American Society of Pharmacognosy

Fall 2023

Discovering Nature's Molecular Potential

ASP Newsletter: Fall 2023, Volume 59, Issue 3

New ASP President McKee Addresses Membership

Dr. Tawnya McKee
PHOTO: NCI

By Tawnya McKee, PhD

First, I'd like to thank Amy Wright for the excellent job this past year as president. It was a great learning experience working with her and the EC over the last year as vice president. We just completed another interesting and successful annual meeting at the Northern Bethesda Conference Center in Bethesda, Maryland.

When I was asked to run for vice president I thought long and hard before I said yes. While flattered by the request, I had more questions than answers, and what kept going through my mind was, "Where is the Society?" and "Where did I think we needed to go to continue to be relevant and a home and resource for the next generation of natural products scientists (our up-and-coming students, post docs and young professionals)?" Since the Portland meeting in 2017, I have been heartened by the determined efforts of the Society, especially the Diversity, Equity and Inclusion Committee, the scientific and local organizing committees, and with the support of the Executive Committee to be intentional about diversity, equity and inclusion. With all of this in mind, I ultimately settled on three issues/areas of focus for the upcoming year.

1 **Membership.** As vice president I led the Membership Committee. This spring we generated a poll, well actually two, one for established members and one for younger members. The goal is to gather information about what the ASP adds to your career and development as a natural product chemist; that is, why do you make the choice to join and sustain your membership? Why would we ask these questions? One reason is that in my 30+ years of membership, nobody ever asked me, and I have never seen a survey addressing these questions. Frankly, I'm curious to see the responses. Secondly, while we have a stable membership, we aren't really growing as much as we should, especially with the large number of younger scientists that attend the annual meeting each year. So, to me, there is a disconnect between what the Society adds to established members versus elucidating and promoting the values of our Society as a resource and support system to our younger members.

Asking these questions is a way to gather the data we need to make intentional choices of how the Society can serve its membership while supporting and enhancing their careers. I am hoping you will help us gather this information by taking the time to fill out and submit this survey. When I began to write this article for the newsletter, we only had 17 responses. Here is the QR code you can scan to access the poll. It also has been posted to the ASP website: https://www.pharmacognosy.us/?s=poll.
It is completely anonymous; we are not tracking any personal information, only the number of responses.

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American Society of Pharmacognosy

Discovering Nature's Molecular Potential

***ASP Newsletter*: Fall 2023, Volume 59, Issue 3**

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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/

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PHOTO: CUNY

Editor's Corner

American Society of Pharmacognosy

By Edward J. Kennelly, PhD

The fall *ASP Newsletter* welcomes ASP President Dr. Tawnya McKee as the incoming president of our society. As part of her presidency, McKee is asking members to complete a poll to find out how ASP adds to your career and development as a natural product scientist. I hope you will take a moment to complete this poll and provide insights about what membership means to you. I have spoken with many members over the years who have recounted how much the Society has been important in their careers, especially by providing opportunities to present their science or expanding their scientific networks.

The *Journal of Natural Products*, now with its highest-ever 2-year impact factor (5.1), is the flagship publication of the ASP, published jointly with the American Chemical Society since 1995. McKee describes how ASP will be renegotiating the publishing agreement with ACS that is now almost three decades old. Revenues from *JNP* help to facilitate many ASP activities, so we will hope for a new agreement that will continue to provide benefits to ASP and its members. I hope you will take time to read the entire message from ASP President McKee.

The 2023 annual meeting in Rockville, MD was a great success. If you were not able to attend, please look at the wrap-up provided by the organizing committee. One of the great pleasures is seeing so many award winners (page 11). The Farnsworth Research Achievement Award was presented to ASP member Dr. Sheo Singh. Singh's long and storied career in natural product drug development is described in detail in an article written by Gordon Cragg and David Newman. Incredibly, Singh's early work on dolastatin 10 has led to four antibody drug conjugates that have been approved by FDA for cancer treatments.

The Diversity, Equity and Inclusion Committee was approved at the annual meeting to be elevated from an ad hoc to a standing committee. This committee has been very active in recent years and continues to describe its achievements in its ongoing "Taking Action" column in the *Newsletter*. The 11-week summer program, now in its third year, continues to be a tremendous opportunity for Black, Indigenous, and Latinx students to conduct research in natural products and also have the opportunity to attend the 2023 ASP Annual Meeting through a special donation.

There are many other issues covered in this newsletter, from *JNP* award winners to memories of the ASP "Honest Herbal" expert, the late Professor Varro Tyler. I hope you have a wonderful autumn, and please contact us if you have any ASP-related news. ■

New ASP President McKee Addresses Membership

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2 Renegotiation of the ACS-ASP journal contract. We first teamed with the ACS to begin co-publishing the *Journal of Natural Products* in 1995. This has been a very successful collaboration with the ACS with our journal now at an all-time high Impact Factor of 5.1. It is also the primary source of money for the Society. In the 28 years since, our agreement has not altered, but the publishing world of scientific journals is rapidly changing, and we should anticipate that this model will not be sustainable. There is increasing pressure to allow free access to the publications and scientific data generated by publicly funded research, like that from NIH, NSF and DOD. Currently, NIH requires public access to this no more than 12 months after publication. In this model, a PI pays a fee, often of several thousand dollars, to provide immediate access to their work. As many have pointed out, since these fees are generally obtained from grant funds, the government is actually paying twice for the same data. The publishing world has become aware of this and is adapting to this emerging reality, and so should we. Therefore, it makes sense that a renegotiation is needed. This renegotiation will address how the Society and the ACS will cover the costs and earnings of the *JNP* moving forward. The goal is to reduce the administration burden on the Society while ensuring the cost and revenue is equitably shared by both parties. A committee has been selected for this process. Phil Proteau as *JNP* editor, Douglas Kinghorn as member of the original negotiation team and *JNP* editor during these negotiations, Jimmy Orjala as ASP treasurer, Susan Mooberry as a former ASP president and ASP Fellow, and myself as current president will work with the ACS on a new agreement. I will be sharing information about our progress as negotiations proceed.

3 Communication. Communication is probably one of the most important tasks we have, both as individual scientists but also as a Society. I believe the current structure of separate committees that has evolved/developed over time and focused on the many aspects of communicating the Society activities makes integration, consistency, and efficiency difficult. I'd like to see them work together in a more unified and cohesive manner that benefits from a shared infrastructure. To do this, I am proposing combining the Website, Social Media, Job Service and Newsletter Committees into a new ad hoc Communications Committee. This will make us more nimble, adaptable to changes in technology/platforms/tools and responsive to our changing environment and membership needs. It will begin as an ad hoc committee because a standing committee will require changes to the Constitution and By Laws, and it will take at least a year and a half to complete this process. This stepwise approach will allow us to test and evaluate the best combinations or formats and determine their effectiveness. Our decision as a Society on whether this change is truly effective should take several years. I think this is an area where we can engage our junior members, and they can lead the way for our Society. As a group they are comfortable, savvy, and more knowledgeable about social media; they have the computer skills to both update and modernize our website and newsletter and can envision efficient and effective ways and methods to communicate across the Society, and especially, with each other. The basis of this new communication system will be a state-of-the-art website, a streamlined html-based newsletter, and a vibrant new social media presence on at least Instagram and X (the service formally called Twitter).

I am excited about these opportunities for the Society this year. I hope you will join me by volunteering on a committee, attending webinars (like the wonderful webinar on July 10th highlighting the work of this year's Student Research Fellows) and attending our international meeting next year in Krakow, Poland. I welcome your suggestions and comments as well. Please reach out to me at: tawnya.mckee@gmail.com. ■

ASP 2023 Annual Meeting: Innovation through Interaction

Meeting Report

By Nandakumara Sarma, PhD

The Local Organizing Committee (LOC) for the 2023 ASP Annual Meeting is glad to report a very productive meeting in Rockville, MD during July 22- 26! The meeting included a dynamic slate of speakers, including many who presented for the first time at ASP. The meeting was attended by 445 people, including 166 attendees who are postdocs or students.

The meeting logo illustrates the Chesapeake Bay area which includes Rockville, MD, designated by the star. The Chesapeake Bay's ecosystem is a large estuary that impacts the health and safety of thousands of species of animals and plants, as well as the 18 million people who live in the Chesapeake Bay watershed. Thanks to LOC member Dr. Barry O'Keefe, NIH and his family connections for their help in designing and making the logo.

Besides the recurring themes, such as the Young Members symposium and awards symposia, the meeting included the following symposia and scientific sessions which represent the breadth of natural products areas of current interest and encompass the conference theme of ***Innovation through Interaction***:

- Where Chemistry and Biology Meet
- Natural Products that Modify Macromolecular Interactions
- Old Molecules/New Purposes
- Microbiome/Probiotics Interactions
- Bridging the Gap: Collaborations with Predominantly Undergraduate Institutions
- Public/Private Partnerships
- Unique Environments
- Fungal Biosynthesis and Chemodiversity
- Who's Your Partner: Symbiosis and Natural Products
- Cannabis and Cannabinoids
- Recent Advances in Traditional Herbals — Quality/Authenticity and Analysis
- Natural Products and Infectious Diseases

The Saturday workshops on July 22 included the following topics with presentations and panel discussions to help inform research:

- Botanical Drugs: A Regulatory Approach on How FDA Reviews a Botanical Application
- Biochemical and Biophysical Assay Design for Natural Product Discovery Campaigns
- Current Topics in Botanical Safety
- Fungal Identification Using Molecular Tools
- Public Speaking for Scientists

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ASP 2023 Annual Meeting: Innovation through Interaction: *Meeting Report*

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Thanks to LOC member Dr. Emily Mevers for successfully submitting an NCCIH grant proposal for $30,000 to support registration costs for students, postdoctoral fellows and junior investigators with the goal of promoting diversity based on the guidelines established by the NIH NOT-OD-20-031: Notice of NIH's Interest in Diversity. Registration waivers were provided to 70 diverse early career researchers, including 10 oral presenters receiving full registration waivers, 60 poster presenters receiving 50% registration waivers, and one member of the organizing committee receiving a 25% waiver. This grant helped 38 graduate students, 22 postdoctoral research fellows, nine assistant professors, and two associate professors attend the meeting.

In addition to the exciting scientific program, equity and diversity were important conversations at the meeting. There was also an array of social events, such as the trip to Smokey Glen Farm which included great food and a variety of games and activities. The Younger Members Committee met at Pinstripes across the street from the hotel for an evening of bowling, bocce, and beer.

Meeting attendees also provided positive feedback about things to see and do outside of the meeting, both around the meeting location in Rockville, MD and the attractions in Washington, DC, which was well-connected to the meeting venue.

The ASP annual meeting presented a wonderful opportunity for network among the attendees by providing an intellectually stimulating opportunity for ***Innovation through Interaction***! ■

Local Organizing Committee:

Drs. Craig Hopp, NIH (co-chair); Nandu Sarma, USP (co-chair); Carole Bewley, NIH; Amit Chandra, Amway; Lin Du, NIH; Ikhlas Khan, NCNPR; Emily Mevers, Virginia Tech; Barry O'Keefe, NIH; Tim Ramadhar, Howard University; Barbara Sorkin, NIH; Laura Stoll, ASP Business Manager.

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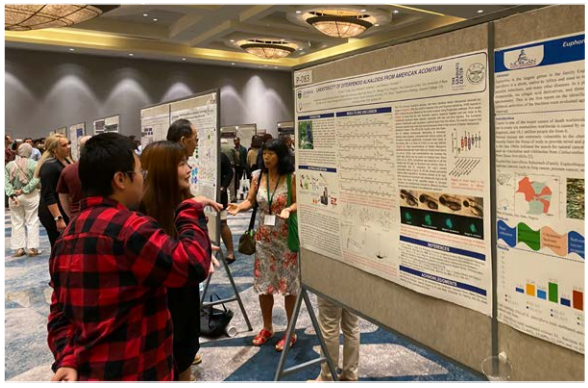
Presentations, awards, and friendships!

PHOTOS: ED KENNELLY



The meeting included a dynamic slate of speakers, including many who presented for the first time at ASP.

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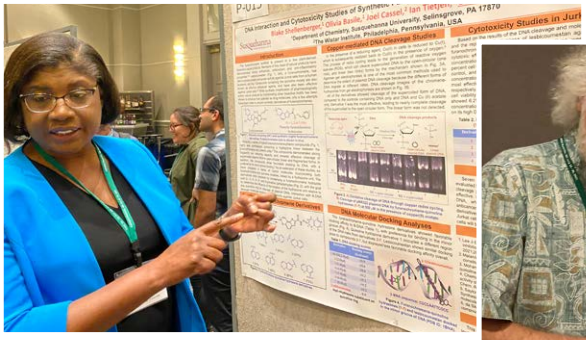

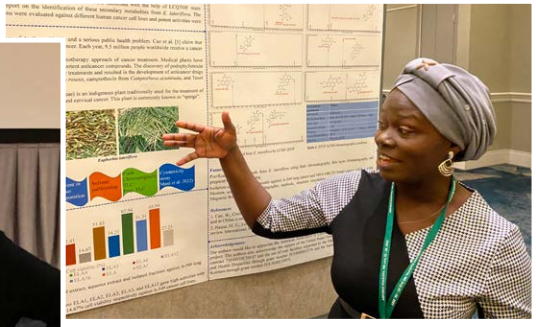
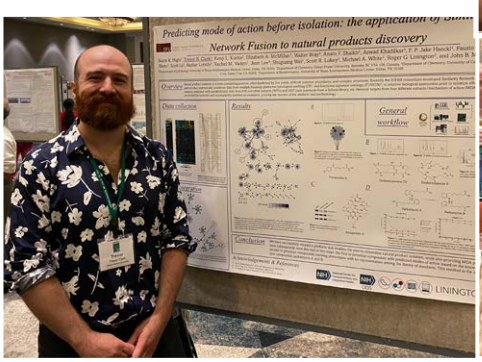

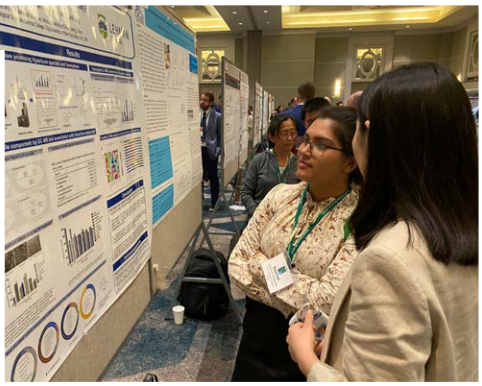
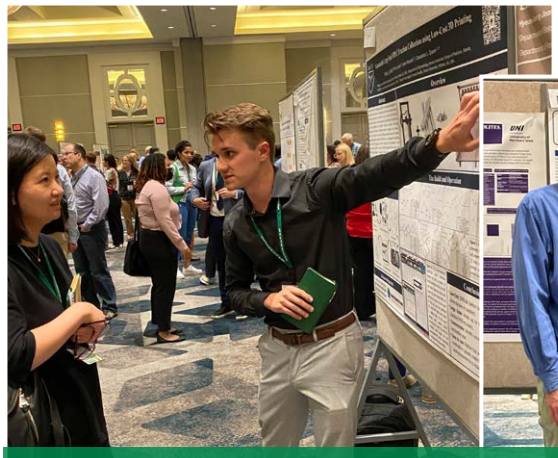
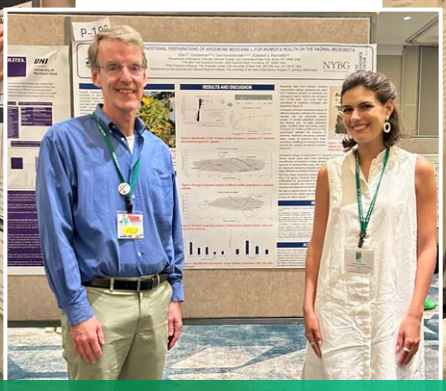

Singh Conferred the 2023 Farnsworth Research Achievement Award

By Gordon Cragg, PhD and David Newman, DPhil

Dr. Sheo B. Singh received the 2023 Norman R. Farnsworth Research Achievement Award at the ASP Annual Meeting in Bethesda, Maryland. Singh has had an outstanding natural products research career spanning over 30 years, including 24 years in Merck Research Laboratories in Rahway, New Jersey. After obtaining his BSc and MSc degrees at Gorakhpur University in India, he attended the Central Institute of Medicinal Aromatic Plants at Lucknow and Avadh University in Faizabad where he completed his PhD in 1981. The late Professor Norman Farnsworth, founding member of ASP, visited India during this period and was the first American Singh ever met, so this award, named in his honor, seems especially appropriate for Singh to receive.

Singh worked as a postdoctoral fellow at the University of Glasgow in Scotland in 1982, and in 1983 joined the research group of the late Prof. G. R. Pettit at the Cancer Research Institute (CRI) at Arizona State University in Tempe. It was at the CRI that he really launched his natural products research career. During this period, he carried out the bioassay-guided isolation, purification and structural elucidation of antitumor compounds from plant and marine sources, coupled with the synthesis of several promising lead compounds. These studies resulted in the development of several compounds which were advanced through preclinical and eventual clinical development.

Foremost among the plant products were members of the stilbene family, combretastatins A1 and A4, which he isolated from *Combretum caffrum.* He developed efficient total syntheses for both these compounds, which were then converted to their corresponding water-soluble phosphate prodrugs, combretastatin A4 phosphate (CA4P; Fosbretabulin; Zybrestat) and combretastatin A1 diphosphate (CA1P; OXI4503), which have undergone advanced clinical trials under the auspices of Oxigene, now Mateon Therapeutics. Both these agents were granted orphan drug designation by the FDA: CA4P in 2003 for the treatment of anaplastic thyroid cancer, medullary thyroid cancer, and stage IV papillary or follicular thyroid cancer, and in 2006, for the treatment of ovarian cancer; and CA1P in 2012, for the treatment of acute myelogenous leukemia. Currently there are 13 records related to combretastatins still listed in the clinicaltrials.gov database.[1]

Dr. Sheo B. Singh

PHOTO: STEVENS INSTITUTE OF TECHNOLOGY

His other highly significant contribution while at the CRI was the development of efficient total

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syntheses of dolastatins 10 and 15, members of a family of peptides originally isolated from the marine mollusk, *Dolabella auricularia*. While neither of these compounds proved to be effective clinical candidates due to unacceptable toxic side effects, structure activity relationship studies of dolastatin 10 by Singh led to synthetic analogs which have been linked to monoclonal antibodies (mAbs) by companies, such as Seattle Genetics, to give a range of Antibody Drug Conjugates (ADCs) showing promise in clinical trials against a number of cancers. Currently four ADC analogs of dolastatin 10 (MMAE structure) are FDA approved drugs (plus one recently approved in China). The first of these, brentuximab vedotin (Adcetris®), was approved in 2011 by the FDA for the treatment of certain lymphomas, and the second one (polatuzumab vedotin; Polivy®), using the same vedotin warhead but a different monoclonal antibody, received FDA approval in 2019 for the treatment of diffuse large B-cell lymphoma. One using the MMAF version of dolastatin 10 was approved by the FDA but was recently withdrawn after less than two years by GlaxoSmithKline. A search of clinicaltrials.gov database using "cancer" and "vedotin" as the search terms, accessed 357 clinical trials of ADCs containing vedotin as the warhead, indicating the significant promise of these conjugates as potential treatments for a range of cancers, often used in combination with other chemotherapeutic agents.[2] Singh recently published a review of the discovery and development of dolastatin 10-derived antibody drug conjugate anticancer drugs.[3]

In 1989, Singh moved to Merck Research Laboratories in Rahway, New Jersey, where he started as a research fellow and advanced through the ranks to become director and global head of natural products chemistry as well as director of medicinal chemistry, later serving as team leader of the chemistry program.

His other highly significant contribution while at the CRI was the development of efficient total syntheses of dolastatins 10 and 15, members of a family of peptides originally isolated from the marine mollusk, *Dolabella auricularia*.

During Singh's tenure at CRI, Pettit was fully supportive of his research and acknowledged the significance of his outstanding contributions to the CRI program. The development of these efficacious drugs were surely harbingers to his subsequent highly successful and productive career at the Merck Research Laboratories (MRL). In addition, colleagues who worked closely with Singh at CRI as members of his team in the synthesis of dolastatin 10 praised his excellent leadership, guidance and mentorship, which were later reflected in his leadership roles at MRL.

In 1989, Singh moved to Merck Research Laboratories in Rahway, New Jersey, where he started as a research fellow and advanced through the ranks to become director and global head of natural products chemistry as well as director of medicinal chemistry, later serving as team leader of the chemistry program. At his retirement in late 2013, he occupied the rank of senior principal scientist. He became increasingly involved in the leadership of multidisciplinary teams in the development and execution of strategies in programs for the discovery and development of agents covering a wide range of therapeutic areas. These areas included anticancer, cardiovascular, hypertension, anthelmintic, antiparasitic, coccidiostat, antimalarial, immunoregulatory, antidiabetic, and antiviral, including HIV and influenza, and during his last ten years at MRL his focus was on the discovery and development of antibiotics to treat bacterial resistant infections. His leadership roles included managing collaborative programs with many contract research organizations as well as with collaboration partners in China, India and Japan. As a senior and key member of the Merck team, he led the chemistry efforts of the Gates Tuberculosis Drug Accelerator project,

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identifying a series of novel anti-TB compounds that are undergoing further evaluation.

While at MRL, Singh discovered over 240 novel natural products. These included the antibiotics, platensimycin and platencin (fatty acid synthase/FAB inhibitors) and thiazomycin (protein synthesis inhibitor); the anticancer agents, clavaric acid and chaetomellic acids (Ras and FPTase inhibitors); apicidin, an HDAC inhibitor having coccidiostatal, antimalarial, and anticancer activity; the HIV integrase inhibitor, completstatin; and nodulisporic acid, an ion channel modulator with antiparasitic activity, all of which entered lead optimization and preclinical development. These studies included the total synthesis and SAR studies of a range of natural products, with a prime example being the lead optimization of apicidin which led to the development of multiple oncology candidates by Merck teams. He also co-discovered kibdelomycin, a potent gyrase inhibitor and developed an analog as an oral non-systemic *Clostridium difficile* agent exhibiting a potentially better spectrum of selectivity and efficacy than the current standards of care. Another significant achievement was the rational correlation of the liver specific FAS inhibition of platensimycin with glucose lowering, thereby repurposing it as an antidiabetic agent and qualifying it for development as a preclinical candidate.

Singh's research has led to the publication of over 230 papers and 34 reviews and book chapters, an impressive record given that he spent most of his career working in the pharmaceutical industry where the publication of research results is limited for proprietary reasons. The granting of 55 patents, however, reflects the importance and potential value of the discoveries made during his productive research career. He has also committed himself to serving the scientific community in various capacities and currently is on the editorial boards of the *Journal of Natural Products* (from 2004), *Journal of Antibiotics* (from 2007) and *Natural Product Reports* (from 2011). In addition, he has served on NIH Study Sections and as a member of the scientific advisory boards of several national and international institutions and organizations. His accomplishments and service have been recognized by a number of academic and professional awards, including several MRL Awards of Excellence, the Percy Julian Memorial Award (2007), the ASP Arthur E. Schwarting Award (2004), and the *Journal of Antibiotics* Medal (2014); and in 2006 he received an Honorary Doctorate of Philosophy in Chemical Biology from the Stevens Institute of Technology.

Last but not least, Singh has been a loyal ASP member since 1985. From 2005 to 2007 he was a member of the Norman R. Farnsworth Research Achievement Awards Committee, serving as chair in 2007, and on the Nominating Committee in 2014. He also served as an integral member of the 2012 International Congress of Natural Products Research in New York City.

Singh's outstanding research contributions were strongly lauded by Dr. Malcolm MacCoss, past vice president and head of basic chemistry at MRL, who also emphasized his exceptional leadership and mentoring qualities. MacCoss stated, "*Sheo's leadership at the group leader level, and later as a Director and Head of the Natural Products Group at Merck has been superb, and the number of Natural Product drug candidates that he has been responsible for bringing forward into development, is second to none,*" and this is perhaps the ultimate tribute to the overall level of excellence and achievements of Singh's career.

On behalf of ASP we congratulate Sheo Singh for his many accomplishments in natural product drug discovery. It has been an honor and pleasure for the authors to work closely with him for many years and to follow his outstanding career. ■

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2 clinicaltrials.gov. (*clinicaltrials.gov/search?term=vedotin&cond=Cancer* (Accessed July 28, 2023)

3 Singh, S.B. Discovery and development of Dolastatin 10-derived antibody drug conjugate anticancer drugs. *J. Nat. Prod*. **2022**, *85*, 3, 666–687.

ASP Award Winners 2023

Norman R. Farnsworth Research Achievement Award

Sheo B. Singh
Stevens Institute of Technology (2023)

Varro E. Tyler Prize

Djaja Djendoel Soejarto
University of Illinois at Chicago (2022)
Robert Verpoorte
Leiden University (2023)

Matt Suffness Young Investigator Award

Laura Sanchez
University of California, Santa Cruz (2022)
Jason Christopher Kwan
University of Wisconsin-Madison (2023)
Sandra Loesgen
University of Florida (2023)

Undergraduate Research Grant

Rodrigo Carrillo
Centro de Investigación Científica de Yucatán A.C.
Marvin Rositzki
University of Hawai'i at Hilo

Research Starter Grant

Benjamin Naman
San Diego Botanic Garden

D. John Faulkner Travel Award

Yuanyuan Ji
University of Maryland, Baltimore
Jeffrey Rudolf
University of Florida

David Carew Student Travel Award

Jose Alberto Gutiérrez- González
Universidad Nacional Autonoma de Mexico

Jerry McLaughlin Student Travel Award

Marcio Barczyszyn Weiss
Sao Paulo University
Vitor Lourenzon
University of Illinois at Chicago

Lynn Brady Student Travel Award

Riley Blue
University of California, Santa Cruz
Timothy Bushman
University of Alabama
José D.D. Cediel-Becerra
University of Florida
Cole Gannett
Virginia Tech
Kabre Heck
Auburn University
Thanh-Hau Huynh
Seoul National University
Eunah Jeong
Sookmyung Women's University
Lois Kwane Kyei
Virigina Tech
Diana Łomowska- Keehner
University of Florida
Huong Thi Pham
Sookmyung Women's University
Herma Pierre
University of North Carolina Greensboro
Liana Zaroubi
Simon Fraser University

Robert Krueger Travel Award

T'ea P. Cameron
University of North Carolina Greensboro
Maricarmen Corona
Centro de Investigación Científica de Yucatán, A.C.
Erin Marshall
University of Florida
Samuel Tanoeyadi
Oregon State University

Waqar Bhatti Student Travel Award

Logan Breiner
Virginia Tech

2023 Arthur E. Schwarting Award

Frederikke D. Andersen, Katja D. Pedersen, Dennis Wilkens Juhl, Tobias Mygind, Paul Chopin, Esben B. Svenningsen, Thomas B. Poulsen, Marie Braad Lund, Andreas Schramm, Charlotte H. Gotfredsen, and **Thomas Tørring.** Triculamin: an unusual lasso peptide with potent anti-mycobacterial activity. *J. Nat. Prod.* **2022**. *85*: 1514–1521.

2023 Jack L. Beal Award

Daniel Back, Brenda T. Shaffer, Joyce E. Loper, and **Benjamin Philmus**. Untargeted identification of alkyne containing natural products using ruthenium catalyzed azide alkyne cycloaddition reactions coupled to LC-MS/MS. *J. Nat. Prod.* **2022**. *85*: 105-114.

ICNPR 2024: Historic Kraków Hosts Cutting-edge Pharmacognosy Conference

By Stefan Gafner, PhD and Krystyna Skalicka Wozniak, PhD

We cordially invite you to the ICNPR 2024 meeting in Kraków, which will take place from **July 13-17, 2024**. This is a joint meeting of the American Society of Pharmacognosy (ASP), Association Francophone pour l'Enseignement et la Recherche en Pharmacognosie (AFERP), Japanese Society of Pharmacognosy (JSP), Korean Society of Pharmacognosy (KSP), Phytochemical Society of Europe (PSE), Società Italiana di Fitochimica (SIF), and Society of Herbal Medicine and Natural Product Research (GA), hosted by the PSE. Every four years these seven societies, which share a common interest in natural products research, meet to exchange expertise, discuss state-of-the-art science, and network.

The congress will bring together experts and researchers from all over the world to share their latest findings and discuss the latest developments in the field of natural products research. It will offer the opportunity to learn about cutting-edge research, network with other professionals in the field of natural products research, and explore the beautiful city of Kraków. Registration and abstract submission pages will be live starting November 7, 2023.

Kraków is the second-largest city in Poland with a rich history and culture. The old town, with its beautiful architecture and narrow streets, is a UNESCO World Heritage site. Some of the finest examples of European architecture can be found here, including Wawel Castle and the Cloth Hall, one of the city's most recognizable buildings. The Cloth Hall, located on the city's large market square, used to be a major trading center in medieval times. Looking over the market square is St. Mary's Basilica, a cathedral built with red brick in 1347. It is famous for its wooden altarpiece and colorful murals. Kraków is also the home of world-class museums like Oskar Schindler's Enamel Factory and the Wieliczka Salt Mine, one of the biggest mining heritage museums in the entire world.

The official venue for ICNPR 2024 is the ICE Kraków Congress Centre - the business and cultural flagship of the city, located in the very heart of Kraków.

On behalf of the organizing committee, we hope that you can join us in Kraków, and we look forward to hosting you. ■

The congress will bring together experts and researchers from all over the world to share their latest findings and discuss the latest developments in the field of natural products research.

Cloth Hall, the central feature of the main market square in Kraków's Old Town.

Taking Action: Annual Report from the ASP Diversity, Equity and Inclusion Committee

By Lesley-Ann Giddings, PhD and Christine Salomon, PhD

The three main goals of the ASP Diversity, Equity and Inclusion Committee are to (1) build a pipeline that overcomes structural barriers of entry for underrepresented groups of scientists who wish to engage in natural products research, (2) work with members of the ASP to create a more equitable, inclusive, and supportive community, and (3) recognize and highlight the contributions that members from underrepresented communities make to the ASP. The ASP Executive Committee has recognized how important this work is and that it will never be finished. As a result, at the 2023 meeting they approved our recommendation that the DEI Committee be converted from an ad hoc to a standing committing. Below are updates on what our committee has accomplished in 2022–2023.

1 Build a Pipeline to Overcome Structural Barriers of Entry

- We accepted our third cohort of students to our ASP Summer Research Fellowship (SRF) program to increase the representation of Black, Indigenous, and Latinx (BIL) scientists in natural products research. This program funds summer research experiences for undergraduates from historically underrepresented groups in our membership. The ASP Fellows and the ASP Foundation generously provided funds to support this program. Our third cohort was comprised of eight fellows, and Dr. Lesley-Ann Giddings continued to lead weekly virtual professional development workshops with the assistance of several ASP members (meeting for 11 weeks) to help foster community and provide a series of training seminars and exercises designed to prepare the cohort for applying to graduate school. Through an anonymous donation for travel for fellows, we were able to sponsor travel and accommodations to the annual ASP meeting in Rockville, MD, and all eight students attended and presented posters at the conference. The program concluded this summer with a highly successful webinar on August 10, 2023 in which each of the trainees presented their summer research to the ASP community (more than 80 participants). To ensure that the program continues, we applied for an NSF REU grant to secure three-year funding to support up to ten fellows per year with stipends, travel, housing, and lab materials. Drs. Brian Murphy (PI) and Marcy Balunas (Co-PI) worked with Drs. Christine Salomon, Eduardo Caro, and Lesley-Ann Giddings to develop the application.

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2023 ASP Summer Research Fellows and DEI committee members at the ASP meeting in Bethesda.

Front row (left to right): Roxana Gonzalez, Ma. Andrea Gatmaitan, Jacqueline R Vargas-Ulloa, Aria Gonzalez, Anna Pons, Jaylin A McCollum, and Selome Banini.

Back row (left to right): Eduardo Caro, Marcy Balunas, Brian Murphy, Lesley-Ann Giddings, Christine Salomon, Melvin Osei Opoku, and Jorge Hernandez Garcia.

PHOTO: NADJA CECH

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We received highly favorable reviews, and it was scored as "excellent" but was not funded. We have just resubmitted the application and are optimistic that it will be funded in this round.

- We are grateful for the significant investment into the SRF program from both the ASP Foundation and ASP and for the additional generous donations from ASP Fellows and members. These funds have allowed us to pilot the SRF program for three summers, which has supported and trained 19 students. Out of the 11 students from the first two cohorts, nine students have enrolled in graduate or professional programs. The Executive Committee recognizes the importance of maintaining this program and recently voted to continuously support two SRF students each year.
- We wrote a proposal for the Executive Committee outlining a new mentoring award. The Phillip Crews Mentorship Award is intended to recognize those ASP members who, like Dr. Crews, have prioritized providing premier mentorship to many individuals from diverse backgrounds who represent the next generations of scientists in fields associated with pharmacognosy. The Phillip Crews Mentorship Award includes recognition and a podium presentation during the annual meeting of the ASP. The details of this award will be forthcoming.

2 Create an Equitable Community/Educate

- Dr. Malika Jeffries-El, associate dean of the Graduate School in Arts and Sciences, Boston University, gave a webinar on Thursday, March 23rd, 2023, hosted by Drs. Eduardo Caro and Elizabeth Kaweesa. A recording of this webinar is available to ASP members on the website, and a summary article was published in the summer *ASP Newsletter.*
- We organized a workshop titled *How to Build Innovation and Creativity in Your Team: Perspectives from USP and NIH*. This workshop will discuss data-driven initiatives federal agencies have taken to diversify their workforce and provide steps we can take to diversify the workforces at our home institutions. The presenters are Dr. Pamela Tamez, health science policy analyst in the NIH Office of Workforce Diversity, and Dr. Debra Joy Perez, chief equity officer and senior advisor to CEO at USP (United States Pharmacopeia). The discussion was moderated by Drs. Eduardo Caro Diaz and Elizabeth Kaweesa.
- Drs. Eduardo Caro Diaz, Lesley-Ann Giddings, Christine Salomon, Brian Murphy, C. Benjamin Naman, Jaclyn M. Winter, Marcy Balunas, and Kevin Tidgewell wrote an article entitled *Unveiling Part of the Hidden Curriculum: Perspectives on How to Successfully Navigate Scientific Conferences*. The manuscript was submitted to the *Journal of Natural Products* as a means to educate young scientists about how to attend academic conferences and get the most out of these professional experiences.
- We continue to provide content for the Taking Action column in the ASP Newsletter. Over the last year, we have published five articles covering the work of the DEI committee, our events, as well as how to successfully apply for federal funding.

We would like to thank the ASP Executive Committee, the ASP Fellows, and the ASP community for their contributions and support that allow us to do this important work. ■

The ASP Executive Committee has recognized how important this work is and that it will never be finished.

JNP Recognizes Outstanding 2022 Papers

By Vanessa Nepomuceno, PhD

The Arthur E. Schwarting and Jack L. Beal awards began in 2001 to recognize the stellar work published in the *Journal of Natural Products* and to memorialize two former distinguished editors of the journal. Each year, a two-tier process is used to determine the winners of the best papers published in the JNP, which is published jointly between the ASP and the American Chemical Society. The Schwarting Award is open to all papers published in the journal within a given year (either in print or electronically). In turn, the Beal Award is awarded to younger investigators, i.e., persons within 12 years of receiving their PhD degree or within 10 years of gaining their first professional appointment (e.g., assistant professor or an equivalent position in industry or government).

2023 ARTHUR E. SCHWARTING AWARD - DR. THOMAS TØRRING

Dr. Thomas Tørring
PHOTO: AARHUS UNVERSITY

Dr. Thomas Tørring is an associate professor at Aarhus University in Denmark. His lab focuses on microbial biosynthesis and is particularly interested in understanding the mode of action and optimizing the production of bioactive compounds. Tørring and his team investigate compounds with antibiotic potential like triculamin, described in their publication. Lasso peptides such as triculamin are of particular interest to the Tørring lab both as an interesting biosynthetic product and promising drug scaffold. Tørring is very proud to receive this year's Arthur E. Schwarting Award. "I enjoy really reading old papers and the project was started based on two very short papers from 1958 and 1967. The genome sequences of the producing bacteria and the structures of the isolated compounds gave us some nice surprises, became the start of several new collaborations, and now also this award." ■

Andersen, F. D.; Pedersen, K. D.; Juhl, D. W.; Mygind, T.; Chopin, P.; B. Svenningsen, E.; Poulsen, T. B.; Braad Lund, M.; Schramm, A.; Gotfredsen, C. H.; **Tørring, T**. Triculamin: An unusual lasso peptide with potent antimycobacterial activity. *Journal of Natural Products*. **2022**. *85* (6): 1514-1521. doi.org/10.1021/acs.jnatprod.2c00065

2023 JACK L. BEAL AWARD - DR. BENJAMIN PHILMUS

Dr. Benjamin Philmus

Dr. Benjamin Philmus is an associate professor at Oregon State University. He and his team use a combination of computational tools and wet lab-based approaches to connect orphan biosynthetic gene clusters to molecules, ultimately aiming to discover novel pathways and molecules. Their publication highlights the use of click chemistry to derivatize alkynyl natural products coupled to LC-MS to detect them in an untargeted manner.

"We have found that identifying alkynyl natural products was problematic due to their low ionization efficiency, and we thought that there would be more of them produced by bacteria based on looking at published bacterial genomes. So, we worked out this technique to find alkynyl natural products in bacterial extracts."

Philmus says being awarded the Beal award was a very humbling experience and reflects the hard work and dedication of the team that he works with. "I am extremely proud of Daniel (the lead author) for his work, and the immense contributions of our co-authors Brenda and Joyce. I am also grateful for the support of the College of Pharmacy, my colleagues, and NIH for funding our work." ■

Back, D.; Shaffer, B.T.; Loper, J.E.; **Philmus, B**. Untargeted identification of alkyne-containing natural products using ruthenium-catalyzed azide alkyne cycloaddition reactions coupled to LC-MS/MS. *Journal of Natural Products*. **2022**. *85* (1): 105-114. DOI: 10.1021/acs.jnatprod.1c00798

JOURNAL OF NATURAL PRODUCTS

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Hot Topics in Pharmacognosy

Recent Musings Through the Literature

By David J. Newman, DPhil

There are four discussions below that result from recently published papers. These cover use of novel chemometric systems, a nominally simple modification of vancomycin giving activity against non-TB mycoplasma infections, the derivation of metallo-β-lactamase inhibitors, and synthesis of a modified marine natural product that yielded potential agents against Omicron variants (CoV-2).

1 The discovery of the first nitrogen-containing phomactin from the Berlinck group in Brazil utilizing a clever combination of metabolomics and chemometrics.

In a recent paper in the *Journal of Natural Products*,[1] the Brazilian group led by ASP member Dr. Roberto Berlinck demonstrated that diverse phomactin-based terpenoids could be expressed by, and then isolated from, the marine-derived fungus *Biatriospora* sp. CBMAI 1333. Initially the group focused on work around a predicted biosynthetic intermediate (**1**) that had been proposed in 2018 by Kuroda et al.[2] Using various metabolic variations in the fermentation of the potential producing fungus, they discovered multiple phomactin "skeletons" that were initially difficult to analyze due to their high spectral similarity, thus producing a single consensus spectrum when using GNPS in attempts to identify/separate the initial fermentation products.

Due to the initial inability to identify some components of the initial fermentation products, the group turned towards the application of metabolite association networks to aid in the identification of the fermentation products. These techniques are often used in systems biology, biochemistry, and molecular biological studies of closely related molecules in primary metabolism. Only a few investigators have applied this combination of techniques to identify products of secondary metabolism.[3,4] Then, by using a revised fermentation technique on a 30 liter scale and analyzing the products using a modified chemometric system, two new molecules were isolated: phomactin C and the first nitrogen-containing phomactin which the authors named as phomactinine (**2**).

Though the molecule was barely active as a platelet-activating antagonist, the real take-home lesson is in the novel application of multiple chemometric techniques, and the utilization of a reasonably large scale for an academic laboratory (30 liters) but in a minimal medium, rather than the usage of a "regular" medium which is often used due to the lack of scientists experienced in "large"-scale fermentations due to the demise of industry-based fermentation programs. Unfortunately, today people do not go back and consult the massive amounts of media data often found in the patent literature in the heyday of antibiotic discovery in the 1950s to early 2000s.

2 A relatively simple modification to vancomycin that opens up its mycobacterial activity.

Though they are described in one of my more recent freely available reviews,[5] the totally synthetic variations that the Bolger laboratory published demonstrated how subtle modifications in the peptide backbone (in red) of vancomycin (**3**) plus addition of side-chains from later approved glycopeptides (not shown), generated molecules that were highly active against vancomycin-resistant microbes with the compound in (**4**) demonstrating excellent activities against "regular microbes," but no data was shown of activity against non-tubercular mycobacteria (NTM).

The major problem with this "class" of infectious microbes is the significant increase in infection by NTM in patients suffering from cystic fibrosis (CF) or chronic obstructive pulmonary disease (COPD). This is primarily due to the biofilm-forming potential of these infective agents. That "class" is composed of the *M. avium* complex plus *M. kansasii* and *M. abscessus*. Strains of the latter organism have been identified by whole genome studies on infected CF patients, with no significant antibiotic treatment(s) currently identified.

Vancomycin itself is effective only against Gram-

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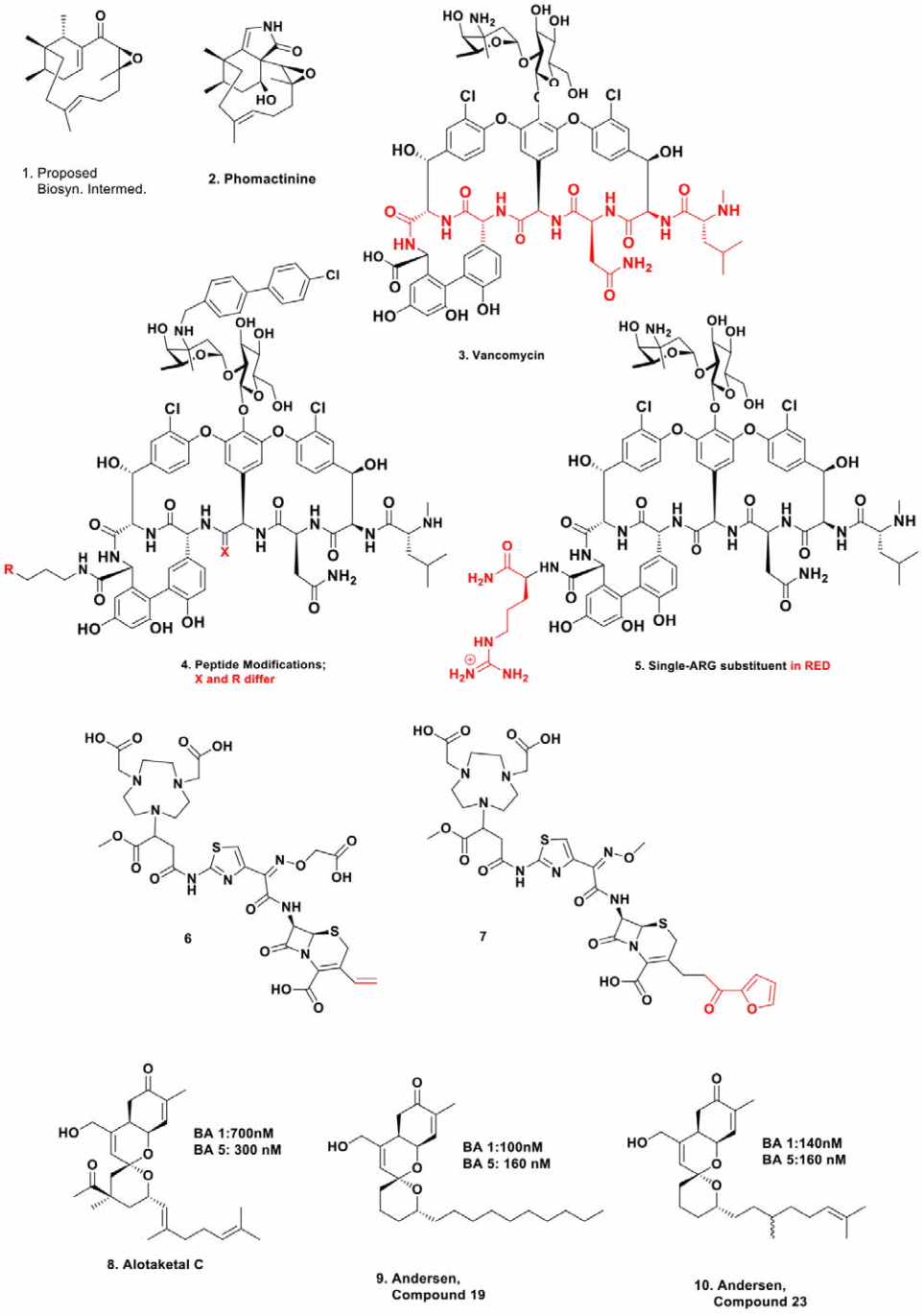
STRUCTURES



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positive organisms though as reported by van Groesen et al.[6] a vancomycin linked to polymyxin (vancomyxins) demonstrated activity against Gram-negative organisms. Rather than use a complex nominally charged peptide, Bricic et al.[7] reported that the simple linkage of a single arginine residue on the left-hand side of the conventional vancomycin structure (**5**), extending the internal polypeptide, generated a simple vancomycin derivative with decreases in the MICs ranging from 10-fold to 4-fold against *M. smegmatis, abscessus* and *kansasii* but not against *M. avium* strains, with no difference seen between the arginine derivative and vancomycin itself.

Further experiments both *in vitro* and *in vivo* (mouse models) lent credence to their molecular modelling since the presence of meso-diaminopimelate, rather than the L-lysine in the usual tripeptide target in the cell wall found in most Gram-positive microbes except *Bacillus* species, led to improved binding to the cell-wall tripeptide.

The work described in this paper should definitely lead to different treatment modalities for the non-TB mycobacterial infections. It will be interesting to see if the later glycopeptide antibiotics (early 2000s) will have similar or better activities as seen with this "elderly antibiotic" if/when similar modifications are made.

3 Metallo-β-lactamase inhibitors

Perhaps the major problem with the use of beta-lactams, recognized almost from their first release into general usage in the 1940s, was the realization that beta-lactamase enzyme production by the "target microbes" was the major cause of resistance seen at the time. Initially these were known as the serine-β-lactamases (SBLs), then much later in time that class was followed by the metallo-β-lactamases (MBLs). Although there are a significant number of SBL-inhibitors in general use, usually as a mixture with the antibiotic, there are no MBL-inhibitors in clinical use and very few inhibitors directed against MBLs undergoing specific or general clinical trials currently.

Beta-lactamases are divided into four classes depending upon their amino acid homologies and molecular properties. The known SBLs (classes A, C and D) have a serine residue at their active site that hydrolyses the β-lactam, whilst the Class B enzymes (MBLs) have one or two Zn atoms at their active site that produce a hydroxide ion that acts as a nucleophile in their ring-opening operation. In a 2023 paper in *RSC Advances* by Shungube et al.,[8] a multidisciplinary and multi-country group with a substantial number of South African scientists, have identified synthetic MBLs that have significant activities against microbes producing MBLs.

In that report they identified 11 potential MBL inhibitors and emphasized two that are Zn-chelators and have activity against the New Delhi variant of MBLs when co-administered with meropenem against *Klebsiella pneumoniae*. Also in this paper is a harrowing map of the world demonstrating the incidence of resistant *K. pneumoniae* to Carbapenems, of which meropenem is one that is used worldwide. Major resistance was reported in Russia, Egypt and India with effectively 100 percent of invasive isolates, and at the 50 percent level were China and parts of Central and South American countries.

The two molecules (**6, 7**) from the 11 that are referred to above that demonstrated little to no toxicity *in cellulo* at the levels administered with time-kill kinetics demonstrated sterilizing activity for the two compounds (**6, 7**) with doses in the 0.5 to 2 μg.ml range. Similar levels of either compound were able to restore sensitivity to meropenem in *E. coli* and *K. pneumoniae* isolates exhibiting both NDM-1 and NDM variants of Class B NBLs. Thus, these compounds are potential candidates for entering preclinical trials with the hope of further development. Though as shown, they differ only in a substituent on the terminal β-lactam.

4 Potential CoV-2 Inhibitor(s)

One of the major problems with perhaps most of the compounds that were gleaned from repurposing libraries of pure and modified natural products and synthetic compounds in the early days of the COVID pandemic was the ultimate realization that, even though the compounds in two excellent studies (one led by Shokat and the other by Shoichet) were tested extensively *in cellulo* in human cell lines to identify potential agents, it subsequently was realized that drug-induced phospholipidosis by the "active" compounds gave a very large number of spurious results. Due to the 29 authors on the 2021 *Science* paper identifying the problem(s) and cause, only the first author is given, though this paper and its two predecessors are excellent examples of authors realizing that they were incorrect, and the reason(s) for the revision.[9]

Recently the Andersen group at the University of British Columbia published[10] data derived from synthetic analogues of alotaketal C (**8**). This compound was initially isolated from a Canadian-sourced sponge and subsequently became part of a large collection of natural products from all sources, plant, marine organisms and microbes. This collection was subsequently assayed in a screen designed to be studied against SARS-CoV-2 that had been engineered to function in Calu-3 lung epithelial cells, which contained an mNeonGreen

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fluorescent reporter. One molecule that was very potent exhibited an EC_{50} of 110nM, and it was alotaketal C (**8**) with a selectivity ratio of activity to cytotoxicity (against the host cell) of ~900 fold. In addition, except for the Delta variant of CoV-2, it demonstrated EC_{50} values of 300-700 nM against the other viral strains under the same assay conditions.

This natural product had first been isolated from a *Phorbas* sp. sponge collected in Howe Sound and earlier was shown to be a PKC activator that was more active than prostratin as a potential HIV-1 latency reversal compound. Interestingly, there were other data implying that that agent encouraged shedding of the presumed target of CoV-2, the ACE2 receptor. Thus, this compound might actually reduce the "target of the virus" rather than attack the virus itself.

Synthetic modification of the original structure yielded two derivatives (**9, 10**) that gave significant activities *in cellulo* (human lung cells) against both the Omicron BA.1 and BA.5 SARS-CoV-2 variants. The activity figures are EC_{50} values in nM in the figures. Notably, the more active compounds were in fact simpler in structure than the natural product, though the base spiro-structure was still maintained. ■

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New Members of ASP Fall 2023

ASP would like to welcome our 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 six full members and 25 associate members. We look forward to meeting you and learning more about you and your work. Information on ASP membership is available here.

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American Society of Pharmacognosy

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, at **asp.newsletter@lehman.cuny.edu**.

ASP Natural Product Sciences Webinar

Zoom Seminars

Thursdays 4 PM ET / 1 PM PT

www.pharmacognosy.us/natural-product-sciences-webinar/

C&EN Webinars

Various Days and Times

cen.acs.org/collections/webinars.html

Gordon Research Conference: Marine Natural Products

March 10-15, 2024

Ventura, California

www.grc.org/marine-natural-products-conference/2024/

22nd International Conference on the Science of Botanicals and the 7th World Congress on Medicinal and Aromatic Plants

April 15-18, 2024

Oxford, Mississippi

www.oxfordicsb.org

International Congress on Natural Products Research (ICNPR 2024)

July 13-17, 2024

Kraków, Poland

www.icnpr2024.org

American Society of Pharmacognosy

Capital Communiqués

Natural Product-related News from NIH and Beyond

By Barbara C. Sorkin, PhD

NEWS FROM THE US

Updates from the National Institute of Standards and Technology (NIST)

- Artificial intelligence in NIH peer review? On June 23 NIH published NOT-OD-23-149, "The Use of Generative Artificial Intelligence Technologies is Prohibited for the NIH Peer Review Process."

- The NIH Data Management and Sharing (DMS) policy that went into effect earlier this year requires that applications for NIH funding include a DMS plan. The NIH Scientific data sharing webpages (sharing.nih.gov) include a list of NIH-supported scientific data repositories, information on selecting a repository appropriate to the data you propose to generate, and, as noted in the last newsletter, information on how to include costs of data sharing in your application budget.

Drs. Noni Byrnes and Mike Lauer
PHOTOS: NIH

- Results of the NIH's Request for Information (RFI) on simplifying the research grant application peer review process are described in a mid-May blogpost from Drs. Noni Byrnes, Director of NIH's Center for Scientific Review, and Mike Lauer, Deputy Director for Extramural Research. The proposal is to reorganize the five review criteria into three factors: Importance of the Research (including the Significance and Innovation criteria), Rigor and Feasibility (corresponding to the Approach criterion), and Expertise and Resources (corresponding to Investigators and Environment). Over 800 responses to the RFI were received. A trans-NIH committee is developing implementation and evaluation plans. The blogpost discusses the issues of blinded review and equity. Dr. Byrnes described the planned changes following from the RFI in a recent presentation to the National Advisory Council for Complementary and Integrative Health (beginning at 1:56 in the videocast).

NIH-SUPPORTED RESOURCES

- Currently over 20% of cases of drug-induced liver injury in the United States are due to herbal and dietary supplements rather than conventional medications. LiverTox, a resource supported by the NIH National Institute of Diabetes, Digestive and Kidney Disease's Liver Disease Research Branch in collaboration with the National Library of Medicine provides an online resource on drug induced liver injuries, including up-to-date, accurate and easily accessible information on the diagnosis, cause, frequency, patterns and management of liver injury attributable to more than 1200 prescription medications and more than 100 botanical products, vitamins and nutritional supplements.

PRESENTATIONS, WORKSHOPS, WEBINARS

- Dr. Patrick C. Still, a program director at the NIH's National Center for Complementary and Integrative Health (NCCIH) presented a concept for a resource center for cannabis and cannabinoid research at the May 2023 NCCIH Advisory Council meeting.

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Dr. Patrick Still
PHOTO: NIH

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- A concept for a future Consortium Advancing Research on Botanicals and Other Natural Products (CARBON) initiative was presented to the open session of the National Advisory Council for Complementary and Integrative Health on September 8, 2023. The Advisory Council's meeting is available for viewing.

- NIH Office of Dietary Supplements (virtual) Seminar:
  - **November 8, 2023,** *Botanical Use for Health in the Caribbean and Mexican Diasporas* **Ina Vandebroek,** University of the West Indies, Mona, Jamaica

Dr. Ina Vandebroek
PHOTO: NYBG

FUNDING OPPORTUNITIES

- **NIGMS Biomedical Technology Optimization and Dissemination (BTOD) Program**

  The National Institutes of General Medical Sciences (NIGMS) encourages BTOD Center proposals focusing on technology research areas within the NIGMS mission. The NIGMS BTOD Program supports the optimization and broad dissemination of late-stage technologies. The BTOD Centers also have collaboration opportunities for the biomedical research community to address the technological challenges in their research areas. Please visit the NIGMS BTOD website and Notice of Funding Opportunity (PAR-23-110) to learn more about this program and the awarded Centers. The next application due date is January 26, 2024. Potential applicants are strongly encouraged to consult with NIGMS staff before application submission. After reviewing the relevant documentation, please contact **NIGMS_BTODMailbox@nigms.nih.gov** with any questions.

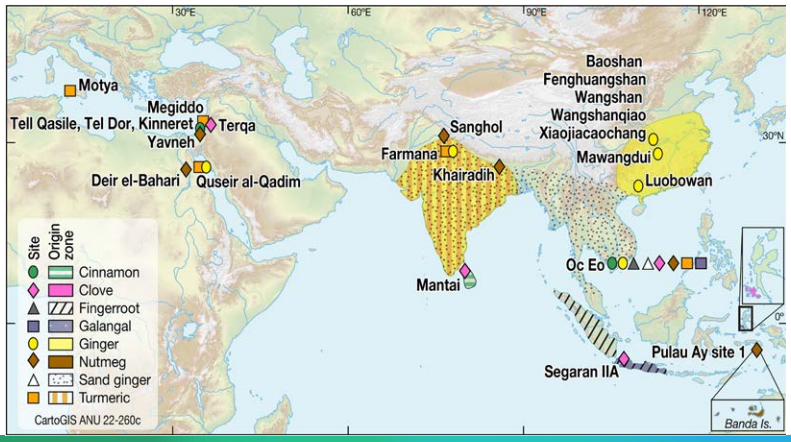
- **NIGMS National and Regional Resource Program**

  NIGMS supports National and Regional Resources to provide the biomedical research community access to NIGMS-mission-related, state-of-the-art, unique, and mature research capabilities. Please visit the NIGMS National and Regional Resource website and Notice of Funding Opportunity (PAR-22-065) to learn more about this program and the awarded National and Regional Resources. The next application due date is June 14, 2024. Potential applicants are strongly encouraged to consult with NIGMS staff before application submission. After reviewing the relevant documentation, please contact **R24mailbox@nigms.nih.gov** with any questions.

ODDS AND ENDS

- Dating spice? Curry lovers, did you know that consumption of curries and the trans-Indian Ocean trade in curry spices may date back at least two millennia? Weiwei Wang, et al. report in the July 21 issue of *Science Advances* that plant micro-remains recovered from the surfaces of stone grinding tools excavated "from the archaeological site of Oc Eo in southern Vietnam, an entrepôt of the state of Funan that was occupied during the early centuries CE," included "turmeric, ginger, fingerroot, sand ginger, galangal, clove, nutmeg, and cinnamon."

  The authors suggest this find reflects trans-Indian Ocean spice trade in the ancient world.
  DOI: 10.1126/sciadv.adh5517



From the Archives:

The Honest Herbalist and Rational Phytotherapy

By Christine Jankowski, MA

While reviewing the American Society of Pharmacognosy Foundation Papers, I came across two pages cut from a 1997 edition of *USA Today*. One sheet was a full-page advertisement for a new Celestial Seasonings® product, echinacea lozenges. The other was an article on deceased ASP Honorary Member Varro E. Tyler entitled "Medicine Catches up to 'Honest Herbal' Expert." In the article, author Nanci Hellmich asks Tyler his thoughts on the increased interest in natural products in the United States. Tyler gives his insights on phytomedicine and about his upcoming book, *Rational Phytotherapy*. He takes the opportunity to educate an American audience by sharing information on herbal medicine backed by scientific research collected in Germany.

As many know, Varro E. Tyler (1926-2001) was a pharmacognosist, a consultant, a professor, and the dean of pharmacy at Purdue University from 1966 to 1986. He was a prolific writer of hundreds of articles on medicinal plants and an orator of numerous presentations on natural products at meetings and conferences across the nation.[1] Of his eighteen books, one of his most popular was *The Honest Herbal: A Sensible Guide to the Use of Herbs and Related Remedies*, and many editions followed its initial release in 1981.

Tyler was an advocate for herbal medicine that was backed with scientific evidence supporting its safety and effectiveness.[2] In the *USA Today* article, Tyler explains that before World War II there was interest in using natural products for medicine or treatments in the United States. As the drugs of that time became more synthesized, the public interest died down. Meanwhile, outside of the United States, the use of natural wellness products was commonplace. As Tyler states, "In Germany, the use of plant drugs is a science."[3]

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HEALTH

Medicine catches up to 'Honest Herbal' expert

By Nanci Hellmich
USA TODAY

Varro Tyler wasn't surprised by this week's news that ginkgo biloba extract improves brain function in Alzheimer's patients.

The public is just learning about medicinal plants like ginkgo, St. John's wort and echinacea, but Tyler has been studying them all his life.

Now, the growing fascination with botanical supplements has made Tyler, at age 70, an overnight sensation, a popular lecturer and consultant in this field. His book, *The Honest Herbal* (Pharmaceutical Products Press, $17.95), published in 1982, is now in its third edition. And he has another book due out next month.

A former academic, Tyler is one of the country's premier experts on herbal medicine. He has long been a strong advocate of the appropriate use of herbs that are backed with adequate scientific evidence supporting their safety and effectiveness.

The herbal revolution in this country is long overdue, he says. Natural remedies are extremely popular in other countries, but they fell out of favor in the USA during World War II, when the public became enamored with the new synthetic drugs.

Now, the United States is playing catch-up. Doctors, nurses, dietitians and other health professionals are pounding on Tyler's door seeking information. His message: be open-minded. Herbs can be effective for a variety of conditions. They're usually less expensive than drugs and often have fewer side effects.

But he's a loud critic of what he considers outrageous and hyperbolic claims that some herbal manufacturers make about their products. Tyler sees himself as "in the middle on most occasions. I'm too conservative for many of the people in the herbal products field who claim *everything* is good for *everything*. And perhaps I'm too liberal for conservative physicians who haven't read some of the clinical research on herbs."

It's a balance that has earned him wide respect. He is "reliable, meticulous intellectually," says Jean Carper, author of the herb book *Miracle Cures* (HarperCollins, $25). "He knows the data. He talks to the foreign scientists."

Tyler "has been a voice of authority and responsibility in taking a conscientious approach to this field," says Marc Micozzi, executive director of the College of Physicians of Philadelphia and author of the first medical school textbook on complementary medicine.

Now retired, Tyler was the dean of pharmacy at Purdue University in West Lafayette, Ind., for 20 years. He ...

Honest herbalist: Longtime expert Varro Tyler is a strong advocate for the use of botanicals to treat a variety of conditions.

Popular botanicals for relief

Herbs that expert Varro Tyler believes will become increasingly popular as the population ages:

▶ **Saw palmetto.** Widely used in Europe for treatment of the conditions associated with benign prostatic hyperplasia, a nonmalignant enlargement of the prostate. Relieves some of the symptoms of the condition, including frequent urination, especially at night.

▶ **Kava kava.** A plant from the South Pacific, believed to help relieve anxiety. Popular in Europe for years.

▶ **Black cohosh.** An American plant that has been researched in Germany. Used there for various symptoms associated with menopause, including hot flashes.

▶ **Chasteberry.** According to German research, may be useful for women who suffer from premenstrual syndrome.

▶ **Milk thistle.** Used for many years for a variety of conditions, especially liver complaints. Believed to prevent toxins from entering the liver cells.

15% to 20% annually, the survey says.

"In a big wholesale catalog you can find more than 500 different herbs that are being sold for medicinal reasons," Tyler says.

So it's no wonder that consumers are often baffled when they go into a health food store, drugstore or discount store to buy a supplement. They often don't know which herbs work for which conditions. They don't know what strength or form of the supplement to buy, and they don't know which manufacturer is putting out the best products.

It's "chaotic" out there, Tyler says. He has made it his job to help consumers sort through the confusion.

There are a few products on the market that are "downright dangerous," Tyler says. Comfrey is one. It should not be used for internal consumption because it contains toxic alkaloids that cause liver cancer, he says. "It's regulated in every civilized country in the world except the United States. The FDA should take it off the market" for internal use.

(The FDA's Arthur Whitmore says, "We have some concerns about the safety of comfrey, but we're not at this time preparing any regulatory restrictions on it.")

Most of the herbal preparations "are reasonably safe" if used in the correct doses, Tyler says, and the couple dozen best sellers are backed by clinical evidence. Among them:

▶ **Ginkgo.** "There have probably been more studies on ginkgo in Europe than any other herb." He says ginkgo is good for the ailments associated with cerebral blood flow, particularly in geriatric patients. These conditions include short-term memory loss, headaches, dizziness, vertigo.

▶ **St. John's wort.** "There's very good evidence to support using St. John's wort to treat mild and moderate depression, and now the National Institutes of Health are going to do an extensive study on it."

▶ **Garlic.** The most popular herb worldwide, "garlic is useful in lowering cholesterol by 10% to 12%."

▶ **Echinacea.** "It's quite useful for the prevention of colds and influenza symptoms. There's good evidence it strengthens the immune system. The best way to take it is when you feel symptoms coming on."

USA should consider German system, Tyler says

Herbal expert Varro Tyler thinks U.S. dietary supplement regulations need to be revamped so consumers can get more accurate information about herbs. Germany, he believes, would be a good role model for U.S. officials.

Botanical supplements here are loosely regulated by the Food and Drug Administration. They fall into the dietary supplement category and are governed by regulations different from those for drugs.

Drug manufacturers must prove that a product is safe and effective before it goes on the market. Not so with dietary supplements. They can be sold with no government screening, and some arrive at stores with very little scientific evidence to support their effectiveness, Tyler says. To get a supplement off the market, the FDA must prove the supplement or its ingredients pose a hazard to consumers.

Supplement makers are not allowed to make claims that their products treat diseases; they can make structure and function claims.

For example, the manufacturers of feverfew products can say they are good for the brain but can't claim usefulness in treating migraines, he says.

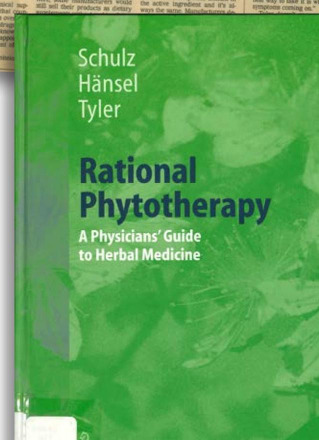
Germany treats botanical supplements differently. In that country, they are approved as over-the-counter and prescription drugs by a committee of scientists known as Commission E, which is appointed by the German equivalent of the FDA.

Over the years, Commission E has reviewed 300 herbs and found about 200 are safe and effective. The Germans publish monographs (essays) on each herb that outline exactly what the herb is, possible uses, safe dosages, possible side effects and drug interactions. In Germany, natural substances are manufactured to pharmaceutical standards and carry informative labeling.

If a similar system was adopted here, some manufacturers would still sell their products as dietary ...

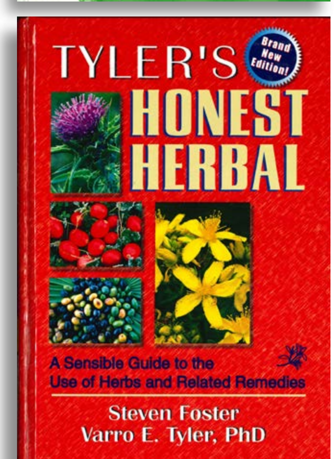
... ing dietary supplement labels, says she agrees with Tyler that "Commission E is a good model to be added to our current system but not to replace our system."

Until there are some changes, Tyler recommends consumers use "standardized" products — those that are clearly labeled "standardized extract" or "standardized herbal extract," which means each dose contains a specific amount of the active ingredient and it's always the same. Manufacturers de...



ABOVE: The *USA Today* article which featured Tyler and *Rational Phytotherapy* from 1997.

RIGHT: Cover of *Rational Phytotherapy* from 1998 as found in the Lloyd Library and Museum's collection.



BELOW: Cover of the fourth edition of *Honest Herbal* authored by Steven Foster and Varro E. Tyler.

Varro E. Tyler (1926-2001) was a pharmacognosist, a consultant, a professor, and the dean of pharmacy at Purdue University from 1966 to 1986.

From the Archives: The Honest Herbalist and Rational Phytotherapy

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At the time of the article, Germany had more regulations and standardizations for phytomedicine than the United States. Commission E of the German Federal Health Agency (later known as the Federal Institute for Drugs and Medical Devices) is comparable to the US Food and Drug Administration. The commission researches and conducts clinical studies to determine regulations of plant-based drugs. Their labels are clearly printed with information on how to use supplements, the recommended dosage to be administrated, and any possible side effects. Here in the US, the FDA oversees the regulation of products, but with fewer standards. An example Tyler used was feverfew. A company could say that their feverfew product is good for the brain but could not label it as a migraine reducer.[2] As interest in using natural products resurged, many Americans purchasing these herbals had little guidance regarding a product's strength, frequency of use, or even what it treated.

In its introduction, Tyler states, "*Rational Phytotherapy* may be called the world's first qualitatively complete, science-based herbal in the English language."[3] *Rationale Phytotherapie: Ratgeber für die ärztliche Praxis* was originally written by Drs. Volker Schulz and Rudolf Hänsel in 1996. The translated version, *Rational Phytotherapy: A Physicians' Guide to Herbal Medicine* (1998), was based on the third German edition of the publication. The English version is fully revised, expanded, and includes an introduction written by Tyler. The guidebook gives detailed information on the data collected from Commission E, who conducted clinical research on 300 herbs, 200 of which were found to be safe and effective. Each chapter focuses on a different body system, with subchapters covering different ailments or diseases within those systems and the natural products used as treatment or therapy. An index at the end provides a table of 100 of the most prescribed natural products in Germany for 1994-1995.

Tyler was an advocate for herbal medicine that was backed with scientific evidence supporting its safety and effectiveness.

TYLER'S PREDICTIONS FOR POPULAR HERBS

In 1997, Varro E. Tyler predicted the following herbs would become more popular for the aging U.S. population. Did his predictions hold up for 2023 ?

Saw palmetto
Kava kava
Black cohosh
Chasteberry
Milk thistle

Tyler predicted the publishing of *Rational Phytotherapy* would be "a milestone of achievement" for phytomedical science for human health[3] and he was right. Multiple editions of *Rational Phytotherapy* have been released by Springer Nature. This includes updates for a fourth edition in 2001 and a fifth for 2004, a softcover edition released in 2011, and an e-book version in 2013.[4] Mark Blumenthal of the American Botanical Council, and an ASP member, contributed to the fifth edition, renaming the secondary title *A Reference Guide for Physicians and Pharmacists* and updating the list of phytomedicines from 2002.[5]

As interest in phytomedicine, herbal medicine, and natural products continues to grow across the world, resources like *Rational Phytotherapy* and Tyler's publications remain important guides for laymen and professionals alike, ensuring that ailments are effectively treated with natural products backed by science. ■

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