auto. University Mexico

ASP Kilmer Prize

Fatma Alawadhi

University of Florida

Student Research Award

Samantha Gromek

University of Connecticut

Research Starter Grant

Matthew Bertin

University of Rhode Island

Laura Sanchez

University of Illinois at Chicago

Katharine Watts

Cal Poly, San Luis Obispo

Jaclyn Winter

University of Utah

Tyler Johnson

Dominican University of California (2016 Recipient)

Suthananda Sunassee

University of Cape Town (2016 Recipient)

Undergraduate Research Award

Abo Aoun Mohamed, University of Winnipeg Haylee Padget, University of Oklahoma

Andrew Whiteley, Cal Poly, San Luis Obispo

Wagar Bhatti Student Travel Award

Anam Shaikh, UT Southwestern Medical Center

Student Travel Award

Lindsay Caesar, University of North Carolina Greensboro Chase Clark, University of Illinois at Chicago Camila Crnkovic, University of Illinois at Chicago

Maryam Elfeki, The University of Illinois at Chicago Jake Haeckl, Simon Fraser University

Christopher Leber, Scripps Institute of Oceanography Catherine McCaughey, Simon Fraser University Corena Shaffer, UT Health Science, San Antonio

Mariam Salib, University of California, San Diego

Hannah Whitmore, University of Surrey

Fabien Schultz, Technical University of Berlin er Ruiz Vargas. Centro de Investigación Científica de Yuc

Javier Ruiz Vargas, Centro de Investigacion Cientifica de Yucatan (2016 URG Recipient)

2017 Arthur E. Schwarting Award

Per Juel Hansen & Thomas Ostenfeld Larsen's manuscript, "Silas Anselm Rasmussen, Sebastian Meier, Nikolaj Gedsted Andersen, Hannah Eva Blossom, Jens Øllgaard Duus, Kristian Fog Nielsen, Per Juel Hansen,* and Thomas Ostenfeld Larsen.* Chemodiversity of Ladder-Frame Prymnesin Polyethers in Prymnesium paryum. J. Nat. Prod. 2016. 79, 2250-2256"

2017 Jack L. Beal Award

Adam S. Duerfeldt's manuscript, "Nathan P. Lavey, Jesse A. Coker, Eliza A. Ruben, and Adam S. Duerfeldt.* Sclerotiamide: The First Non-Peptide-Based Natural Product Activator of Bacterial Caseinolytic Protease P. J. Nat. Prod. 2016, 79, 1193-1197"

Stephen Chamberland's manuscript, "Stephanie J. Conn, Shannon M. Vreeland, Alexandra N. Wexler, Rebecca H. Pouwer, Ronald J. Quinn, and Stephen Chamberland.* Total Synthesis of *Clavatadine A. J. Nat. Prod.* **2015**, 78, 120-124." – (2016 Recipient)

Carter Receives Farnsworth Award

By Dr. Leonard McDonald

r. Guy T. Carter was honored with the Norman R. Farnsworth Research Achievement Award on August 2, 2017 at the annual meeting of the American Society of Pharmacognosy in Portland, Oregon. This prestigious award is given to a member of the Society who has made "outstanding contributions to research on natural products."

ASP President Cedric Pearce commented, "Guy has been a leading natural products researcher for over three decades, successfully exploring terrestrial and marine organisms, and later in his career leading one of the most productive industrial groups. His reputation is international. I consider myself very fortunate to have him both as a friend and past colleague and congratulate him for winning the Norman Farnsworth Research Achievement Award."

Dr. Carter received a Ph.D. in Biochemistry from the University of Wisconsin-Madison and pursued marine natural products research as a post-doctoral fellow with Prof. Kenneth Rinehart, University of Illinois ASP President, 1995-1996, who encouraged him to become more involved with the ASP. Since then Dr. Carter has served the Society in various roles including Executive Committee member (1998-2001) and President (2008-2009), and was inducted as an ASP Fellow in 2013.

He has over 30 years of experience working in Pharmaceutical R&D, primarily in the discovery and development of microbial products for use as potential agricultural, anticancer, antimicrobial, and immunosuppressive agents. From his start at Lederle/Cyanamid as a natural products scientist, Dr. Carter advanced through various levels of scientific management to the leadership of the Natural Products Discovery program at Wyeth Research (now part of Pfizer); his responsibilities were later expanded and



Dr. Guy Carter, (left), being presented the Farnsworth Achievement Award art work by ASP President Cindy Angerhofer and ASP Foundation Chair. John Cardellina.

RICHARD TEHAN

he was named Assistant Vice President of Chemical Technologies. Dr. Carter is currently CEO of Carter-Bernan Consulting, LLC, and Chief Scientific Officer at Biosortia Pharmaceuticals.

In his award lecture entitled "Natural Products in Pharma 1980-2010: A Personal Perspective," Dr. Carter presented an overview of the evolution of industrial natural products research, focusing on his and his teams' efforts—from antibiotics at Lederle Labs, to agricultural agents (crop protection and animal health) at American Cyanamid, to anticancer and antibiotic compounds at Wyeth. Among early discoveries by Dr. Carter and his teams were a series of antiparasitic macrolides in the nemadectin class from which the semisynthetic anthelmintic moxidectin was derived; dioxapyrrolomycin which inspired the synthesis of chlorfenapyr (Pirate®), a pyrrole insecticide used in agriculture with potential utility in a malaria prevention product; and ganefromycin, an elfamycin class of narrow-spectrum antibiotic acting as a growth promoter in livestock by inhibiting protein synthesis via impairment of elongation factor Tu function.

Following the earlier successes in the agriculture area, Dr. Carter spearheaded the so-called "Look-Back" program strategy that was implemented at Lederle/Cyanamid/Wyeth between 1996 and 2003. The program was designed to find new antibiotics to combat emerging resistant organisms. By focusing on leads acquired over 50 years at Lederle/Cyanamid and using newer separation and spectroscopic technologies, Dr. Carter and his team fully characterized the structures of several antibiotic classes including the translocase-inhibiting uridyl peptide muraymycin antibiotics, the saccharosamine-containing continued on page 10

He has over 30 years of experience working in Pharmaceutical R&D, primarily in the discovery and development of microbial products for use as potential agricultural, anticancer, antimicrobial, and immunosuppressive agents.

Carter Receives Farnsworth Award

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saccharomicin, and the transglycosylase-inhibiting mannopeptimycin glycopeptides. From the last class a viable semi-synthetic pharmaceutical lead was identified, and served as an example that showcased the synergy that can be achieved between natural products isolation and semi-synthetic derivatization.

Dr. Carter further described the Wyeth team's efforts with internal collaborators: Drs. Philip Frost, Lee Greenberger, Valerie Bernan, Michael Greenstein, and Semiramis Ayral-Kaloustian, and external: NCDDG-Dr. Raymond Andersen, U. of British Columbia, Dr. Chris Ireland, U. of Utah, Dr. Jon Clardy, Harvard, and ICBG Dr. Louis Barrows, U. of Utah, in collaboration with U.

of Papua New Guinea to access diverse microbes for the generation and screening of novel natural products. Collaboration with Dr. Raymond Andersen's group (UBC) resulted in the biological profiling of the antitubulin agent hemiasterlin, which led to the discovery of HTI-286, an anticancer agent that progressed into clinical studies.

A similar collaboration with Dr. Ireland's group (University of Utah) led to the search for an elusive enediyne isolated by the Utah group. In an effort to find the putative microbial producer of namenamicin, the first enedivne isolated from a marine tunicate. the team embarked on studies to isolate and culture the microbial inhabitants of the tunicate. While the enediyne was never isolated from an isolated microbe, a number of microbes were isolated and cultured to produce interesting natural products, the most interesting of which is the exquisitely active DNA-cleaving diazobenzofluorene glycoside Iomaiviticin A. Finally, the ICBG collaboration with Dr. Barrows was established to access, isolate, and culture endophytes to increase the diversity of the strain collection. A number of endophytic



Dr. Guy Carter with former colleague Dr. Leonard McDonald at 2017 ASP Annual Meeting

actinomycetes from tropical plants were isolated and characterized to reveal some rare and novel genera among the isolates which remain part of the Pfizer collection.

The final part of the talk related to the discovery of analogs of the immunosuppressive agent rapamycin with new indications. Dr. Carter described the team's efforts in discovering and synthesizing ILS-920, a non-immunosuppressive neurotropic rapamycin analog with indications for stroke. Mechanistic experiments showed that the new "rapalog" bound to FKBP52 and not to the rapamycin binding target FPBP12. Additional efforts spearheaded by Dr. Carter and his group include the engineered substitution of various functionalities in the rapamycin molecules including the cyclohexane starter unit, the piperidine ring, and various macrocyclic tailoring. A new source of diverse rapalogs was accessible via collaboration with Biotica (Isomerase) using starter unit knockout mutants that produced novel compounds when fed suitable starter units. Furthermore, a general approach, coined "accelerated evolution" of modular gene clusters, afforded both ring-contracted and ring-expanded rapamycin analogs.

Themes of sustained excellence, persistence, flexibility, and collaboration in science emerged during Dr. Carter's talk. He has a reputation as a productive natural products scientist with broad experience in pharmaceutical R&D. His accomplishments show that a willingness to adapt to changing corporate cultures and project priorities is one of the best ways to succeed in pharma.

Dr. Carter is quick to credit his success to working effectively with colleagues and collaborators and modestly credited Wyeth colleagues—Drs. Donald Borders, Gerhard Schlingmann, Anokha Ratnayke, Magid Abou-Gharbia, Leonard McDonald, Fangming Kong, Haiyin He, Valerie Bernan, Edmund Graziani, Min He, Mr. Jeffrey Janso and others in his talk,

stating: "I am truly grateful to the ASP for the recognition that the Farnsworth Award represents. I am deeply indebted to dozens of co-workers who were responsible for the bulk of the discoveries that were made at Lederle/Cyanamid and Wyeth, and I share this honor with them."

As consistent with his reputation for excellence in natural products research, Dr. Cindy Angerhofer, outgoing ASP President, concisely summed up Dr. Carter's achievements in a statement: "Sincere congratulations to Guy in winning the NRF Research Achievement Award! The breadth and depth of his career has touched many areas of natural products research, and his discoveries continue to deliver potential for additional success. I'm so happy that such a valued member of the Society has been recognized for his accomplishments with this premier award."

From a perspective of working with Guy for over 16 years and knowing him for over 24 years, he is a strategic thinker and does excellent, curiosity-driven science. I whole-heartedly congratulate Guy on receiving this award.

The breadth and depth of his career has touched many areas of natural products research, and his discoveries continue to deliver potential for additional success.

Van Breemen: Tyler Award Recipient and New Director of Linus Pauling Institute

By Dr. Edward Kennelly

SP member Professor Richard van Breemen of the University of Illinois at Chicago (UIC) was presented the Varro Tyler Award at the 2017 ASP Annual Meeting in Portland Oregon on August 2. Less than two weeks later, his appointment as the new director of the Linus Pauling Institute was formally announced by Oregon State University.

ASP President Cedric Pearce commented, "Professor Richard B. van Breemen is such an appropriate Varro E. Tyler Prize winner, and the Society is very fortunate to have him as a member. He has worked on botanical dietary supplements and natural products his whole career; data generated by him and his colleagues has developed our understanding of so many natural products, and impacted the lives of ordinary people everywhere. Varro Tyler would be very happy with our selection of Richard for this award. We look forward to Dr Brennan's continuing to be involved with the ASP and to discussing his latest data with him at our annual conferences."

Dr. van Breemen became the Director of the UIC/NIH Center for Botanical Dietary Supplements Research in 2011, succeeding Professor Norman Farnsworth, the first Vice President of ASP. Dr. van Breemen's award lecture, "From Botanical Authentication through Clinical Evaluation, Safety, and Efficacy of Botanical Dietary Supplements" covered a wide range of botanically inspired research that he has been part of for several decades.

During his Tyler lecture, Dr. van Breemen reflected upon his long career in natural products and biomedical research, beginning with his doctoral advisor, Dr. Catherine Fenselau (Johns Hopkins University School of Medicine), and postdoctoral mentor Dr. Robert Cotter, also at Hopkins, who played a major role in his approach to biomedical questions using state-of-the-art techniques in mass spectrometry.

Carotenoids have been a major focus of Dr. van Breemen's career, and he worked diligently to enhance the accurate quan-



Dr. Richard van Breemen being presented the Tyler Prize artwork.

RICHARD TEHAN

In his Tyler talk, Dr. van Breemen also discussed the many botanical dietary supplements he has worked on as part of the UIC/NIH Center. The Center focuses on botanicals for women's health.

such as Angelica sinensis, Humulus Iupulus, Actaea racemosa, Valeriana officinalis, and others. His research includes the metabolism and safety of selected botanicals in women, such as PK analysis, influence of botanicals on P450s, botanical metabolism, and safety testing. He noted that one of the greatest legacies of the UIC Center has been the number of scientists that have trained in botanical research, including 51 graduate students and more than 50 postdoctoral researchers.

Van Breemen said, "I am grateful to the American Society of Pharmacognosy and honored to receive the Varro E. Tyler Prize

He has worked on botanical dietary supplements and natural products his whole career; data generated by him and his colleagues has developed our understanding of so many natural products, and impacted the lives of ordinary people everywhere.

tification of carotenoids in biological samples using APCI LC-MS techniques. He discussed working with Dr. Clive West (Wageningen University) to develop a stable isotope labeling approach to resolve the issue of beta-carotene bioavailability and bioconversion to retinol. He also developed plateau isotope enrichment for more accurate results. For example, in a study published in 2001 of Indonesian school-aged children provided labeled beta-carotene in sunflower oil, Dr. van Breemen and colleagues found that the bioefficacy of beta-carotene was 27% better than that estimated by the World Health Organization, but 20% worse than that estimated by the US IOM.

for my translational research concerning botanical dietary supplements."

Shortly after the ASP Annual Meeting, Dr. van Breemen was named as director and endowed chair of the Linus Pauling Institute at Oregon State University in Corvallis. The research programs at the Linus Pauling Institute include the examination of the role that vitamins, essential minerals, and phytochemicals play in human aging, immune function, and chronic disease. Dr. van Breemen is scheduled to begin his position on January 1, 2018. The ASP congratulates him both for this Tyler Award and for his new position!

Art for ASP Awardees

By Dr. Barry O'Keefe

he Norman R. Farnsworth Research Achievement Award and the Varro E. Tyler Prize for Research on Botanicals are the highest awards bestowed by the ASP. Along with a monetary honorarium, the recipients of these awards have traditionally been given a plaque or clock as a sign of the esteem from the ASP. This year, and in future years, the ASP has decided to provide a more personal touch to the awards. Both awardees at the ASP Annual Meeting in Portland received framed original artwork inspired by their research achievements.

The ASP Foundation commissioned two print artists, Mr. Barry W. O'Keefe and Mr. Jacob Parker, to provide original pieces for the Farnsworth and Tyler Awardees, respectively. The selected artists had responded to an ASP Foundation call for proposals. They were provided with the nomination files for each award recipient as well as their contact information and photographs. The art was left to the individual artist's interpretation—to be inspired by the research of the recipient scientists.

Mr. O'Keefe is an artist from Richmond, VA. He works in a variety of media including woodcut, letterpress, bookmaking, murals, and public sculpture. Mr. O'Keefe has exhibited nationally and internationally, and his work can be found in several institutions including the Valentine Museum in Richmond VA, the Black History Museum of Virginia, the Library of Virginia, and El Mina University in Egypt.

Of his work for the Norman R. Farnsworth Research Achievement award, Mr. O'Keefe stated, "In researching Dr. Guy Carter's work I was attracted to images of the different microorganisms referenced in his published articles. [Many of these microbes bear a strong resemblance to pills of different shapes and sizes, and their ghostly outlines and transparent forms, when photographed through a microscope





O'Keefe art work top; Parker art work below.

O'Keefe



Parker



which reminded me of cyanotypes, an early photographic process.] The title, a Latin binomial, translates to 'The Bountiful Ocean' or 'The Generous Ocean,' a reference to Dr. Carter's conviction that the marine environment is a great laboratory for drug discovery, an enormous resource whose potential must be unlocked, and whose diversity must be preserved."

Mr. Parker is a printmaker from Wilmington, NC. He received a Bachelors in Fine Arts from East Carolina University in 2014 and is currently finishing his Masters in Fine Arts at Ohio University in Athens, OH. His work has been exhibited in juried exhibitions and print publications nationwide.

Of his work for the Varro E. Tyler Prize Mr. Parker states, "Larks, the bird featured prominently in this print, is considered the 'Bird of Discovery.' In mythology, they herald the dawning of a new day and the hope it brings. The lark is carrying budded hops in his talons. While hops figure in some of Dr. Richard van Breemen's research, they are also symbolic of healing and peace of mind."

Mr. Parker's work produced a screen print in which every color is hand drawn using a brush and India ink. Every color was printed separately by hand with varying amounts of transparency and overlap to produce new colors and subtle blends.

The artists also provided a limited production of 100 numbered, signed prints of each of the award artworks; these were for sale at the ASP meeting and can now be purchased through the Society. In addition, both the artists and the awardees along with the art will be featured on the ASP website

It is anticipated that this program of matching art and outstanding science will continue in the future with new artists selected each year. We hope the members of the ASP will support this new initiative and that it will add an innovative aspect to our Society.

Two Fire Alarms Herald Suffness Awardee Ryan's Hot Research

By Dr. Alessandra S. Eustaquio

he recipient of this year's Matt Suffness Award was Katherine S. Ryan of the University of British Columbia. The Matt Suffness Award recognizes outstanding contributions by young investigators and ASP members. Her award talk, "Using Cofactors in New Ways in Natural Products Biosynthesis," was on August 2, and afterward she was presented with the award by ASP President Cindy Angerhofer and ASP Foundation Chair Dr. John Cardellina. In between, two fire alarms sounded

that left the young investigator unfazed.

Dr. Ryan said, "I'm grateful to the ASP for recognizing our work; it's especially exciting to receive an award in honor of Matt Suffness, who played an important role in the development of taxol."

Dr. Ryan has a B.S. with honors in Biological Chemistry from the University of Chicago, and a Ph.D. in Biophysical Chemistry and Macromolecular Structure from Massachusetts Institute of Technology with Professor Catherine Drennan. After being a Merck-sponsored, Life Sciences Research Foundation postdoctoral fellow with Professors Bradley Moore and Julian Davies, Dr. Ryan joined the faculty of the University of British Columbia in 2011, where she was re-

cently promoted to Associate Professor in the Department of Chemistry.

Dr. Ryan's research seeks to understand biological routes to construct unusual chemistry. During this year's ASP annual meeting, she presented two stories covering enzymes that use cofactors in unexpected ways. The first was of a heme-dependent piperazate synthase that catalyzes nitrogen-nitrogen bond

formation during piperazate biosynthesis. Despite the presence of N-N bonds in over 200 known natural products, the piperazate synthase KtzT from *Kutzneria* sp. is the first enzyme shown to catalyze N-N bond formation *in vitro* and to use heme to do so. The second was about an $\rm O_2$ and pyridoxal phosphate-dependent oxidase that catalyzes the formation of a carbon-carbon double bond during indolmycin biosynthesis. The oxidase Ind4 from *Streptomyces griseus* unprecedentedly uses molecular oxy-

gen and pyridoxal phosphate to catalyze a challenging oxidation of an unactivated C-C bond.

The two examples Dr. Ryan presented during her Matt Suffness Award talk illustrate her ingenuity in uncovering microbe's enzymatic secrets, ultimately leading to a greater understanding of how natural products are made. A greater understanding of biosynthesis can, in turn, aid genome mining towards the discovery of natural products, and can also lead to the development of new biocatalysts.

"I had a lot of fun giving the talk. Thanks to everyone for coming back to listen, even with all the fire alarms!" She went on to note, "I'm still pretty stunned that I would be recognized with this award!" Nominations for this award are reviewed



Katherine S. Ryan

RICHARD TEHAN

carefully by an appointed ASP committee.

The Matt Suffness Award is the latest in a growing list of achievements for Dr. Ryan, including being recognized with the 2016 *Natural Product Reports* Emerging Investigator Lectureship and as a 2016 Sloan Research Foundation fellow.

The ASP extends congratulations to Dr. Ryan on this important award, and is proud to count her as a member of the Society! ■

Dr. Ryan's research seeks to understand biological routes to construct unusual chemistry.

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Khan Named Honorary ASP Member

Dr. Khan is an uncommon combination of exceptional scientific achievement and service to his scientific discipline, the University of Mississippi, ASP, and the community at large.

By Dr. Ray Cooper

his year the ASP proudly welcomes Professor Ikhlas Khan as an Honorary Member.

Dr. Khan is a long-standing

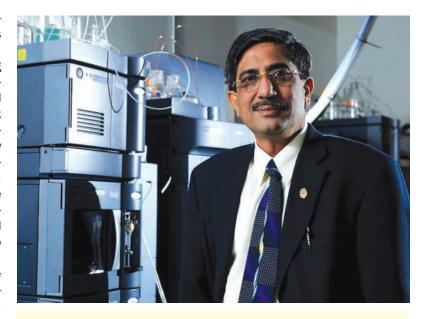
Dr. Khan is a long-standing member of the ASP and a highly accomplished and internationally recognized pharmacognosist. His research work and influence at the University of Mississippi have been recognized nationally and abroad, and Dr. Khan was awarded the Tyler Botanicals Prize in 2013. Furthermore, his contributions to the International Consortium for the Standardization of Botanicals has helped bring botanicals for healthcare back into the public spotlight in a positive way.

Honorary ASP members are those who have been distinguished and recognized for their service to the Society. This service may take various forms: outstanding support and contributions to the Society, lifelong support to the ASP executive. long-time service to

pharmacognosy, education, the promotion of good science, and the good name of the Society.

Dr. Khan has continued a tradition at the University of Mississippi of hosting an annual International Conference of the Science of Botanicals. This annual conference, now in its 16th year, is co-sponsored by ASP, and has been enormously successful in bringing scientists, clinicians, and regulators together to discuss developments in the science of medicinal plants and the current problems of the botanical industry, leading to the development of an International Consortium for the Standardization of Botanicals.

Dr. Khan is an uncommon combination of excep-



Professor Ikhlas Khan

tional scientific achievement and service to his scientific discipline, the University of Mississippi, ASP, and the community at large. He infuses high scientific and ethical standards in his many students and research associates, most of whom become ASP members, encouraging their participation and presentation of their scientific work at every annual meeting. Thus Dr. Khan's extensive direct service to the Society deserves the recognition of Honorary ASP Member.

The Society wishes to recognize the scope and manner of his service, which have had a major impact far beyond the boundaries of our organization. ASP is proud and honored to have Dr. Khan join the distinguished rank of Honorary Member. ■

...his contributions to the International Consortium for the Standardization of Botanicals has helped bring botanicals for healthcare back into the public spotlight in a positive way.

Planning for 2018 Annual ASP Meeting Underway



By Drs. Jurgen Rohr and Joe Chappel

rganizing for the 2018 ASP Annual Meeting in Lexington, Kentucky is well underway with an exciting scientific program and a variety of social events to welcome everyone to the charm and hospitality of the Bluegrass region already planned.

The "Riding High with Natural Products" meeting will take place at the Hilton Hotel in downtown Lexington July 21-25, 2018, consisting of plenary symposia and concurrent sessions surrounding cutting-edge topics in Natural Products Discovery, Biosynthesis, Targeted Therapeutics, Synthetic Biology, and Emerging Technologies. Internationally acclaimed innovators will kick-off each of the more than a dozen symposia sessions, followed by a selection of speakers from the submitted abstracts and poster sessions designed to facilitate social mingling and professional networking.

No less important will be the excursion opportunities. Join us for the banquet dinner at Keeneland, one of the world premier racetracks, to learn more about the beauty of the thoroughbred horses, and of course to place your bet on your favorite in live simulcast races. The junior scientists event will take place at another trademark venue for the Bluegrass, the Buffalo Trace distillery, where you can learn about the secret crafts behind this venerable tradition and taste some of the finest bourbons made. And for those who have never experienced the beauty of this part of the US, you can take a horse farm tour or walk among the amazing nature of the Appalachian foothills.

Mark your calendars now for July 21-25, 2018 to continue your exploration of natural products and the fun at the 2018 ASP Annual Meeting. ■

Mark your calendars now for July 21-25, 2018 to continue your exploration of natural products and the fun at the 2018 ASP Annual Meeting.





ASP Members Cech and Oberlies Named Distinguished Professors

By Dr. Edward Kennelly

SP members Drs. Nadja Cech and Nicholas Oberlies were each named as the inaugural Patricia A. Sullivan Distinguished Professors of Chemistry at the University of North Carolina, Greensboro (UNCG). Both are professors in the Department of Chemistry and Biochemistry, and prominent members of ASP.

ASP President Dr. Cedric Pearce commented on this remarkable recognition of two ASP members, "I know I speak for the membership in general when I wish both Distinguished Professors Cech and Oberlies congratulations on this fine achievement. Both Nadja and Nick have excelled with their research into natural products and have made many fine discoveries. They also had a significant role in developing the graduate program in the Department of Chemistry and Biochemistry at UNCG, and continue to train a new generation of natural products researchers and ASP members. It is exciting to see two of my closest collaborators being recognized by the university in this way, and I wish them both the best of luck as they continue with their careers."

When asked how ASP has contributed to his career development, Dr. Oberlies, who joined UNCG in 2009, responded, "The ASP has been an instrumental part of my career, both when I was a young, long-haired graduate student nervous about the questions I might get during a poster session, through the early stages of my independent career when I would hope that my abstract would be picked for an oral presentation, through today where I plan my entire summer around when and where the next meeting will take place and how I can manage to bring as many students as possible. I was fortunate in that all of my early mentors did not only encourage attendance, but insisted that I 'be involved.'"

Dr. Oberlies noted that neither he nor Dr. Cech formally applied to be Distinguished Professors. They were both pleasantly surprised when their Dean invited them to lunch, and sprang the good news on them. Dr. Oberlies reflected, "It is so great to be awarded this at the same time that my friend, colleague, and collaborator, Nadja Cech is also honored. She is the one who first invited me to UNCG about a decade ago to give a presentation and then helped recruit me here when the Ph.D. program was started. I can say with great conviction that I am a better scientist today (and certainly a better educator and mentor) due to the countless things I have learned from her..."



Drs. Nadja Cech and Nicholas Oberlies at the University of North Carolina, Greensboro.

Dr. Cech, who joined UNCG in 2001, credits Dr. Oberlies for encouraging her to become an ASP member. She commented, "It is truly an honor to be awarded the Sullivan Distinguished Professorship of Chemistry. Patricia Sullivan was a pioneering woman, biologist, and unwavering advocate of science education, and I am thrilled and honored to be charged with carrying on her legacy. It is particularly lovely to share this award with my longtime collaborator and colleague, Dr. Nicholas Oberlies."

Dr. Cech considers ASP to be important for both her and her students' career development. This year, she and Dr. Oberlies brought 20 students to the ASP Annual Meeting in Portland, Oregon. Dr. Cech noted, "Involvement with the Society is critical for expanding our young scientists' perspective on the breadth and depth of the field of natural products, and for giving them the opportunity to build connections with their peers and with senior members of the field."

The Patricia A. Sullivan Distinguished Professor is named in honor of former UNCG Chancellor Sullivan (1995-2008) who was trained as a biologist, and was especially committed to expanding the sciences and research at the university. Dr. Oberlies noted, "She was a great leader and a beloved individual. We have excellent scientific research facilities at UNCG, and she set us on that path during her tenure at the helm of this institution."

Both Nadja and Nick have excelled with their research into natural products and have made many fine discoveries.

Assistant Editor Keller Departs Newsletter

By Dr. Edward Kennelly

r. Amy Keller, Assistant ASP Newsletter Editor, resigned effective August 1, after 11 years helping to run the quarterly publication. Dr. Keller said she wants to focus more time on her research because she has recently been awarded a Career Development Award through the Veteran's Administration.

Dr. Keller started editing the ASP Newsletter in 2006 (Volume 42, Issue 1) when she was a doctoral student at the City University of New York, under the supervision of ASP Newsletter Editor, Dr. Edward Kennelly. For more

than a decade, she edited the *Newsletter*, first in New York, and then in the Denver area where she went to work as a postdoctoral fellow and continues to live.

Dr. Keller noted that when she joined the *Newsletter*, there was a new editor and a new layout editor, so although she did not know what to expect, she was sure it would be different than the previous incarnation of the *Newsletter*. She noted, "My biggest surprise, but proudest aspect of the work over time, was the longevity of being in the position as long as I was. This gave me the opportunity to forge connections with members, watch the Society grow and change, and make a larger contribution."

Dr. Keller has been instrumental in shaping the *Newsletter* into its current form. In 2006, the *Newsletter* had no regular columns or columnists, and the staff did much of the original writing. Over time, Drs. Keller and Kennelly worked to develop regular columns and were able to find a small and dedicated group of ASP members to write them. Dr. Keller looked back and remembered a few of her favorite subjects she covered, including: ASP members who were featured in the national press, like Drs. Brian Bachmann and Cassandra Quave; ASP members who have contributed to the Society, like the Bhatti Travel Award and the Brady Estate bequeath; and also the close relationships she forged with regular columnists like Dr. Dave Newman.

One of the very first columnists to join the ASP Newsletter



Dr. Amy Keller holding prickly pear fruit (Opuntia phaeacantha)

PHOTO BY MS. LESLIE KNAUB

was Dr. Georgia Perdue, who had formerly edited her own Newsletter known as Washington Insight. Dr. Perdue wrote of her interactions with Dr. Keller over many years, "Even though I have not met her, Amy was very professional in her work coediting the Newsletter. She was always gracious in accepting my requests on certain aspects of my column, 'Brief News from Washington'. It was truly a delight to work with her. While I will miss her, I wish her all the best in her new endeavor."

Another unflagging contributor to the ASP Newsletter

has been Dr. Dave Newman, who writes the popular "Hot Topics in Pharmacognosy" column. He commented, "Amy was always gentle with me even when she should have been 'tearing her hair out' as I missed deadlines. She was (and still is) very courteous in her dealings with authors and the ASP Newsletter will definitely miss her 'delicate touch.'"

An important mission of the ASP Newsletter is to support the mission of the Society, and its flagship publication, the Journal of Natural Products. Dr. Keller was the main force in the column "Behind the Scenes in Pharmacognosy" by selecting recent peer-reviewed articles by ASP members, typically published in J. Nat. Prod., and interviewing the corresponding author about the research. She also worked with J. Nat. Prod. Editor-in-Chief, Professor Douglas Kinghorn in promoting the journal's annual awards. Dr. Kinghorn noted, "Over the years, Amy has added a lot of value to information I have provided about the Journal of Natural Products, and she has been able to take basic details from me and then to expand on these to formulate polished final articles for the ASP Newsletter. For example, she has contacted authors who have won our annual Schwarting and Beal Awards, and has obtained quotes and photographs from them. I have always found Amy a delight to work with on a personal level, and I wish her well as she enters the next step of her career".

continued on page 18

"Over the years, Amy has added a lot of value to information I have provided about the *Journal of Natural Products*, and she has been able to take basic details from me and then to expand on these to formulate polished final articles for the ASP Newsletter..."

-Dr. Kinghorn

Assistant Editor Keller Departs Newsletter

continued from page 17

In 2014 the ASP Newsletter Committee was formed to provide advice on the content of the publication. The Committee consists of Ms. Devhra BennettJones, Dr. Gordan Cragg, and Dr. Kevin Tidgewell. Dr. Keller has interacted considerably with this Committee; for each issue of the Newsletter Drs. Keller and Kennelly develop a list of potential articles, and run it by the Committee. In addition, any questions or controversial items are run by them as well. Dr. Cragg wrote, "It has been a great pleasure to be associated with Amy as a member of the ASP Newsletter Committee. She has been a great source of inspiring, novel ideas, and has introduced important features to the Newsletter such as 'Behind the Scenes in Pharmacognosy'. I and many readers have enjoyed her superbly written articles and interviews with members of the natural products community, both in the US and overseas, about their research programs and significant contributions to our discipline. Thank you, Amy. We will miss your regular articles but look forward to your continued participation in ASP activities. Every best wish for continued success in your career."

Other ASP Newsletter Committee members echoed some of Dr. Cragg's sentiments. Dr. Tidgewell said, "Amy is one of those special people who remains calm in the face of chaos and is able to bring everyone together and on task. Working with her these last few years on the Newsletter committee and her help in editing my articles for the Newsletter has been wonderful."

Ms. BennettJones wrote, "Her expertise in pharmacognosy and editorship combined with her pleasant disposition, and great sense of humor has made writing 'From the Archives' an endeavor that I look forward to every few months...I and all of the staff at the Lloyd Library wish Amy the very best as she embarks on establishing her laboratory."

Many ASP Newsletter contributors have commented that they will miss Dr. Keller's kind and laid back personality. Patricia A. Sullivan Distinguished Professor Nick Oberlies put it this way, "I wish her all the best with her developing career. But, simultaneously, I will very much miss her involvement with the Newsletter. Besides being an excellent writer, she has such a pleasant, 'hippy-dippy' personality. It was a joy to work with her on countless stories, where her influence, both in actually drafting the text, or more importantly, coaxing the proper verbiage out of long winded scientists, was invaluable."

Dr. Keller noted, "The best thing about being involved with the *Newsletter* were all the positive and enlightening interactions I had with members and their work. I loved being integrated into the Society in this way, and will miss being in direct contact with such fascinating people and scientists."

On behalf of the ASP, we all wish you continued success in your work, and hope to see you at the annual meetings, and perhaps even contribute to the *Newsletter* in the future.

Chatham Fellowship Announcement: Deadline January 31

By Dr. Wendy Applequist

The Garden Club of America's Anne S. Chatham Fellowship in Medicinal Botany provides at least one grant award of \$4,500 annually to support research related to medicinal plants. An important aspect of the award is that it is intended to enable a student to pursue an avenue of research that might otherwise prove closed. Accordingly, the funds may be used to cover direct costs associated with travel, field studies, or laboratory research. However, fellowship funds may not cover indirect costs, overhead, or student stipends, and should not be used to pay for lab space or supplies normally provided by universities.

Eligible candidates include U.S. citizens or permanent residents who are currently enrolled in Ph.D. programs in U.S.-based institutions, in any field of specialty, or who have received a doctoral degree within the last five years. The fellowship is administered by the Missouri Botanical Garden. Fellowship recipients will be selected by a panel of botanists with expertise in economic botany or ethnobotany, subject to approval by the Garden Club of America Scholarship Committee.

Please submit the following:

a brief application letter
 an abstract of 200 words or less

• a one- to two-page research proposal, set in 12 pt. type, giving the project's background and purpose and describing activities to be conducted (proposals will be treated as confidential; proposals longer than two pages will be considered ineligible) • a one-page budget that explains how funds would be used • a current curriculum vitae • for graduate students, a letter from a major advisor certifying enrollment in a Ph.D. program • copies of permits for field work or studies including animals, research clearances, and permission from governmental agencies for foreign research (if permits are being applied for but have not yet been obtained, please ensure that the proposal explains the situation)

Proposals must be received by January 31, 2018.

Mail applications to:
Dr. Wendy Applequist
Missouri Botanical Garden
PO. Box 299

Saint Louis, MO 63166-0299 USA

Additional information may be obtained by contacting Dr. Applequist at the address above or by email at: wendy.applequist@mobot.org

Pharmacognosy Field Notes: Random Encounter Leads to Cameroon Adventure

By Dr. Kevin Tidgewell

r. Telesphore Nguelefack is an unassuming figure when you first meet him but it quickly becomes apparent that he is a force when it comes to natural products research in Cameroon. Dr. Nguelefack is the head of the Department of Animal Biology, the Laboratory of Animal Physiology and Phytopharmacology (LaPhyPha), and the Research Unit of Neuroinflammatory and Cardiovascular Pharmacology (RUNICaP) at the University of Dschang in Dschang, Cameroon. His lab consists of 13 Ph.D. students and 7 Masters students along with some undergraduate researchers to round out the

including tropical parasitic diseases, pain, epilepsy, cancer, and other non-communicable diseases. Cameroon has eight public universities and a number of smaller private universities spread throughout the country.

Despite his busy schedule, Dr. Nguelefack made the drive from Dschang to Douala, one of the economic centers and home to one of the major international airports, to meet Dr. Kolber and me, and then turn around the next morning to drive back north to Dschang. While in Dschang the two US professors taught some seminar courses for first year graduate stu-



This extensive habitat diversity has led to a large number of researchers studying pharmacognosy in the country and utilizing plant extracts to study a wide range of diseases including tropical parasitic diseases, pain, epilepsy, cancer, and other non-communicable diseases.

group. A chance encounter between Dr. Benedict Kolber and Dr. Nguelefack while at the International Association for the Study of Pain (IASP) meeting in Tokyo led to discussion about collaboration in looking at Cameroonian plant natural products for the treatment of pain. This brief encounter at IASP led to the writing and submission of a small research grant through the Duquesne University Center for African Studies to fund the collaboration and a trip for Dr. Kolber and me to Cameroon.

For those unfamiliar with Cameroon, it is a Central African country that sits at the Bight of Biafra where West Africa begins to turn southward. It spans an incredible diversity of habitats from northern deserts near the

Dr. Nguelefack's Lab with Drs. Kolber and Tidgewell

border with Chad, down through savannah and grasslands, then to volcanic mountains which are surrounded by highland and lowland forest, and ending with an extensive coastline and black sand beaches. This extensive habitat diversity has led to a large number of researchers studying pharmacognosy in the country and utilizing plant extracts to study a wide range of diseases

dents in biomedical sciences and chemistry on topics ranging from optogenetics (using light to activate neurons) to marine natural products.

They also spent time working with and learning about the projects being conducted in Dr. Nguelefack's lab. Highlights of working with the Nguelefack lab included touring his lab and

Pharmacognosy Field Notes: Random Encounter Leads to Cameroon Adventure



Touring the animal facility where
Dr. Nguelefack created a separate lab space
to avoid noise disturbances for his animals.





Pius with P. pinnata in the field



Francis and Dr. Nguelefack inspecting a bee hive

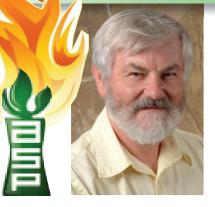
animal facility. A small team spent one day going to different areas to see the collection sites for Paullinia pinnata and other plant species which they have been studying and have shown to be analgesic in in vivo models. Mr. Pius Tseuguem Pum, a 3rd year graduate student exploring the analgesic and anti-depressant effects of P. pinnata, showed us his collection sites near his hometown of Bandjoun. Francis Bomba Tatsinkou, a 5th year Ph.D. student about to defend his thesis on NfKB and TNF-a dependent effects of Petersianthus macrocarpus extracts, showed us the forest near his family home in Bamoungoun and also his bee hives spread throughout the property. He has a side project studying the properties of propolis from the bee hives which he has tended since he was a child to earn extra money and currently uses to help pay for his graduate studies. In addition to Dr. Nguelefack there are a number of researchers involved with LaPhyPha at the University of Dschang who are exploring local ethnopharmacological knowledge to find treatments for infectious diseases, epilepsy, diabetes, and other non-communicable diseases.

Following a week in the mountains of Dschang, Dr. Kolber and I grabbed a ride from Mr. Basile Piegang Nganmegne, another of Dr. Telesphore's graduate students who spends time teaching at a private University near Douala to help pay for his studies, to

the University of Buea in the English speaking part of the country and spent time working with researchers there. Research talks and discussions were had with a number of students and professors that are using the plants local to their part of the country for treatments against infectious and non-communicable diseases, utilizing animal models to evaluate extracts and then leveraging foreign collaborators to help with the identification aspects. Despite the wealth of habitat diversity and their proximity to the ocean, there has been little work on bacterial or marine natural products due mainly to limited resources and ethnopharmacological knowledge. Buea has centers for research on neglected and emerging tropical diseases as well as a number of people working on natural products and medicinal chemistry.

This collaborative project among the Nguelefack, Tidgewell, and Kolber labs should prove beneficial to all three labs and could result in discovery of novel treatments for pain, something that is in high demand given the current opioid epidemic. This project would not have been possible without the team being open to collaboration and willing to introduce themselves to someone new at a conference halfway around the world. So the moral of the story is to make sure and branch out while at conferences and meetings because you never know what scientific doors a random conversation might open.

Research talks and discussions were had with a number of students and professors that are using the plants local to their part of the country for treatments against infectious and non-communicable diseases, utilizing animal models to evaluate extracts and then leveraging foreign collaborators to help with the identification aspects.



By Dr. David Newman

n February 17, 2017, the World Health Organization published a list of twelve microbes that were of concern as they were all resistant to a significant number of antibiotics in current use. This list was meant to be a "wake-up call" to the pharmaceutical industry/scientists involved in discovery of new antibiotics (be they natural products, semisynthetic or totally synthetic) showing how widespread resistance is.

On the list (www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/), the first three (priority 1 and listed as critical) were all Gram-negative organisms, but the next 6 (with a priority of 2 and listed as high), contained two very well-known Gram-positive pathogens, Enterococcus faecium and Staphylococcus aureus with resistance to vancomycin in the first and to methicillin (MRSA) and vancomycin in the second.

As may be known to some of the ASP members, vancomycin (1) was first introduced into medicine in the middle to late 1950s by Eli Lilly and Company (though there is some confusion as to the formal date as the Integrity™ database shows 1955 but the 2014 review by Butler et al.1 states that the FDA approved vancomycin as a "certifiable antibiotic" in late 1958). Although in clinical use for over 20 years, it was not until 1982 that the full structure was identified when Harris and Harris correctly identified an asparagine residue in the antibiotic.2 Subsequently, this molecule was used predominately as the "treatment of last resort" when resistance to methicillin in S. aureus arose, giving rise in due course to the soubriquet MRSA for this resistant organism. Relatively recently, in order to help overcome the side effects of the normal iv administration of vancomycin, today there is an oral formulation "vancocin pulvules" now marketed by Shire Pharmaceuticals.

As with all antibiotics, resistance arose to vancomycin and, for a fair amount of time, the reason for this resistance was not known. Vancomycin and similar molecules predominately function as antibiotics by binding to the L-Lys-D-Ala-COOH terminals of the cross-links in the Gram-positive cell

6. Boger $R^3 = -NH(CH_2)_3N(CH_3)_3^+$

wall. In the late 1970s the author (and colleagues) then at Smith Kline and French, devised a very simple screen for discovering the vancomycin-like glycopeptides, by initially competing their activity on a simple disc assay on a test plate of the well-known S. aureus strain 209P. We used a sacculus preparation from the Gram-positive bacterium B. subtilis, as the cost at that time of Acetyl-L-Lys-D-Ala-D-Ala-COOH was prohibitive. This was published using the tripeptide method, many years later as Smith Kline and French ceased antibacterial discovery in 1985.3 This resulted in the discovery and then subsequent development of the aridicins.4 We also discovered how easy it was to induce vancomycin resistance in S. aureus 209P and rapidly disposed of all of the resistant clones. Subsequent work, though not by Smith Kline and French, demonstrated that the Van^R phenotype was simply due to a change in the terminal D-Ala residue to D-Lactate in the vanA, vanB, van D or D-Ser in the vanC, vanE, vanG phenotypes.

The rise of the vancomycin-resistance phenotype in clinical practice was such that new antibiotics were required to deal with it as one now had an increase in infections where MRSA continued on page 22

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This list was meant to be a "wake-up call" to the pharmaceutical industry/scientists involved in discovery of new antibiotics showing how widespread resistance is.

was also exhibiting resistance to vancomycin. The D-Lac modification increased resistance by roughly 1000-fold, with the D-Ser modification being roughly 7-fold less sensitive. Although use of glycopeptide antibiotics in animal feeds was often thought to be associated with increased resistance, work by D'Costa *et al.*⁵ and Wright and Poinar⁶ indicated that the resistance genes were seen in microbial extracts from Arctic sources that were >10,000 years old.

RISTOCETIN AND TEICOPLANIN

However, microbiologists and chemists had not been idle during those years, as other molecules with the vancomycin mechanism of action had been found, with at least two going into clinical use. Ristocetin A (structure not shown) which entered use in the 1960s was withdrawn due to toxicity involving platelet aggregation, which was shown to be due to a rhamnose moiety on the pendant tetrasaccharide.7 In addition, teicoplanin (structure not shown) was launched in 1988 in Italy and was and is still used extensively in Europe, with an oral formulation reported to have efficacy in geriatric patients with C. difficile infections in Serbia as recently as 2015.9 A similar report on the same disease in geriatric patients was reported from France in 2017.10 It was approved for use in Europe and in many other countries world-wide, and there are clinical trials involving this agent in the NIH Clinical Trials database in the last 10 years with a recent one being used in dermatologic infections under NCT02652169 sponsored by the Medical University of Vienna. Teicoplanin does maintain resistance against strains with the vanB operon, and there are strains with resistance against teicoplanin that retain sensitivity to vancomycin but more usually strains are resistant to both. A potential problem with the current formulation is that it is not a single compound but is a mixture of five compounds, TA2-1 to TA2-5, which differ in their fatty acid side chains as well as the presence of TA3-1 which is deacylated. The use of such a mixture in the US may not be feasible at this moment.

APPROVED SEMISYNTHETIC GLYCOPEPTIDE ANTIBIOTICS (GPAS)

Three semisynthetic GPAs have entered clinical use in the US and other countries. These are: telavancin (2) approved initially in 2009, and derived from vancomycin; dalbavancin (3) derived from a teicoplanin-like compound that was part of the A40926 complex approved in 2014; and oritavancin (4) derived from chloroeremomycin, which was also approved in 2014.

TELAVANCIN (2)

To synthesize telavancin, a long-chain amino lipid was coupled as the Fmoc protected aldehyde with vancomycin producing a substituted aminosugar moiety (NE corner as written), following removal of the Fmoc group, led to the N-decylaminoethyl derivative of vancomycin. Then using a Mannich condensation with aminomethyphosphonic acid and formaldehyde yielded telavancin (2). This synthesis was reported by Leadbetter et al. in 2004 and that paper should be consulted for further information.¹⁰ Currently there are 14 trials listed in the NIH clinical trials database, with three recruiting. One of these (NCT02013141) is a Phase 4 open trial in pediatric patients to study the PK of a single dose of IV telavancin, the second (NCT03172793) is also a Phase 4 open study to investigate adult CF patients with MRSA infections, and the third (NCT02208063) is a Phase 3 open study multicenter, randomized, open-label, noninferiority trial of telavancin versus standard IV therapy control (e.g., vancomycin, daptomycin, anti-staphylococcal penicillin (PCN), or cefazolin) in the treatment of subjects with complicated Staphylococcus aureus bacteremia and SA right-sided infective endocarditis (RIE). So as is customary, even 8 years after approval, the drug is still being investigated to see if its activity can be extended to other patients with more complex illnesses involving resistant Grampositive microbes, in particular, MRSA-related.

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DALVABANCIN (3)

In 1995, Malabarba *et al.* reported the isolation and structures of a series of glycopeptide antibiotics that closely resembled the teicoplanin complex.¹¹ The origin of this series of compounds leading to the approval of dalvabancin, is an example of the takeover climate of the late 1900s and early 2000s amongst pharmaceutical houses. It was originally developed at the Italian Lepitit Research Centre then owned by Marion Merrell Dow (which was a US-based conglomerate from the 1980s). The Lepitit Centre was then purchased by Hoechst in 1995 and spun off as Research Italia SPA two years later. In 2003 Versicor acquired Research Italia and renamed the combined company as Vicuron Pharmaceuticals. In turn, Vicuron was purchased by Pfizer in 2005. Durata Pharmaceuticals then acquired the compound after three Phase III trials, as the FDA required yet more testing at the Phase III level to establish a non-inferiority endpoint by com-

3. Dalbavancin

paring 2 doses of IV dalbavancin given 7 days apart against 2 daily doses of vancomycin for 14 days. Only the *vanA* phenotype shows resistance.

ORITAVANCIN (4)

This compound also had a very checkered past, starting with its semisynthesis as LY-333328, an N-alkylated derivative of LY-264826 (formerly A82846B, and also known as chloroeremomycin), a naturally occurring structural analog of vancomycin.

LY-333328 contains a chlorodiphenyl side chain and an additional aminosugar residue on the phenylserine hydroxyl group when compared to vancomycin (1). Following acquisition by Inter-Mune in the USA in 2001, in 2005 it moved to Targenta Therapeutics which in turn was acquired by The Medicines Company in the US in 2009. After two Phase III trials with over 900 patients

4. Oritavancin

each, the FDA approved the drug in 2014. The drug has excellent activity against vancomycin-resistant strains but there are difficulties in measuring the actual MICs, so recently a surrogate method utilizing vancomycin comparisons was published by the Medicines Company.¹²

CEFILAVANCIN HYDROCHLORIDE (TD-1792) (5)

This is a chemical combination of vancomycin and a cephalosporin that is in Phase III clinical trials in Russia. The compound was originally synthesized as part of a number of such agents by Theravance. 13, 14 The compound was licensed to R-Pharma for further development in 2014. If the development is successful, then this will be the first such agent approved as an anti-bacterial, though combinations of uncoupled agents have been investigated for many years, with classic examples being a beta-lactam and an aminoglycoside, or the many beta-lactams plus beta-lactamase inhibitors.

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"TOTALLY SYNTHETIC" VANCOMYCINS

The major group involved in such agents is that of Dale Boger at the Scripps Research Institute in San Diego. Following excellent work over the last 10 plus years on total syntheses of very interesting and active variations on the base vancomycin structure, with all being made by total synthesis not by modifying the

5. Cefilavancin trihydrochloride

natural product, though as will be seen, they are very close in structure to the known agents. Very recently his group reported the synthesis of a chlorobiphenyl derivative of vancomycin that following subtle modifications, including the conversion of a carbonyl to a methylene and the addition of a $\rm C_{14}H_{29}$ alkyl chain via a tertiary amine substituent (6), yielded an exceptionally potent

antibiotic with activity against both D-Ala-D-Ala and D-Ala-D-Lac end groups, increased membrane permeability and more than a 1000 fold increase in activity over vancomycin, and no significant resistance after 25 passages. The development of this molecule should be extremely interesting.

CONCLUSIONS

Although vancomycin has been in clinical use for almost 6 decades, even today, subtle modifications to this natural product are still being investigated in order to cure patients of infections due to resistant microbes. This work demonstrates that in addition to searching for new active structures, modification of old agents may also be of utility. One is reminded of the work done in the late 1990s and reported in 2000, on the synthesis of modified everninomicins by Nicolaou et al., ¹⁶ and the slight

This work demonstrates that in addition to searching for new active structures, modification of old agents may also be of utility

modifications to this base structure that were not continued with by the then Schering-Plough (everninimicin; Ziracin®) 17 due to the requirement by the FDA for more Phase III trials, a request reminiscent of the development of oritavancin 10 plus years later.

Thus, do not throw away those older compounds since working with very competent synthetic chemists may well resuscitate interest in them.

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Meet a New ASP Member

Dr. Kenji Kurita is our featured new member in this fall issue of the ASP Newsletter. Dr. Kurita is an Associate Scientist at Genentech, having completed his doctoral studies with ASP member, Dr. Roger Linington, and recently he has joined Genentech's Small Molecule Pharmaceutical Sciences Department as part of the Structure Elucidation Group. Dr. Kurita was an invited speaker at the ASP Annual Meeting in Portland this year, and wants to remain connected to the pharmacognosy community. We are grateful for a chance to further welcome Dr. Kurita into the ASP.

By Dr. Dan Kulakowski

How did you hear about the ASP?

I first heard about the ASP in 2011 when I started graduate school at the University of California, Santa Cruz in Professor Roger Linington's Lab. The 2011 meeting was in San Diego and the entire lab piled into a van and drove 10 hours from Santa Cruz. I presented a poster on using direct analysis in real-time mass spectrometry to sequence natural product peptides directly from solid phase resins.

Why did you join ASP, and what would you like to achieve through your membership?

I joined the ASP because I was invited to give a talk at this year's conference in Portland and thought that

becoming a member and attending meetings would help me remain in contact with academic collaborators and to stay current in structure elucidation, chemical biology, 'omics, and biosynthesis as they apply to natural products. It is also nice to put some faces to the authors of papers you read over and over again.

Do you belong to any other scientific societies?

I do not belong to any other scientific societies; however, I plan to join the American Society for Mass Spectrometry next year.

What are your current research interests in pharmacognosy?

My current interests in pharmacognosy are in the chemical ecology of the human microbiome, structure elucidation, and bioinformatics approaches towards the discovery of compounds and their mechanisms of action from large natural



Dr. Kenji Kurita

product libraries. I believe that community methods for sharing data, creating standardized bioassays that are accessible to all laboratories around the world, and providing mechanisms for these data and libraries to be ethically leveraged will start a new wave of interest in natural products.

What is your scientific background?

I studied Chemical Biology at UC Berkeley and was lucky to participate in undergraduate research in the lab of Professor Matthew Francis. Then I graduated from the Program for Biomedical Science and Engineering at UC Santa Cruz with a Ph.D. in Chemistry. My thesis, supervised by Professor Roger Lin-

ington, was focused on directly integrating biological and chemical profiling data from natural product libraries. These projects gave me many opportunities to practice de novo structure elucidation of complex natural products. This skill allowed me to provide isolation and structure elucidation support to multiple collaborative projects with Professor Michael Fischbach at UC San Francisco. My role included large scale microbial fermentation, prep-scale and analytical scale chromatography, and finally full structure elucidation of highly unstable, low abundance, and large molecules. Within days of graduating, I helped Professor Linington move his lab to Simon Fraser University in Burnaby, British Columbia and to establish a new research program. The Linington lab is part of the NIH-NCCIH Centers for Advancing Research on Botanical continued on page 27

I believe that community methods for sharing data, creating standardized bioassays that are accessible to all laboratories around the world, and providing mechanisms for these data and libraries to be ethically leveraged will start a new wave of interest in natural products.

Meet a New ASP Member

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and Other Natural Products (CARBON), and I worked for CARBON as a postdoc. During this time I worked closely with Waters Corporation to engineer a platform to characterize the chemical constitution of natural product libraries using data independent acquisition ion mobility mass spectrometry.

Recently I joined Genentech's Small Molecule Pharmaceutical Sciences Department as part of the Structure Elucidation Group. Here I use my knowledge of mass spectrometry, NMR spectroscopy, and organic chemistry to assist the process, analytical, and formulation groups. One of the outstanding benefits of being a scientist at Genentech Research and Early Development (gRED) is that we are encouraged to perform cutting edge research, publish, and attend conferences.

What inspires you in your work?

Even just the idea that the projects I am working on might one day be a therapy that could help someone is pretty inspiring. Patient stories and testimonies are extremely motivating, and I enjoy working further down the development pipeline.

What is your favorite organism?

My favorite organisms are humans. We are only at the very edge of understanding how we tick, and how we interact with the billions of microbes we carry around with us.

What do you like doing in your spare time?

Some would describe me as a cyclist, but I would say I am more of a militant bike commuter and National Public Radio enthusiast. There is pretty much nothing better than drinking an embarrassingly expensive cup of coffee, and listening to Rachel Martin read the news. When the sun is low on the horizon you will probably find me surfing or climbing. Finally, just as every other chemist, I really enjoy cooking and fermenting things.

Making an Effective Presentation at an ASP Meeting

By Dr. James McChesney

e have just completed a very successful annual ASP meeting in Portland. There were about 500 registrants, and the attendance at the oral sessions was notable. The symposia and oral contributions were timely, well organized, and conveyed solid science.

I have a suggestion to improve presentations. A number of speakers tended to be poorly heard and thus did not optimally always convey their work. ASP meeting registrants have made a considerable investment in time and resources to be in attendance to learn about the latest progress in natural products research and development efforts, and have elected to attend a presentation specifically to learn of the progress and results.

ASP annual meeting speakers spend hours preparing the PowerPoint slides for a presentation; however if they do not communicate their verbal explanations to be heard and understood beyond the first few rows of the audience, much is lost. ASP speakers likely practice their presentations extensively beforehand, but probably do so in a small venue where it seems they are easily heard and before familiar colleagues. When they get to the annual meeting and find the venue is huge (seating 500 or so) and the audience is composed of many senior ASP members as well as students and post-doctorals, they may be a little intimidated and are not prepared to be heard by the entire audience.

Use of the sound system is thought to overcome this issue, but many speakers may fail to realize it is important to speak directly into the mike for the system to amplify their words. (This is also true of audience members who wish to ask questions). Many people have soft voices (culturally and naturally) so it is especially important to be mindful to use the sound system optimally.

I hope in future meetings we can prepare so as to overcome this issue and make our oral presentations even more valuable, informative, and exciting.

New Members of ASP 2017



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 22 full members and 8 associate members. We look forward to meeting you, and learning more about you and your work.

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Dr. Kanglun Liu

Hong Kong Baptist University Hong Kong, Hong Kong

Dr. Molly Megraw

Oregon State University Corvallis, Oregon, USA Assistant Professor

Dr. Ruth Muchiri

University of Illinois at Chicago Chicago, Illinois, USA Postdoctoral Researcher

Dr. Lilibeth Salvador-Reyes

University of the Philippines Quezon City, Philippines Assistant Professor

Dr. Kerri Smith

Waters Corporation Milford, Massachusetts, USA Senior Scientist

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ASSOCIATE MEMBERS

Mr. Mario Augustinovic

University of North Carolina at Greensboro Greensboro, North Carolina, USA Undergraduate

Ms. Valria Gimenez

Universidade de Franca (UNIFRAN) Beaverton, Oregon, USA Ph.D. student

Ms. Sonja Knowles

University of North Carolina at Greensboro Greensboro, North Carolina, USA Graduate Student

Ms. Loveth Linus

China Pharmaceutical University Nanjing, China Master's student

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Chapman University Lake Forest, California, USA Ph.D. student

Mr. Nicholas Pflug

University of Iowa Iowa City, Iowa, US Graduate student

Mr. Peter Sullivan

University of Illinois at Chicago Chicago, Illinois, USA

Yixuan Xia

Hong Kong Baptist University Kowloon Tong, Hong Kong Ph.D. student



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.pharmacognosy.us. 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.

3rd International Conference on Natural Products Utilization: from Plants to Pharmacy Shelf October 18-21, 2017 Bansko, Bulgaria www.icnpu.com/2017 Gordon Research Conference
in Marine Natural Products
March 4-9, 2018
Four Points Sheraton/Holiday Inn Express
Ventura, California
www.grc.org/programs.aspx?id=11555

International Conference on Natural Products
for Cancer Prevention and Therapy
November 8-11, 2017
Kayseri, Turkey
npcpt2017.org

American Society of Pharmacognosy
Annual Meeting
July 21-25, 2018
Lexington, KY
www.pharmacognosy.us

2nd International Conference on Natural Product Discovery and Development in the Genomic Era January 21-24, 2018 Clearwater Beach, Florida www.simbhq.org/np/ Gordon Research Conference on Natural
Products and Bioactive Compounds
July 29-August 3, 2018
Proctor Academy
Andover, New Hampshire
www.grc.org/natural-products-and-bioactive-

Keystone Conference
Natural Products and Synthetic Biology:
Parts and Pathways
January 21-24, 2018
Olympic Valley, California
www.keystonesymposia.org/18J1

66th International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research jointly with the 11th Shanghai TCM conference

compounds-conference/2018/

August 26 - 29, 2018 Shanghai, China www.ga-online.org



Brief News from Washington

By Dr. Georgia Perdue

- On August 10 Dr. Francis Collins issued a statement announcing the retirement of Dr. Josie Briggs, Director of the National Center for Complementary and Integrative Health since 2008. "...I am truly sorry to see her go," noted Dr. Collins. "She has been an outstanding director, a trusted advisor to me and others at NIH and a trusted friend. She is among the most accomplished leaders at NIH and is [universally] respected within and outside the agency." Dr. Briggs has been at NIH since 1987. She will be the Editor-in-Chief of the Journal of the American Society of Nephrology (her specialty). Dr David Shurtleff, NCCIH Deputy Director, will serve as Acting Director while a new director is sought.
 - [On a personal note, I admired Dr. Briggs and the backbone she exhibited in running what was at times a controversial agency. She was gracious, superb and forthright when I interviewed her!]
- > On June 8 at the two-day meeting of the Advisory Committee to the (NIH) Director (ACD), Dr. Francis Collins announced that just two days prior to the ACD meeting, President Donald Trump asked him to stay on. Dr. Collins noted he had met with the President once before the inauguration and three times subsequently. More recently there was an "important and useful" meeting at the White House with "experts and leaders from FDA and NIH," and members from academia, industry and government agencies as well as the newly confirmed Secretary of Health and Human Services Dr. Thomas Price. Vice President Mike Pence led the meeting. Dr. Collins said he pointed out the major role NIH plays in biomedical research and explained the importance of basic research carried out both at NIH and academia. all of which was "well received." A side note from Dr. Collins: "Ivanka Trump is very interested in basic research."
- > Secretary Price visited NIH just a few days after he was appointed as head of HHS; his interest was seen as a positive sign.

- Dr. Collins was very upbeat about the appointment of Dr. Scott Gottlieb as FDA commissioner and is "very optimistic about their relationship..." as they work together.
- One directive in the Cancer Moonshot portion of the 21st Centuries Cancer Act: "any publications as a result of this effort must be made available right away."
- Dr. Anthony Fauci, Director of National Institute of Allergy and Infectious Diseases (NIAID), spoke at the **ACD** meeting about an accelerated Pathway Towards a Universal Influenza Vaccine. In his comments Dr. Fauci noted that "Yellow Fever is 99% eradicated." The current influenza vaccine is only 0-20% effective. In 2008-09 there was an increase in influenza cases. Former President Bush provided \$5 billion for a pandemic influenza vaccine. In 2013 a vaccine made by ID Biomedical (a GlaxoSmithKline subsidiary) was approved. Now NIAID has H7N9 and H9N9 influenza vaccines, but "they need to be improved. " ... we are going after a broadly protective universal vaccine, with a 'breadth of 5-10 years." The end of June, NIAID had a meeting regarding the development of this vaccine and "brought in the best and brightest, ... and all specialties together." Dr. Collins invited Bill Gates. The effort is now hailed as "an NIH-led bold initiative towards the development of a universal influenza vaccine." The Science Philanthropy Alliance wants to put money in this type of research. Stay tuned!!
- "Dissolving the Fogarty Center makes no sense," noted Dr. Collins at his ACD meeting. "Consider all the research contributions made for about a \$70 million budget...." Stay tuned.
- On the second day of the ACD meeting, Dr. Lawrence Tabak, NIH Principal Deputy Director, provided interesting information regarding "R01 awards by degrees"
 - Number of PhDs is high
 - Number of MDs peaked in 2000 and has steadily been going down

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Brief News From Washington

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- Number of MDs-PhDs—concentrated primarily on research-has remained stable
- There are fewer younger physicians (in their 40s) receiving RPGs and interested in research
- Number of those in their 60s-70s is going up
- A new area of research of interest to NIH about to be launched is "pathways to conduct dedicated research while residents." "This pathway works," said Dr. Tabak adding, "People who go through these types of programs do well."
 - Fund 10-12 programs with R28, K28 over four years. The R28 is the institutional part, i.e., provides support to institutions for the research and teaching opportunities
 - After one-two years, if the person does well they are eligible for K28, for dedicated research during residency.
 Even if the person goes to another institution, they can take the K28 with them.
- At the June 20 National Cancer Advisory Board and Board of Scientific Advisors (NCAB/BSA) meeting Dr. Tabak talked about "Enhancing Stewardship-The Next Generation Researchers Initiative" which will be included in the NIH-wide Strategic Plan. In addition to enhancing stewardship, its aim is to train and retain researchers. "The current environment is turning off young people and we need to do something about it." Dr. Tabak added that there has been a decline in the number of those in their 40s-60s because they are having a tough time sustaining their research careers. "Baby boomers will ultimately fade away... but not quite yet because established researchers are out-performing others. Senior investigators are more resilient because they have funding from different resources." Currently NIH policy is to "provide a boost for first time applicants." Under the New Proposed Plan NIH is committed to ensure support for highly meritorious early stage and mid-career investigators. Based on 2016 figures, \$210 million will be needed to fund them in the first year of a 5-year grant. The money will come from reprioritization of funds. Some IGs use R56; for the most part the R35 is used because it provides a "bit" more money and is for a longer term.
- NIH-Wide Strategic Plan 2016-2020 "NIH cannot afford to support everything. Good stewardship is essential," said Dr. Collins at his ACD meeting. A few details:
 - Recruit and retain outstanding workforce
 - Rescuing U.S. biomedical research from its systemic flaws—we have a problem here...
 - Hypercompetition—applicants and awardees –number of awardees is constant; the number of applicants keeps going up

- The 21st Century Cures Act advocates policies that will promote earlier independence and increased funding to new investigators. The how of this has yet to be worked out!
- The 21st Century Cures Act has a loan repayment program, LRP Expansion, which provides \$65,000/ year. "There is increased attention to this type of program....We get outstanding scientists from this," said Dr. Tabak. NIAID is also participating in this program.
- Dark chocolate lovers take heart: its good effects on memory, blood pressure, hardening of the arteries etc. has prompted NIH to launch a 5-year study to evaluate the flavanols in reducing the effects /risks of cardiovascular disease.
- Once again St. John's Wort, Hypericum perforatum, is in the news again. While the plant has been used since ancient times, especially in Greece, as an anti-inflammatory, antidepressant and antiseptic, recent concerns deal with its psychotic properties. (See J Med Case Reports, 11 (137), 2017.)
- "The High Overhead of Scientific Research" is the title of an article written by Rep. Lamar Smith, (R-TX). The subtitle is very telling: "Taxpayers shouldn't have to pay for new buildings and fat salaries." A couple highlights: "Indirect costs are supposed to pay for utility bills for university laboratories, security services.... Over time universities have included university president's salaries and benefits, and new university buildings....Universities and non-profits should be reimbursed for reasonable costs of sponsoring federally funded research." The Government Accountability Office warned that "indirect costs are taking a larger and larger share of funds for scientific research." "Many universities are pressing to raise indirect costs even higher...." The article ends with the following sentence: "Every dollar we spend on scientific research must count." [I highly recommend reading the entire report at https://science.house.gov/news/in-the-news/high-overhead-scientificresearch.]
- As unbelievable as it sounds, in mid-August health officials in Arizona confirmed that fleas in at least two counties "have tested positive for plague." ABC news carried the story in mid-August (http://abcnews.go.com/US/fleas-testing-positive-plague-parts-arizona/story?id=49177920). Imagine a disease from the Middle Ages re-appearing!! Human transmission of the disease is either from an infected flea bite or transmitted by direct contact with rabbits, rodents or other animals upon which the fleas enjoyed a meal! Stay tuned!!

Dark chocolate lovers take heart!

From the Archives: Pettit's 1974 Groundbreaking Journey to the People's Republic of China, Part II

By Ms. Devhra BennettJones

wo years following the Nixon Administration's lift on the 22-year travel-ban to the People's Republic of China esteemed ASP members Drs. Norman R. Farnsworth, S. Morris Kupchan, Thomas H. Maren, George R. Pettit, and Michael A. Schwartz were among the medicine and pharmacology ambassadors that formed the 1974 National Academy of Sciences Delegation. 1-2 These leaders met with Chinese scientists, toured universities, pharmaceutical manufacturing facilities, hospitals, and met with practitioners of Traditional Chinese Medicine.3 Dr. Pettit composed a travel log of their 27-day journey in the People's Republic of China.4 The following is the second of three excerpts that will appear in From the Archives.5

LUNG HUA (DRAGON FLOWER) HOSPITAL OF TRADITIONAL MEDICINE, SHANGHAI, SATURDAY, JUNE 15.6

Our 8 a.m. start was delayed for onehalf hour while two Romanian generals and their wives and staff and Chinese military counterparts left the hotel for a day's excursion. Interestingly, all of the Chinese army personnel including a man of obvious general rank all wear the same uniform without identifying rank markings or other insignia.

A spokesman for the Revolutionary Committee at the hospital reviewed the history for us over tea. This is the teaching hospital of the Shanghai College of Traditional Medicine and it was established in 1960.8 Presently the staff numbers 400 and includes about 100 doctors and 100 nurses. The hospital has 250 beds and handles 2,000 out-patients per day. Some 40-50 personnel are assigned to rural areas or to factories each year.

Next, we were taken on a tour of the hospital. The first stop was the traditional pharmacy for out-patients. We witnessed another busy operation concerned with filling medicinal plant prescriptions for



home extraction. This was followed by a trip to the hospital dispensary for in-house prescriptions. Here, the mixture of plant materials is extracted in approximate 3-liter size copper kettle as follows. The prescription is placed in the kettle with water. After 15 minutes of boiling the solution is strained through an approximate 60 to 80 mesh sieve and the solution is poured into an approximate 1 liter thermos bottle. More water is added to the origi-

nal mixture and boiling is continued for 40 minutes. The solution is again strained and added to the thermos. The hot solution is then transported to the patient for oral ingestion.

We then began the ward rounds which included seeing a woman in her 60's with a 20-year history of hypertension. When admitted 10 days ago her blood pressure was 160/110 and her cholesterol was at 260. The original complaint was angina pain and after 10 days of treatment (IV) with the Tan Shan medicinal plant mixture, her blood pressure had fallen to 120/70 and her cholesterol level to 175. Also of considerable interest was a series of patients being treated for acute appendicitis.



Above: Dr. Pettit and colleagues visiting the Nanjing College of Pharmacy (now known as China Pharmaceutical University), 1974.

Left: Dr. Pettit in a medical plant garden in China with *Digitalis* species.

The surgeon in this hospital is a man of about 60 who was trained originally by western methods but in 1960 was assigned to this traditional hospital to

learn and continue his skills. Of the surgical patients admitted to this hospital, about 10% have acute appendicitis. On the basis of an earlier study of 350 such patients with simple appendicitis he has found the routine use of Ching hung especially useful. About 70% of appendicitis cases are amenable to this treatment while the remaining 30% with perforated appendixes are sent for the usual surgery. In addition, the serious appendicitis cases, for example with ruptures, are also treated where necessary with penicillin, streptomycin and cantomycin, a Japanese antibiotic. They have found Ching hung (also written as Jing Ching) so continued on page 33

From the Archives: Pettit's 1974 Groundbreaking Journey to the People's Republic of China, Part II

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useful that they are now preparing it in tablet form. The medication is a mixture of *Caulis sargentodoade* (62.4 g), *Herba Tardxaci* (31.2 g), *Rhizoma Rhei* (18.8 g) and *Cortex magnoliase* (0.95 g) and the surgeon has described its use in the *Chinese Medical Journal* No. 1, page 9, 1972. The tablets are prepared in this hospital and distributed to others. Apparently the extract promotes blood circulation in the



Mounting a herbarium specimen.

wall of the appendix and increases peristaltic movement. About 17% of the patients so treated have a recurrence, most in a 6 month to 1 year period. In another group the recurrence rate was 16% overall in an 8-year period. So far, they have experience with 20,000 such cases. In the approximate 350 patients studied, the ages ranged from 12 years to 59 years and symptoms disappeared on an average of 31/4 to four days. The temperature dropped to normal after about 2 days as did the leukocyte count. Generally the patient was discharged from the hospital on the fifth day. The actual prescription used is 12 tablets total taken 3 times a day. Bowel movements soon begin and average 2-3 on the first day.

Among several more patients we observed was a female of 34 years who had been admitted with a leukocyte count of 10,300 and abdominal tenderness and rigidity. She was diagnosed as acute appendicitis and after the Ching hung treatment the pain disappeared. After 20 hours her leukocyte count dropped to about 4,000.

The surgeon noted that she will continue taking the tablets for about 1 week after discharge. Other such patients are seen with original leukocyte counts up to 19,000.

The surgeon responsible for the acute appendicitis treatment and his internist colleague graciously answered a considerable number of questions for us after the ward rounds. We then returned to our hotel for lunch.

SHANGHAI PHARMACEUTICAL FACTORY, NO. 2 (TRADITIONAL MEDICINE), SATURDAY, JUNE 15

Factory No. 2 is located about one-half hour's drive from the hotel (we left at 2:30 p.m.) We were met by the leading member of the Revolutionary Committee who noted that the factory now employs 470 workers and was established in 1958 in the year of the great leap forward. Initially, the factory employs 80 workers. Now it is organized into 4 shops and produces 30 products. About 15% of production is slated for export under the byline, Shanghai Native Medicine Works, Shanghai, China.

An afternoon tour of the production proved interesting and we saw large batches of roots and hardwood being chopped, extracted and the extract dried and screened to a brown powder. The various plant extracts were then formulated as tablets for use as cold remedies and diluted with alcohol (52%) for sale as rheumatism remedies. Obviously this particular factory was engaged in production of palliative type over-the-counter home remedies. The more exotic products such as tiger bone¹¹ and deer antler¹² preparations were relatively high priced and primarily for export.

The only unique items noticed were 2 machines used respectively for pulverizing roots and chipping hardwood. This writer did not recall seeing exactly comparable equipment elsewhere. Preparation of tablets, etc., seemed to be by the usual methods.

As had been our practice at each installation that we visited, the chairman left a series of reprints, picture books about the United States, pictorial calendars, etc., as souvenirs of our visit. Unfortunately, a very small picture book of San Francisco left at this factory, unbeknown to us, contained a picture of Chinatown with a Nationalist China flag displayed.¹³ Unfortunately, this was taken as a grave insult¹⁴ and the next day our chairman and Ms. Tsuchitani delivered our apologies.

That evening we were taken to the Shanghai puppet show which went from 7:15 to 9:15 p.m. The puppets were rather interesting, being about two-thirds life size. One show involved the training of three lions with musical sound effects which was particularly pleasant. Two out of the four skits were political in nature. The first involving capture of a Soviet revisionist spy in China by Chinese children and militia-men. The second involved a former landlord who upset the public tranquility by stealing a goose left in the care of several children.



A 1970's state-of-the-art mass spectrometry laboratory at a pharmacy school.

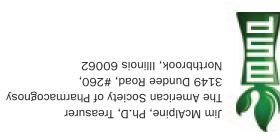
(Read the next excerpt of Dr. George R. Pettit's A View of Medicine, Cancer Treatment And Drug Development In The People's Republic of China, June 1-27, 1974 in the Winter issue of the ASP Newsletter—From the Archives.)

From the Archives: Excerpts from Pettit's 1974 Groundbreaking Journey to the People's Republic of China

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