



American Society of Pharmacognosy

ASP Newsletter: Fall 2021, Volume 57, Issue 3

Fall 2021

**Discovering
Nature's
Molecular
Potential**

ASP President McPhail Addresses Members

By Kerry McPhail, PhD

NOTE: A video of President McPhail's address to members at the July 28th ASP Business Meeting is available at www.pharmacognosy.us/presidential-remarks-asp-business-meeting-2021/

I am profoundly moved and honored to have this opportunity to serve the ASP as president. The ASP has been an anchor like no other for me since shortly after I arrived in the United States from Zimbabwe, twenty-one years ago now. The stated mission of the American Society of Pharmacognosy is “to promote and develop the science of pharmacognosy and all aspects of those sciences related to natural products.” The role of the ASP then is to cultivate interest and participation in, as well as expand the scope of, interdisciplinary natural product sciences. Why? I cannot think of another field of research that so clearly belongs to all people and that intersects so many current critical challenges in human and environmental health and

well-being globally. For many, the turmoil of the COVID-19 pandemic, momentous social justice movements and unprecedented simultaneous weather events around the world have brought an immediacy and focus on what is

important and the need to take action. Natural products research captures the imagination of people of all ages and, as such, has an important role to play in combating the anti-science and education sentiment that is alarmingly pervasive, even as we rely on science and technology to combat an ongoing global pandemic and climate change. Not only do we need to “promote and develop” natural products science but also showcase and leverage it as an inherently diverse and

continued on page 4



Dr. Kerry McPhail

PHOTO: DANIEL SEEMILLER

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IN THIS ISSUE: FALL 2021

ASP President McPhail Addresses Members	1
Editor's Corner	3
Inaugural ASP Vanguard's Virtual Symposium Series	6
a Great Success!	
ASP 2022 Annual Meeting in Charleston	10
<i>Journal of Natural Products</i> Recognizes	12
Outstanding 2020 Papers	
Grants and the People Behind Them: John Daly	14
ASPF Donors 2021	17
Taking Action: One Year after the ASP Diversity,	18
Equity and Inclusion Committee Call to Action	
In Memoriam: Leonard Worthen	20
In Memoriam: Margaret F. Roberts	23
Hot Topics	26
Natural Products in the World of Vaccines:	29
Saponin Adjuvants	
New Members of ASP	33
Conference Calendar	36
From the Archives	37



Dr. Kerry McPhail



Charleston



The flowers of *Quillaja saponaria*

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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Editor's Corner

American Society of Pharmacognosy

By Edward J. Kennelly, PhD

For a second year in a row, the ASP annual meeting has been canceled due to the COVID pandemic. ASP continues to find new ways to interact with members, and one of these was the Vanguards virtual conference that took place in July. Please take time to read about the highlights from this unique approach to video-conferencing that ASP used this year to provide a platform for scientific and social discourse among our members, especially highlighting the research of younger members. The feedback has been encouraging. It is good to know that even in these trying times, ASP has provided innovative ways to connect like this and the monthly webinars: (www.pharmacognosy.us/natural-product-sciences-webinar/).

The ASP Business Meeting also took place virtually this year, and the new ASP president, Dr. Kerry McPhail, was instated, along with new Executive Committee members. Thanks to the ease of recording video conferences, President McPhail's address to members is available on the ASP website, and she has also provided the lead article for this issue of the *Newsletter*. I hope you will take time to read about President McPhail's vision for the ASP, despite the uncertainties of these times.

The fall ASP *Newsletter* is typically jam-packed with coverage of the annual meeting, so this issue is a sad reminder that many of the normal annual traditions of the society, like bestowing awards, did not occur in person this year. However, the 2022 ASP Annual Meeting in Charleston, SC will be a time where the society will make up for this by adding an extra day (Thursday) to the meeting, and certain awards from 2021 as well as 2022 will be given out. Please read about the planning for this meeting that will occur July 23-28, 2022 in Charleston.

ASP continues to mourn the loss of several prominent members. In this issue, the 15th president of ASP, Dr. Leonard Worthen is remembered for his important role in the early days of the society. In the tribute, as well as in "From the Archives," Worthen's role in the health of the finances of the *Journal of Natural Products* (formerly *Lloydia*) are described in great detail. I am reminded how the decisions made by early members of ASP's leadership team have resonated to this day. We also mourn the loss of Dr. Margaret Roberts who was on the faculty of the School of Pharmacy, University of London for 30 years. In a time where few women held faculty positions in professional schools, she stood out for her scholarship and excellent teaching skills. While she was not a regular attendee of ASP meetings, she interacted with many ASP members and will be greatly missed. Before going to press, we learned of the passing of two other prominent ASP members, Drs. George "Bob" Pettit and John Cassady. We plan to include tributes to them in the winter issue of this *Newsletter*.

In his regular "Hot Topics in Pharmacognosy" column, Dr. Dave Newman does a deep dive into the practice of repurposing drugs for the treatment of COVID. In a separate column, Dr. Ray Cooper discusses how saponins from a Chilean bark are being used as adjuvants for boosting immune responses in certain vaccines. As we go to press, reports of COVID infections in the US are dropping significantly, and I hope that with increased vaccinations and better treatments, infection rates will continue to decrease.

I hope all ASP members have a good autumn and keep safe. ■

continued from page 1

I cannot think of another field of research that so clearly belongs to all people and that intersects so many current critical challenges in human and environmental health and well-being globally.

international science that relies on collaboration. Collaboration here implies a tolerance for diverse ideas and a commitment to free, objective inquiry based on a culture of evidence and critique. Certainly, the numerous ASP members named among the 100,000 most influential scientists in a 2020 PLoS Biology article (<https://www.pharmacognosy.us/asp-members-recognized-among-most-influential-scientists/>) evince collaborative, interdisciplinary natural products research.

The ASP directly promotes critical biomedical research for human health by fostering national and international scientific collaborations through its organized events and administration of Society awards. While the pandemic shutdown precluded the usual forum of the ASP annual meetings, twenty-four Natural Product Sciences webinars were offered from April 2020 to June 2021, thanks to members of the Webinar and Publicity Committees as well as ASP Business Manager Laura Stoll. The Natural Product Sciences webinars featured diverse research themes addressed by forty-four presenters, of which twenty-one were women, from Asia, Central and South America, Europe, and academia and industry in the United States. Virtual meetings organized by the Younger Members Committee, such as the recent Fridays in July series “Vanguards of Natural Products,” also encouraged broad international participation. Importantly, significant non-seminar discussion time and poster sessions were facilitated on the interactive virtual platform.

If there is anything positive to have come from the cancellation of the 2020 (ICNPR, San Francisco) and 2021 (Grand Rapids, Michigan) in-person annual meetings, it is the actualization of ranging events in which participation was potentially limited only by time zone rather than by the cost or scheduling of travel. I believe that a majority of us fervently wish for an in-person meeting in July 2022. Regardless, we expect to maintain some frequency of virtual events, including both scientific and professional

development webinars and potentially a second annual Vanguards of Natural Products event highlighting early-stage researchers. The foundations laid in the past twelve to eighteen months for virtual meetings and social media communication and networking will continue to be refined moving forward, as the Society adapts to the COVID-19 pandemic and post-pandemic era. The ASP officers and committees look forward to ideas and participation by any and all ASP members. We are also cautiously optimistic and excited to see the developing program for the 2022 annual meeting in Charleston, South Carolina. Wide-ranging workshops and an extra day of programming will allow us to better catch up with each other and also with presentations from award recipients over the past two years.

This year we will have the opportunity to vote on designating the ad hoc Diversity, Equity and Inclusion (DEI) Committee as a standing committee. This is a necessary step, for which I applaud the past and present co-chairs, as we all seek to understand and take action against enduring systemic racism. Nevertheless, it is a jarring reality that inequity and racism will require the constant attention of a standing committee for the foreseeable future. The Society is indebted to the DEI Committee for their continued work to address critical “leaks” in the educational pipeline for Black, Indigenous and Latinx young people to explore and pursue careers in natural products research.

The work of the DEI committee was most recently evident via the August 12 NPS webinar featuring inspiring talks from the seven women undergraduate ASP summer research fellows (SRFs). In ten minutes each, these seven young researchers gave us a glimpse of the tremendous amount of research and learning accomplished in ten short weeks. Some of them had no prior laboratory experience and all missed components of in-person laboratory training in their degree curricula during the pandemic shutdown. So, congratulations

continued on page 5

Not only do we need to “promote and develop” natural products science but also showcase and leverage it as an inherently diverse and international science that relies on collaboration.

continued from page 4

The Society is indebted to the DEI Committee for their continued work to address critical “leaks” in the educational pipeline for Black, Indigenous and Latinx young people to explore and pursue careers in natural products research.

and thank you to the inaugural ASP summer research fellows: *Ama Boamah (Mentor - Jaclyn Winter, University of Utah), Victoria Casimir (Mentor - Eduardo Caro Diaz, University of Puerto Rico), Michelle Katemauswa (Mentor - Robert Cichewicz, University Of Oklahoma), Nana Obli (Mentor - David Rowley, University of Rhode Island), Jessie Raheisoanjato (Mentor - Amy Lane, University of North Florida), Ariel Richards (Mentor - Erick Leggans, Grinnell College) and Lorena Valentin (Mentor - Jeffrey Rudolf, University of Florida)*. Congratulations and thanks also to the faculty mentors and their lab members, whose engagement and dedication to providing rich research experiences were so evident in the webinar presentations. Lesley-Ann Giddings, Christine Salomon and Brian Murphy critically provided a robust support network, including weekly professional development and networking meetings, throughout the program to maximize the impact of these learning experiences. So what next? It is essential now to establish longer term financial security for the ASP SRF program, and indeed other research awards, so that they may have the sustained impact envisioned by the generous donors and ASP members who worked to enable their successful launch. The Audrey S. Bingel Fellowship for Female Scientists is another recently implemented, successful award program that the Society strives to perpetuate. If you are looking for ways to contribute to equity in our Society and the natural products sciences, or to pay forward to the next generation, please consider donating directly to one of these award programs through the ASP Foundation.

Natural products research is inherently an international science that is rooted in and relies on global biological diversity. Cultures across the world have documented use of natural products as traditional medicines for thousands of years. Many of us have traveled and developed

collaborations across the globe that have been instrumental in our careers. Even when investigating soil microorganisms from our own backyards, we rely on published international data and knowledge and increasingly turn to accessible, globally-curated databases to accelerate our natural product characterizations and to gain insight on metabolic patterns and processes across species and/or environments. The benefit to human health brought about by translation of natural products to medicines and supplements is a tangible message that conveys the importance of conserving and recovering biological diversity.

In addition to broadcasting this ultimate outcome of “discovering nature’s molecular potential,” it is fitting for us to consider the environmental impact of contemporary natural products research practices. Advances in technology have dramatically lowered analytical detection limits for structure determination and allowed miniaturization of biological assays. Combined with sharing and access to open data and software tools for comparative, multi-omic analyses, the outcome ultimately is less travel for less biological material needed for potentially more targeted research driven by more defined hypotheses. Networking with peers and colleagues nationally and internationally leverages, accelerates and broadens the impact of prior and current natural products research.

In the year ahead, I look forward to working with and getting to know many of you as we look to recover from the immediate COVID-19 pandemic and adapt to a post-pandemic era. Thank you to those of you who continue to be involved in ASP committees, and thank you to so many who have newly accepted invitations or volunteered to be involved. Continued work to expand and articulate the tangible benefits of membership in our Society and thus grow our community is not possible without your variety of ideas, skills and talents. ■

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Inaugural ASP Vanguard's Virtual Symposium Series a Great Success!

By C. Benjamin Naman, PhD and Karen VanderMolen, PhD

As we collectively surpass a year and a half together in the global COVID-19 pandemic, many of us suffer from online meeting fatigue and sore monitor eyes. The ASP overcame these challenges this summer and hosted a virtual conference series on July 16, 23, and 30 entitled "Vanguards of Natural Product Research 2021," leveraging the Virtual Chair platform as a venue to increase engagement and personal connection. The program was very successful in building and maintaining meaningful connections and providing important opportunities to younger members of our society at a crucial moment in their careers.

This event highlighted some advantages of conducting virtual meetings, including spotlighting younger members and fostering participation from distant locations (Figure 1). We are thus virtually including members and attendees that would often otherwise be excluded from attending more-costly, in-person events. The tremendous outreach, diversity, and inclusion of the ASP Vanguard's event benefitted altogether more than 450 scientists hailing from nearly 50 countries worldwide, especially including the 18 speakers and 135 poster presenters from the younger membership.

One advantage of the virtual meeting platform and low associated cost has been the greatly increased accessibility of podium presentations for younger members over what tends to be possible during in-person symposia. The Vanguard's program website, reproduced here in part as Figure 2, displayed the diversity of background and geography represented by the selected podium presenters that is reflective of broad demographics in the ASP. Speakers were introduced to the extent possible by their own mentors, who are thanked for providing personal remarks and professional endorsements to job-seeking younger members on the global stage. The Vanguard's presented their cutting-edge research at the forefront of di-

FIGURE 1

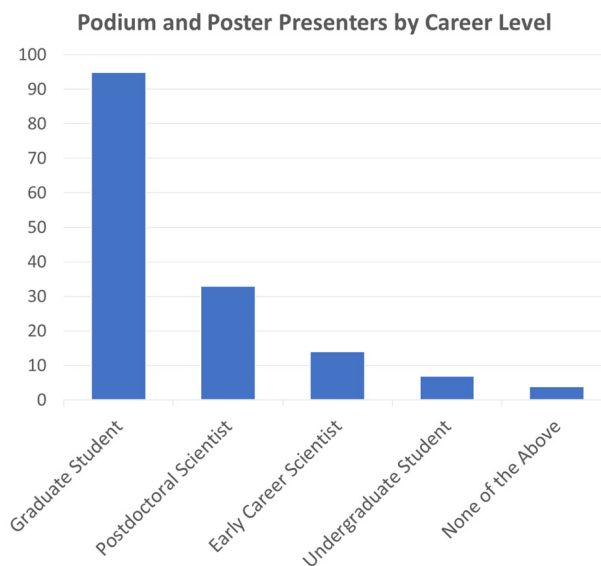
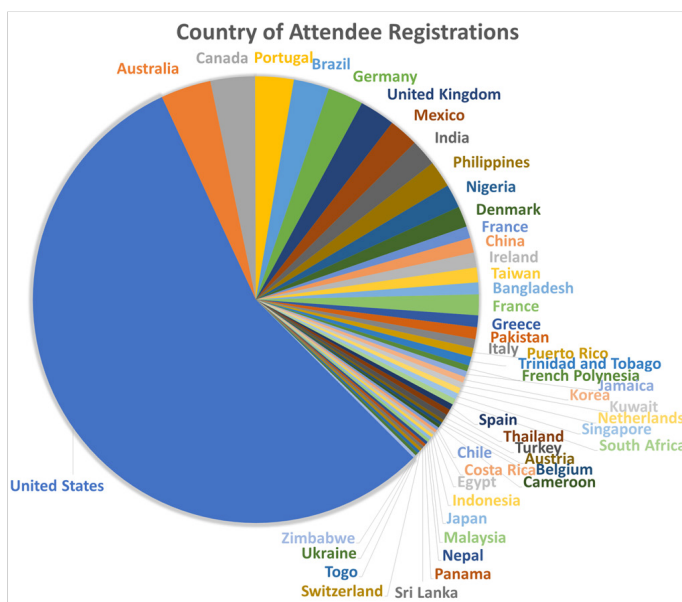


FIGURE 1: Demographics of the conference.

Bar chart shows career level of the podium and poster presenters.

Pie chart shows the country of all attendees' registrations.

All data were self-reported by participants.



continued on page 7

Inaugural ASP Vanguard's Virtual Symposium Series a Great Success!

continued from page 6

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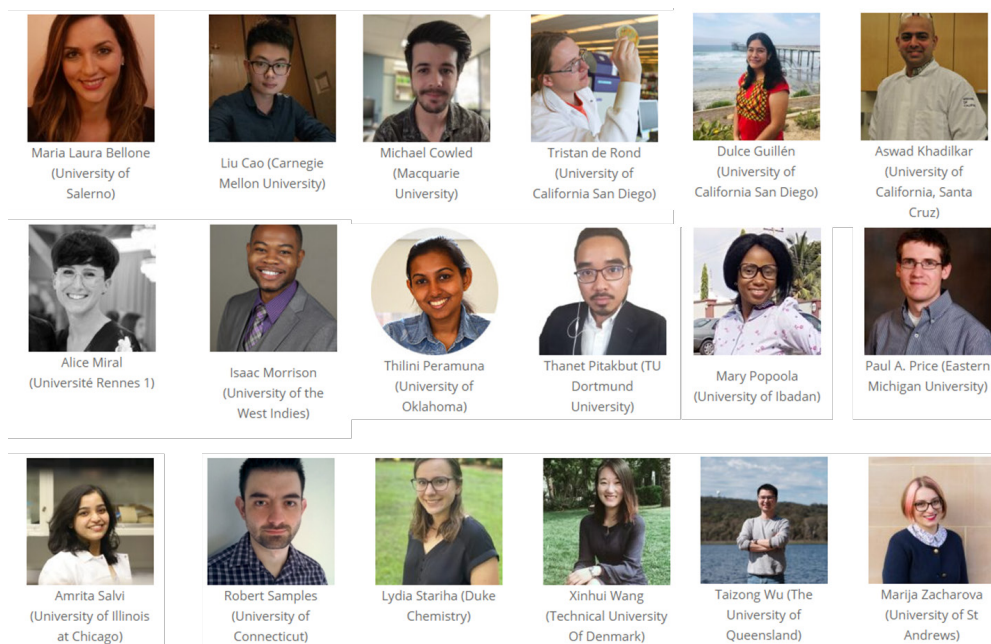


FIGURE 2: Vanguard's of Natural Product Research 2021 podium presenters.

Note: Not able to be reflected on the website in time, Mary Popoola had a last-minute emergency and was substituted by an unrelated presentation from Kathleen Abt (CIIMAR University of Porto).

verse areas of natural product sciences and drug discovery that the ASP brings together, including biosynthesis, chemical ecology, genomics, informatics, metabolomics, natural product isolation and characterization, pharmacology, total organic synthesis and medicinal chemistry optimization, and traditional medicine.

The podium presentations were held via Zoom akin to the ongoing webinar series, and poster sessions and networking hours operated in the Virtual Chair online platform that facilitated direct one-on-one and small group discussions that mimicked typical in-person conference experiences. The motivation for ASP hosting the Vanguard's program was to bring the membership together during a time we could not meet in person for the second consecutive year, and especially provide

opportunities for career advancement to graduating students and postdocs or entry level industrial scientists seeking a new permanent position. The greatest early indicator of the success of this event is that we already have first-hand accounts of job offers for younger members that were made during the Vanguard's symposium series!

In addition to being productive, the program was enjoyable! People were interacting with each other who otherwise might never have had a chance to meet or got together in the conference platform for the first time after a long period of separation. There were surprises built in to the virtual world for careful inspectors. For example, the molecular structure of taxol and discodermolide, among other natural products,

continued on page 8

Inaugural ASP Vanguard Virtual Symposium Series a Great Success!

continued from page 7

The Vanguard presented their cutting-edge research at the forefront of diverse areas of natural product sciences and drug discovery that the ASP brings together, including biosynthesis, chemical ecology, genomics, informatics, metabolomics, natural product isolation and characterization, pharmacology, total organic synthesis and medicinal chemistry optimization, and traditional medicine.



FIGURE 3: Vanguard of Natural Product Research 2021 attendees congregated around the virtual bar for a bit of enjoyable networking among new and old friends.

SCREENSHOT PRODUCED BY CBN.

could be found hiding in certain parts of the virtual conference center. There was also a virtual bar that managed to draw happy crowds (Figure 3). People were seen connecting in from their homes, offices, and lab spaces around the world. Surprise appearances were made by a few family members and pets, and there was even a brief interlude during a podium talk while the presenter glanced out the window to check that a proximal car crash did not need urgent attention before returning in stride to discussing science. We are often reminded, especially during virtual meetings, that we are each human and subject to circumstance even while we are being professional.

Being human in the context of conference planning

also must necessarily involve consideration for the family life of prospective attendees. Dr. Alejandra Prieto-Davo commented during attendance of the Vanguard, “I can’t always find babysitters, funding, time off, and make all the arrangements to go to a meeting, so I usually have to choose one per year to attend. I really love that we can stay connected by webinars and the Vanguard event, and I hope that continues!” This aspect of inclusion is another grand advantage of the virtual platform. The importance of inclusion can also be expanded and applied to earlier exposure of scientists to the ASP. Dr. Simon Jackson reported, “It has been so wonderful to be able to participate in this event from my

continued on page 9

Inaugural ASP Vanguard's Virtual Symposium Series a Great Success!

continued from page 8

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home in Ireland. The online platform allowed me to have an undergraduate student involved who would not have otherwise had the chance to attend an in-person meeting with the travel costs associated." A few more testimonials from attendees of the ASP Vanguard's of Natural Product Research 2021 event are included here to highlight some of the positive feedback and brainstorming ideas received during and after the program:

"It was a bit weird to walk an avatar around the screen of the virtual conference center but it was also quite fun, and the popup interactions were a great simulation of what happens during an in-person meeting. Kudos to the organizers for finding a great platform for the Vanguard's program and fingers crossed for an in-person ASP meeting in 2022!" —Dr. Marcy Balunas

"The Vanguard's program inspired me to think that the ASP and individual researchers should consider using platforms such as Virtual Chair / gather.town to promote outreach to other locations to explain and illustrate how natural products drug discovery impacts everyone. This could be done at the local level (schools) and virtually anywhere else in the country or world." —Dr. Roy Okuda

"The in-person annual meetings always offered a convenient opportunity for lab alumni reunions, and I think this virtual platform can facilitate more people coming together during or after scheduled conference hours. I want to get a lot of people from our old group back together and catch up on what everyone is doing now!" —Dr. Patrick Still

"I don't know that I would have stayed in chemistry research had it not been for my interactions and engagement through the ASP. The importance of the society and its conferences cannot be overstated, even with this and last year's meetings being all virtual. Every meeting has opened up new opportunities for me to develop as a scientist, forge new connections, and walk away inspired." —Dr. Joe Egan

The Vanguard's program benefitted in both planning and ex-

ecution from lessons learned through last year's Zoom-only ASP Younger Members Virtual Symposium 2020, which was summarized previously. [*The ASP Newsletter*, **2020**, 56 (3): 21-23.] The organizing committee for the Vanguard's 2021 symposium series included Drs. C. Benjamin Naman, Karen VanderMolen, Robert Cichewicz II, Cindy Angerhofer, and ASP Business Manager Ms. Laura Stoll, and the newly titled Dr. Joe Egan, who successfully defended his thesis just days before the last part of the conference program. (Congratulations to Joe!) We are collectively thankful to all participating presenters and attendees, as well as Advion X Interchim for corporate sponsorship and the Executive Committee of the ASP for providing financial support to make registration free for all attendees. Presenters were charged a nominal fee of \$10 to offset costs and ensure that only serious abstract submissions would be received and reviewed. The abstracts were evaluated by current representatives of the ASP Younger Members Committee: Drs. Vinayak Agarwal, Fatma Al-Awadhi, Skylar Carlson, Eduardo J. Caro-Diaz, Joe Egan, Jie Li, Joshua Kellogg, Emily Mevers, and Rana Abdelfattah Montaser, who are all thanked for this service to the Younger Members Committee and the ASP.

We look forward now to the next annual meeting, scheduled for July 23-28, 2022, in Charleston, South Carolina (<http://aspmeetings.pharmacognosy.us/>), to reunite in person or meet new members of the ASP and other participants for the first time. Meanwhile, we appreciate having had this opportunity to connect remotely online. We recognize that greater inclusivity and outreach, together with lower costs, are among several advantages of virtual events that merit the consideration of adding online interim meetings to the repertoire of benefits afforded by ASP membership, even after in-person conferences can resume. Be on the lookout for a feedback survey coming your way soon, or reach out directly to members of the Vanguard's organizing committee or the Executive Committee to share your thoughts. ■

We recognize that greater inclusivity and outreach, together with lower costs, are among several advantages of virtual events that merit the consideration of adding online interim meetings to the repertoire of benefits afforded by ASP membership, even after in-person conferences can resume.

ASP 2022 Annual Meeting in Charleston



By Mark Hamann, PhD

The 2022 American Society of Pharmacognosy Annual Meeting will be held in Charleston, South Carolina from Saturday, July 23 to Thursday, 28 (<https://aspmeetings.pharmacognosy.us>). The meeting has been extended by one day to accommodate both the 2021 and 2022 award winners and an anticipated larger-than-normal turnout. The venue for the meeting will be the Charleston Convention Center in the vicinity of downtown Charleston and many nearby attractions. Known for its historic downtown with its cobblestone streets and horse-drawn carriages, Charleston is the epitome of Southern charm and hospitality.

The schedule for the meeting includes sessions addressing topics such as: CyroEM in drug discovery; natural product controls of cancer; emerging infectious diseases (including SARS-CoV2); neglected disease; advances in NMR and MS based informatics; the role of natural products in mitigation of climate change; synthetic biology approaches to NP modifications; and recent advances in the cannabinoids and other botanicals. Natural product leaders from Cameroon, China, Nigeria,



Top: Charleston, downtown

Below: Charleston Convention Center

Panama, Poland, South Korea and Turkey have been identified to help promote the meeting among investigators from these countries active in natural products research and development.

The opening reception and banquet will occur at the Charleston Convention Center. Shuttle service to downtown Charleston will be available. There are many areas in Charleston to explore including Shem Creek, and Middleton Gardens as well as the Sanctuary-Kiawah Island Resort, which includes access to the ocean, Charleston's

continued on page 11

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www.pharmacognosy.us

ASP 2022 Annual Meeting in Charleston

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and recent advances in the cannabinoids and other botanicals.

continued from page 10

historical district, fine dining and shopping as well as the amenities associated with Kiawah Island. The Ocean Course on Kiawah Island hosted the 2021 PGA Championship and will provide world class golfing for golfers. Additional nearby destinations include Fort Sumter National Monument, Patriots Point Military Museum, historic carriage, culinary and ghost tours as well as a diversity of beach parks. Dining, shopping and museums are found throughout downtown Charleston and cater to any budget.

The conference hotel is the Embassy Suites by Hilton Charleston Airport and Convention Center. The hotel and convention center are ten minutes by taxi or Uber from Historical Downtown Charleston. The key airport for the conference will be Charleston International Airport (CHS). CHS is just minutes from the conference site with a free shuttle. Charleston International is a newly renovated and very easy airport to navigate with direct flights to most major cities in the US and some in Europe. ■



**Please plan to join us in
Charleston for an inspiring
and informative program
at a venue rich in charm
and American history!**



Above top: Embassy Suites
Right center: Embassy Suites Rose Garden
Below right: Charleston, historic downtown homes

Journal of Natural Products Recognizes Outstanding 2020 Papers

By Vanessa Nepomuceno, PhD

The *Journal of Natural Products*, published jointly between the ASP and the American Chemical Society, has announced the winners of the Arthur E. Schwarting and Jack L. Beal awards for best papers.^{1,2} Drs. Mary Lynn Trawick and Kevin G. Pinney are the recipients of the Arthur E. Schwarting Award and Dr. Alexander M. Sherwood has received the Jack L. Beal Award.

ARTHUR E. SCHWARTING AWARD RECIPIENTS



Dr. Kevin G. Pinney

PHOTO: BAYLOR UNIVERSITY

Pinney obtained his doctorate in organic chemistry from the University of Illinois at Urbana-Champaign. He completed his post-doctoral studies at the University of South Carolina before continuing to Baylor University in 1993 as an assistant professor of chemistry. Pinney is now a professor of chemistry at

Baylor and has decades of experience in synthetic organic chemistry with additional expertise in medicinal chemistry. His research focuses on elucidating salient features of molecular recognition associated with the binding interactions of small-molecule therapeutic agents with selected bioreceptors, including proteins and enzymes.

"I am tremendously honored and equally humbled to be a co-recipient of the Arthur E. Schwarting Award in recognition of our highly collaborative publication. This award truly highlights the outstanding contributions of the various co-authors on this publication whose areas of research expertise are quite diverse. It is a further honor to join the company of the many outstanding scientists who have previously received the Schwarting Award and to celebrate the tremendous accomplishments of Professor Arthur E. Schwarting who significantly advanced the field of natural products research."



Dr. Mary Lynn Trawick

PHOTO: EA PHOTOGRAPHY

her postdoctoral studies. Trawick joined Baylor University in 1983 as an assistant professor of chemistry. Her research interests include the design, evaluation, and mechanism of action of novel anticancer agents with selectivity for the tumor microenvironment and strategies to inhibit cancer metastasis.

"I am deeply honored to be a co-recipient of the 2020 Arthur E. Schwarting Award. Professor Schwarting's innovative biochemical classification of plants on the basis of their active chemical constituents and his inclusion of chemistry, biochemistry and biosynthesis in his research set the direction of modern Pharmacognosy."

Trawick and Pinney have a well-established and successful research partnership that has led to many publications and shared grant funding. Their co-authored 2020 publication, "Bioreductively Activatable Prodrug Conjugates of Combretastatin A-1 and Combretastatin A-4 as Anticancer Agents Targeted toward Tumor-Associated Hypoxia," is based on the natural products combretastatin A-4 (CA4) and combretastatin A-1 (CA1), which were discovered by Professor George R. Pettit. This article also contains a dedication to Pettit as a tribute and testimony to his lifelong commitment to helping cancer patients through his extensive knowledge of natural products and synthetic chemistry and his tireless passion for translating positive laboratory discoveries towards clinical applications. Trawick tells the society that "both Pinney and I feel that the Schwarting Award will help us drive this research forward."

continued on page 13

Journal of Natural Products Recognizes Outstanding 2020 Papers

continued from page 12

JACK L. BEAL AWARD RECIPIENT



Dr. Alexander M. Sherwood

PHOTO: TARA GIMMER

Sherwood is a medicinal chemist at the Usona Institute where he directs the synthesis and analytical core laboratories. He obtained his doctorate in organic chemistry at the University of New Orleans and completed his postdoctoral studies at the University of Kansas. At the Usona Institute, Sherwood's research efforts involve synthesizing and characterizing compounds most useful to the institute's sponsored

preclinical and clinical research. He has made specific contributions to the design, synthesis, and biological evaluation of psychoactive compounds.

The publication, "Synthesis and Biological Evaluation of Tryptamines Found in Hallucinogenic Mushrooms: Norbaeocystin, Baeocystin, Norpsilocin, and Aeruginascin," aimed to provide the first step toward understanding if other tryptamine natural products present in psychedelic mushrooms, apart from psilocybin and psilocin, could also possess psychoactive properties. This was one of the first projects initiated by the medicinal chemistry group at Usona Institute, a nonprofit medical research organization dedicated to understanding the therapeutic effects of psychedelics.

"Though the Beal Award is given as a personal recognition, I share this honor with everyone who contributed to the selected publication. These experiments

were driven by our mutual enthusiasm toward contributing to contemporary psychedelic research—an area of study that clearly owes its origin to the exploration of natural products."

In 2001, the ASP Foundation began a new initiative to recognize the best papers in the *Journal of Natural Products*, resulting in the Arthur E. Schwarding and Jack L. Beal awards. In this manner, two former distinguished editors of the *Journal* are fondly remembered. The Schwarding Award is open to all papers published in the *Journal* within a given year (either in print or electronically). In turn, the Beal Award is awarded to younger investigators, i.e., persons within 12 years of receiving their PhD degree or within 10 years of gaining their first professional appointment (e.g., assistant professor or an equivalent position in industry or government). A two-tier process was used to determine the winners of the best papers published in the *Journal of Natural Products* in 2020, with editors Daneel Ferreira, A. Douglas Kinghorn, Cedric J. Pearce, Philip J. Proteau, and Joanna E. Burdette having nominated two papers each for the Schwarding Award and one each for the Beal Award. ASP President Nick Oberlies appointed an ad hoc committee comprised of Drs. Tim S. Bugni (University of Wisconsin), chair; Marcy J. Balunas (University of Connecticut), Roger Linington (Simon Fraser University), Robert H. Cichewicz (Oklahoma University) and David J. Newman (special volunteer, National Cancer Institute) to make the final selections.

With the cancellation of the 2021 ASP annual meeting in Grand Rapids, MI due to the COVID-19 pandemic, the distribution of the awards was coordinated with the recipients. Nonetheless, the ASP bestows its warmest felicitations to Drs. Trawick, Pinney, Sherwood and to their co-authors! ■

LITERATURE CITED

Schwarding Award

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Named Awards/Grants and the People Behind Them: John Daly

**This grant honors the late John Daly,
a prolific scientist and longtime member and supporter of the ASP.**

By Kirk Manfredi, PhD and Richard Fitch, PhD

Each year the ASP solicits applications for various awards granted by the Society. Some of these are named (e.g., Matt Suffness Young Investigator Award) while others are not (Research Starter Grants). The intention of this upcoming series of *Newsletter* articles is to inform the ASP membership about the lives and scientific contributions behind named awards as well as the management thereof by the ASP Foundation (ASPF).

The main role of the ASPF is to provide funding for the various Society awards that are formally awarded at the annual meeting. Unnamed awards are sponsored by the ASPF with income from the Foundation's general fund (e.g., Research Starter Grants and Undergraduate Research Grants). Named awards may have a sponsor not directly associated with the ASPF (e.g., Jack Beal Award sponsored by the *Journal of Natural Products*), while others are sponsored by a one-time donation (e.g., the Bingel Fellowship and the Bhatti Travel Award) or are endowed by generous donations from the ASP membership (e.g., Jerry McLaughlin Student Travel Award). The ASPF serves as steward for these endowed funds so that they will last in perpetuity. Based on investment



Daly on a collecting trip in Panama around 2000. A lifelong outdoorsman, Daly was as comfortable in the field as he was in the lab.

performance in recent years, the ASPF board of directors currently sets a 5% payout on endowed awards. In order to help maintain and expand the awards that can be given by the Society, the ASPF relies on good financial management of its assets as well as new donations from members.

How does one donate? The ASPF encourages its members to donate to the ASPF through letters from the ASPF chair or treasurer or articles in the *ASP Newsletter*. If you attend the awards banquet at ASP meetings, you may have noticed donation envelopes on the tables. Inside are donation cards listing the various awards that can be supported, giving options as to how you could direct your contribution. Money not directed to a named award is placed either in a named award that has not reached its target amount or in the General Fund. However, you do not have to wait for the meeting. You can donate any time to the ASPF by contacting the ASPF chair (presently John Cardellina, jhcardellina@aol.com) or treasurer (presently Kirk Manfredi,

kirk.manfredi@uni.edu).

In this installment, we want to let you know about a new grant in development. This grant honors the late John Daly, a prolific scientist and longtime member and sup-

continued on page 15

Work with Solomon Snyder led to the discovery that caffeine inhibited adenosine receptors and opened up the area of purinergic receptors along with collaborator Kenneth Jacobson.

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Daly is most well-known for his work with bioactive alkaloids from amphibians, particularly the brightly colored poison dart frogs of the neotropics.

continued from page 14

porter of the ASP. He is known and remembered fondly by many in our membership.

John William Daly was born in Portland, Oregon in 1933. He obtained his BS from Oregon State College in 1954 and his MA the following year with Professor Bert Christensen on the synthesis of purine and pteridine alkaloids. He earned his PhD at Stanford University with Professor Richard Eastman, studying the terpenes of peppermint oil. Daly then joined the laboratory of Bernhard Witkop in the Laboratory of Chemistry at the National Institute of Arthritis and Metabolic Diseases (NIAMD).

While a postdoctoral fellow, Daly worked with pharmacologist Julius Axelrod on catecholamines, determining the mechanism of methylation with S-adenosylmethionine. Collaboration with Sidney Udenfriend, Don Jerina and Gordon Guroff led to the discovery of the “NIH-shift,” a rearrangement in aromatic hydroxylation via an arene oxide. Work with Solomon Snyder led to the discovery that caffeine inhibited adenosine receptors and opened up the area of purinergic receptors along with collaborator Kenneth Jacobson. Ken Seamon and Daly determined the mechanism of action of the *Coleus* diterpene forskolin as activating adenylate cyclase, leading to further collaboration with Philip Skolnick and Joachim Schultz on cyclic AMP as a second messenger. Fabian Gusovsky, Cyrus (Bob) Creveling, Kenneth Kirk, Edson Albuquerque, and



Daly with a large Dorado caught on a trip near Peru in the late 1990s. Daly was a diehard fisherman and could hardly bring himself to go on a trip if fishing was not involved at some point.

many others worked with Daly on a variety of pharmacological questions, many involving natural products such as the alkaloid reserpine and the polyether maitotoxin. Daly became the founding chief of the Laboratory of Bioorganic Chemistry in 1981. He served as LBC chief (now in NIDDK) until 1997.

Daly is most well known for his work with bioactive alkaloids from amphibians, particularly the brightly colored poison dart frogs of the neotropics. This work began when he was sent to obtain extracts of skins of the frog *Phyllobates aurotaenia* that the Chocó tribe in Colombia used to poison blow darts. The active principle, an alkaloid later named batrachotoxin, had been isolated, purified and characterized in 1963 by Witkop post-doc Fritz Märki, working with field biologist Martè Latham. The struc-

ture was determined in 1968 with chemist Takashi Tokuyama and crystallographer Isabella Karle. Subsequent collaboration with the herpetologist Charles Myers led to novel alkaloids from many dendrobatid species. Over 800 compounds have been described in 20 structural classes from four worldwide anuran families. Together with several key collaborators, Daly demonstrated that most are sequestered from their arthropod diet, though a few are biosynthesized or modified by the frogs. The frog alkaloid program spanned

continued on page 16

Daly authored or co-authored over 700 papers in chemistry, ecology, and pharmacology, including 22 in the *Journal of Natural Products*, one a comprehensive review describing over 800 amphibian alkaloids.

Named Awards/Grants and the People Behind Them: John Daly

continued from page 15

over four decades, producing hundreds of papers on their chemistry and biology, largely in collaboration with his chemist colleagues Martin Garraffo and Thomas Spande as well as biologist William Padgett. A great number of students, post-docs, technicians and other collaborators in chemistry, ecology and pharmacology also helped the program succeed. By all accounts, Daly was a generous collaborator, mentor, and friend.

Daly authored or co-authored over 700 papers in chemistry, ecology, and pharmacology, including 22 in the *Journal of Natural Products*, one a comprehensive review describing over 800 amphibian alkaloids. Daly was also active in the ASP, serving on numerous committees and on the editorial board for the *Journal of Natural Products*.

Shortly after his passing, some ASP members proposed a John Daly Field Research Grant. Because of Daly's interest in "being out in the field" on collections, his ASP colleagues wanted to honor him with a unique grant that would assist researchers in their field work. In 2010, they approached the ASP Executive Committee with a proposal to start a John Daly Field Research Grant. The proposal was approved by the ASPF Board of Directors and ASP Executive Committee, with the understanding that the award would not be activated until it was fully endowed. The current award is proposed to be \$2,000. As of this date, \$20,000 has been raised, with a total of \$40,000 needed to endow the award fully. ■



Daly and colleagues, including longtime collaborator and ecologist Charles Myers (center) and his then student Maureen "Mo" Donnelly (center right) on a collecting trip in Panama around 1995.



Daly and collaborators Marta Adnriantsferana (second from left) and Nirina Rabe Andreamaharavo (right) in the early 1990s.

Because of Daly's interest in "being out in the field" on collections, his ASP colleagues wanted to honor him with a unique grant that would assist researchers in their field work.



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Taking Action: One Year after the ASP Diversity, Equity and Inclusion Committee Call to Action

By Nadja Cech, PhD

The ASP Diversity, Equity and Inclusion Committee operates with three stated goals: (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. In the summer of 2020, we published an article for the *ASP Newsletter* that described a series of actions to support these three goals. Here we provide a status update on what the committee, the society, and the community have accomplished together during what feels like a very momentous year. These activities have been driven by a highly motivated group of committee members, under the leadership of co-chairs Drs. Esther Guzmán and Nadja Cech. We are grateful for contributions and partnership from the ASP Executive Committee, the ASP Fellows, and the ASP community at large. We are excited that the committee will continue in the coming year with Drs. Lesley-Ann Giddings and Christine Salomon taking over as the new co-chairs.

1. BUILD A PIPELINE TO OVERCOME STRUCTURAL BARRIERS OF ENTRY

- We launched an undergraduate summer research assistantship program to increase the representation of Black, Indigenous, and Latinx (BIL) scientists in the natural product discipline. This program funds summer research experiences for students from groups that have historically been underrepresented in our membership. Funds to support this program

were generously provided by the ASP Fellows and the ASP Foundation. Our first cohort of students was recruited for summer of 2021 and included seven trainees. Dr. Giddings led a summer program (meeting virtually on a weekly basis) to help foster community and provide a series of training seminars and exercises designed to prepare the cohort for applying to graduate school. The program concluded this summer with a highly successful webinar in which each of the trainees presented their summer research to the ASP community.

- At the ASP meeting in the summer of 2019 (Madison, Wisconsin) we launched the ASP Ambassador's Program. Three ASP Ambassadors (Drs. Salomon, Katherine Zink, and Sandra Loesgen) were appointed for a three-year term and are working (with support from the ASP) to increase participation of individuals from underrepresented groups in our society. The ASP Ambassador's Program has continued over the past year, although outreach has been somewhat hampered by the conditions of the pandemic. The program has been extended for another year with the existing ambassadors to enable additional activities now that conference attendance is again becoming possible.
- In 2019, we launched the **Natural Products Career Locator App**. This app is an interface that provides resources for students to research natural products-related programs in their area of interest. Over the past year we have continued to encourage group

continued on page 19

We launched an undergraduate summer research assistantship program...
...we launched the ASP Ambassador's Program...
...we launched the Natural Products Career Locator App...



Taking Action: One Year after the ASP Diversity, Equity and Inclusion Committee Call to Action

While we are proud of the accomplishments described above, we recognize that there are many more endeavors that our society could undertake towards the goal of creating a more inclusive and equitable ASP.

continued from page 18

leaders to add themselves to the map. If you are a group leader and would like to be listed on the map, please complete this form:

<https://www.pharmacognosy.us/diversity-equity-and-inclusion-committee/past-ongoing-initiatives/> (It only takes about three minutes!)

2. CREATE AN EQUITABLE COMMUNITY/EDUCATE

- We conducted a webinar titled, “Fostering Diversity, Equity, and Inclusion in Scientific Research Groups.” There were 127 participants from 33 different countries around the world. The recording is freely available at this link: <https://vimeo.com/483614103>.
- We have improved the **ASP Diversity Equity and Inclusion website** and included new information and resources for the community. Please feel free to visit!
- Editorials at *Nature*, *PNAS*, and *Science* (to highlight a few) have stated the reasons why diversity enriches science. As part of the ASP’s ongoing effort to make access to scientific opportunities more equitable, the Diversity, Equity, and Inclusion Committee has drafted a set of guidelines to promote diversity and equity at ASP meetings. These guidelines are now provided to organizers as they embark on the process of planning an ASP meeting.

3. RECOGNIZE AND HIGHLIGHT CONTRIBUTIONS FROM UNDERREPRESENTED GROUPS

- Over the past year, we have written articles (www.pharmacognosy.us/diversity-equity-and-inclusion-committee/past-ongoing-initiatives/) for each ASP *Newsletter* as part of the “Taking Action” column. We will continue this column in the coming year. Anyone interested in writing for the ASP *Newsletter* should contact Dr. Edward Kennelly at: asp.newsletter@lehman.cuny.edu.

- The ASP Diversity Committee is working with conference organizers to ensure that the presenters at ASP meetings include sufficient representation of women, people of color, and others from historically underrepresented groups. The guidelines that we drafted this year include specific suggestions for how to accomplish this. We welcome suggestions for speakers at future meetings!

While we are proud of the accomplishments described above, we recognize that there are many more endeavors that our society could undertake towards the goal of creating a more inclusive and equitable ASP. We invite all of you, members of our community, to reach out to us (contact information below) with ideas and to work with the committee on future initiatives. ■

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We invite all of you, members of our community, to reach out to us ...with ideas and to work with the committee on future initiatives.

In Memoriam: Leonard Worthen

By Roy Okuda, PhD

David R. Worthen, PhD, JD, contributed to this article.

Dr. Leonard “Len” Worthen, 15th ASP president (1974-1975) and professor emeritus of the University of Rhode Island (URI) Department of Pharmacognosy, passed away on April 9, 2020 in Kingston, RI at the age of 94. Worthen joined the ASP in 1962 and was a charter member of the society. He is fondly remembered as a dedicated teacher and mentor, a caring administrator, a practicing community pharmacist, and an expert on New England mushrooms.

Upon hearing of Worthen’s passing, ASP Past President Nick Oberlies wrote, “I was very sorry to learn of the passing of Dr. Len Worthen. He is of a generation that did many great things, and sadly, his generation is quickly (and sometimes quietly) passing. I appreciate his service to the ASP, both as our 15th president and simply as an active member. All of us today owe him, and his generation of colleagues, for what they did to grow what we know of today as the American Society of Pharmacognosy.”

In addition to his service as ASP president, Worthen served as ASP treasurer (1966-1972) and chaired the organizing committees for the ASP annual meetings held at URI in 1965 and 1987. He was a pivotal member of the society in its first decades. Among the notable and long-lasting impacts of Worthen’s tenure as ASP president were the growth of *Lloydia* (along with the Lloyd Library) as the key scientific journal of the Society, and the introduction of the “fleur” logo of ASP, which persisted until the ASP rebranding in 2020. In the biographies of ASP presidents, it stated, “Perhaps his greatest joy as long-time member of ASP has been to witness the phenomenal growth of the Society, both in membership and in scientific scope, as well as the international reputation and financial stability that have been achieved through the dedication and hard work of the members.”¹

In addition to Worthen, two other prominent ASP presi-



Len and Betty Worthen, married 54 years.

dents Dr. Ralph Blomster (1972-1973) and Dr. Norman Farnsworth (1961-1962) were born in the small geographical area around Lynn and Woburn, MA, just north of Boston. In addition, at least three other members, Drs. Frank O’Connell (treasurer after Worthen) Franklin Cole, and Georgia Perdue were born in the same area. “It’s something in the water,” they later claimed. All were among the earliest members of ASP and played important roles in the growth and development of ASP as we know it today.

continued on page 21

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In Memoriam: Leonard Worthen

A microbiologist by training, Worthen's research focused on assessing the antimicrobial and antineoplastic activity of isolates derived from mushrooms and from terrestrial plants, including the *Vaccinium* genus, both in his own laboratory and in collaboration with the NCI and Pfizer.

continued from page 20



After serving in the US Navy in the Pacific in World War II, Worthen received his BS in pharmacy from the Massachusetts College of Pharmacy (1950), went on to Temple University for his MA (1952), and to the University of Massachusetts for his PhD (1957). Worthen went immediately on to be one of the founding faculty of the new URI College of Pharmacy in 1957 under the guidance of Professor Heber Youngken, Jr, a founding member of the ASP.

Worthen was the chair of the Department of Pharmacognosy before his appointment to associate dean to the college in 1985. He retired in 1990 after 33 years of service. In 2019, he was inducted into the URI College of Pharmacy Hall of Fame, where he was recognized as "a consummate teacher, guiding undergraduate and graduate students alike." As a trained and practicing pharmacist, he taught legions of pharmacy students about the origins and roles of natural product drugs in human health.

A microbiologist by training, Worthen's research focused on assessing the antimicrobial and antineoplastic activity



Above left: Worthen, circa 1943, when he enlisted in the US Navy at the age of 17. He served during and after World War II at various locations in the Pacific including Iwo Jima and Okinawa.

Above: The Worthens (left) at the 1987 Annual ASP Meeting in Rhode Island with former ASP President Heber Youngken, Jr. and his wife, Daphne (right).

of isolates derived from mushrooms and from terrestrial plants, including the *Vaccinium* genus, both in his own laboratory and in collaboration with the NCI and Pfizer. He could often be found with friends and family hiking the forests and woods of New England in search of mushrooms and other indigenous sources of bioactive compounds. He sent extracts of mushrooms and other New England plants for testing in the NCI 60-cell line panel.

Worthen also worked on the development of synthetic nitrostyrenes as antimicrobial agents. Trained in industrial pharmacy and a practicing pharmacist for over forty years, Worthen conducted and published research on the extemporaneous compounding of sterile injectables in the hospital setting. He also trained US FDA inspectors in the area

continued on page 22

In Memoriam: Leonard Worthen

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continued from page 21

of sterile product manufacture and quality assurance for many years.

Up to the 1960s, the field of marine natural products chemistry was relatively young but beginning to gain interest as a new frontier of pharmacognosy. Owing to their avid interest in the oceans (Rhode Island is known as the “Island State”), Youngken and Worthen initiated and hosted a series of annual meetings at URI called “Food and Drugs from the Sea” starting in 1969. These were among the earliest conferences in marine natural products and brought a significant amount of attention to this area of natural products, which has since grown to become a major research topic.

In the mid-1980s, the URI Department of Pharmacognosy consisted of Worthen, Yuzuru Shimizu and myself (Okuda), all of us in rather compact space in the basement of Fogarty Hall, then the College of Pharmacy. I got to know them both well and had kept in touch with Len continuously for over 35 years. Our basement labs were adjacent to the Heber Youngken, Jr Medicinal Plant Garden, and I would often run into Len there as we both tried to escape our “real jobs.” He loved to garden and was a fountain of information on local medicinal plants. In retrospect, this was the foundation of my current research work, now on the “left coast.” Len knew all of the



Dr. Hilmar Friedrich of the Society for Medicinal Plant and Natural Product Research (GA) presents a symbolic mug to Worthen in the summer of 1975 as ASP founding member Dr. Arthur Schwarting looks on. The mug commemorates the second joint meeting of the ASP and the GA.

ASP founding and charter members well and told many interesting stories of the early days.

Worthen was married to the late M. Elizabeth (Betty) Worthen for 54 years before her passing. He is survived by three children, Diane Worthen-Hirsch (Eric), Lawrence P. Worthen (Diane) and David R. Worthen. David received his PhD and JD from the University of Kentucky and works as an executive/ independent consultant in the pharmaceutical industry in Rhode Island. ■

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In Memoriam: Margaret F. Roberts

By J. David Phillipson, PhD, A. Douglas Kinghorn, PhD,
Michael Heinrich, PhD and Elizabeth M. Williamson, PhD

Dr. Margaret F. Roberts died at the age of 87 after a long illness. With an over 30-year career at the School of Pharmacy, University of London (now the School of Pharmacy, University College London or the “Square”), she was a pioneering figure in pharmacognosy at a time there were few women with faculty appointments. She will be fondly remembered as an outstanding scientist, cherished colleague, motivating mentor, and nature enthusiast.

Roberts obtained a BA degree from the University of Keele and then an MSc degree at the University of Bristol, where she was a Boots Research Scholar in the Department of Horticulture and Agriculture. She worked next as a research assistant to Dr. B.T. Cromwell in the Department of Botany at the University of Hull, from where she was awarded a PhD degree in 1968. Robert's first research article was on the biogenesis of γ -coniceine in hemlock (*Conium maculatum*).¹

In 1967, she joined the Department of Pharmacognosy at the School of Pharmacy, then headed by Prof. James W. Fairbairn. Her first paper while at the Square was published in 1971,² and this was again on the biosynthesis of γ -coniceine from *C. maculatum*, a topic that she continued to investigate throughout the 1970s, leading to the publication of a series of single-authored research articles. It was at about this time that she first joined the ASP.

Another area of great interest that began early in her



Dr. Margaret F. Roberts

**She will be fondly remembered as
an outstanding scientist,
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mentor, and nature enthusiast.**

tenure at the Square was on the enzymology of alkaloid and other secondary metabolite production in *Papaver somniferum*. This turned out to be a very productive line of inquiry, and several of the later publications were collaborative with others working in the same field, such as a paper on the implication of tyramine in the biosynthesis of morphinan alkaloids in the genus *Papaver*.³

Roberts worked also to great effect for an extended period on studies on cell suspension cultures on species with documented antimalarial activity, in collaboration with one of us (J.D.P.), inclusive of *Ailanthus altissima*, *Artemisia annua*, *Brucea javanica*, and *Cinchona ledgeriana*. Another group of compounds of interest were the flavonoids of *Stevia* species (Asteraceae), including those of *Stevia rebaudiana*, the source of the *ent*-kaurene diterpene glycosides that are now used commercially as sweeteners in many countries.

In addition, Margaret co-au-

thored several published reports with her husband, Curt Homeyer, including an article on dopamine accumulation in *Papaver somniferum* latex.⁴

In 1977, Roberts spent her sabbatical in the laboratory of the late Dr. Tom Mabry at the University of Texas-Austin, where she worked together there with ASP Fellow Dr. Barbara Timmermann, then a graduate student, and now a distinguished professor and chair, University of Kansas, and a former president of ASP. Timmermann recalls: “Above all professional accomplishments, respect and ac-

continued on page 24

In Memoriam: Margaret F. Roberts

continued from page 23

colades received by peers, colleagues and organizations, Margaret was my true and most valued friend. Our friendship started in Austin while in Tom Mabry's laboratory and continued strong during all these years with visits on both sides of the ocean, regular correspondence, her classic Christmas letter, our annual exchange of nature calendars, her accounts and adventures on her beloved *Anhinga* yacht and much more. I will always remember Margaret as my dear friend, mentor, role model and lover of the beauty of nature and the good stuff in life."

Roberts took very great pride in the quality of her teaching at all levels. Prof. Colin Wright, now of the University of Bradford in the UK, was both an undergraduate in the early 1970s and sometime later a graduate student at the Square. He wrote, "I remember Margaret's pharmacognosy lectures in my 2nd year (1973-1974); the content and delivery were of a very high standard. As a PhD student (1986-1989), I remember Margaret (and Curt too!) as very hard working and dedicated to her research; she was meticulous in everything she did, and her lab (the 'enzyme lab') was spotless with everything in its place." Among her former graduate students, Dr. Mikhail D. Antoun (PhD 1974) was previously Professor of Medicinal Chemistry and Pharmacognosy and a Department Head at the School of Pharmacy, University of Puerto Rico in San Juan.

Another major contribution to the natural products literature by Roberts was her role as co-editor of two influential natural products volumes. Initially, she was a co-editor of the volume *The Chemistry and Biology of Isoquinoline Alkaloids*⁵ which included many new perspectives on this important alkaloid class. A later edited volume was *Alkaloids: Biochemistry, Ecology, and Medicinal Applications*.⁶ Many leading alkaloid natural products investigators at the time from several different countries wrote informative chapters for this excellent volume.

Prof. Michael Wink, senior professor at the University of Heidelberg, first met Roberts in 1978 in London and has provided some background on how the 1998 co-edited volume on alkaloids occurred. He wrote, "Although it started with amine biosynthesis, Margaret was interested in alkaloids, as I was at that time. This started a long collaboration with my visits to London (mostly for conferences and a laboratory stay in 1982 for a few weeks) and

Another major contribution to the natural products literature by Roberts was her role as co-editor of two influential natural products volumes.



Roberts in her office at the Square.

"We have the fondest memories of Margaret. She was a great scientist, one of the most generous of friends, and as a woman in academia a sort of a role model for me."

finally a comprehensive book on alkaloids." Dr. Coralie Wink refers to this surprise initial visit in 1978 to London with her husband, Michael, which occurred during the Winks' honeymoon, as "the beginning of a lasting friendship and collaboration." She also noted, "We have the fondest memories of Margaret. She was a great scientist, one of the most generous of friends, and as a woman in academia a sort of a role model for me."

A highlight of her career was in May 1992, when Roberts was awarded an earned DSc degree by the University of London, based upon the quality and depth of her published work. At the graduation ceremony held in the fabled Royal Albert Hall in London, she was among just five honorees out of a convocation of well over a thousand called to the podium to be hooded by the university chancellor. She retired from the University of London as a "Reader Emerita."

After her retirement, Roberts began to take ever-more adventurous sailing trips and frequently would take extended excursions from her adopted hometown of Dart-

continued on page 25

In Memoriam: Margaret F. Roberts

continued from page 24

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mouth in Devon on the English south coast. Wright remembers one of these, "I was fortunate to be invited to join in with a weekend sailing trip with Margaret, Curt and a few of their friends on a chartered yacht –the plan was to sail from Portsmouth across the English Channel to the Channel Islands, but, due to bad weather, the crossing was rough and we ended up in Cherbourg! Margaret enjoyed the ritual G & T at the end of a day's sailing –it was nice to see her in a relaxed setting."

Roberts will be missed greatly as an extremely accomplished and resolute colleague who worked on some of the major challenges in the natural products field in the last third of the 20th century. We extend our deepest sympathies to her husband, Curt, on his very great loss. ■

Roberts with Dr. A. Douglas Kinghorn at the entrance to the School of Pharmacy, University of London, circa 1992.

Roberts will be missed greatly as an extremely accomplished and resolute colleague who worked on some of the major challenges in the natural products field in the last third of the 20th century.

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HOT TOPICS IN PHARMACOGNOSY



Revisions of “Repurposing for CoV-2” and Potential Uses of Cationic Peptide Compounds as Antibiotics and Other Diseases



By David J. Newman, DPhil

REPURPOSING FOR COV-2

In the February 2021 ASP Newsletter I commented on and gave “potted precises” of the work done on large scale repurposing of known drugs in order to try to “short-circuit” the time required to test, and hopefully bring to market, a number of potential candidates as drugs, ideally delivered orally. The idea behind repurposing is that since the toxicities, pharmacodynamics and pharmacokinetics had already been established, and those data led to the approval by the FDA or comparable regulatory agencies, the time required would be materially shortened.

As a result of two very large and subtly different approaches, a number of known, and in some cases not so well-known, structures, a significant number of which would fall under the “NX” series in the Newman and Cragg lexicon where “X” = null, B or D, were published in two *Nature* papers (see earlier article for references/structural types).

However, in a very recent article in *Science*¹ both sets of authors in a joint paper demonstrated that a significant proportion of the compounds identified, including a number of those “pushed by various political figures” in the

early stages of the “pandemic,” were artifacts in terms of being antiviral agents and/or leads thereto.

The “cellular” reason why these compounds, some of which are shown in Figure 1 and fall under the sobriquet of “CADS” or cationic amphiphilic drugs, appeared to be potential antivirals was that they caused a cellular condition known as phospholipidosis. In this side effect there is formation of vesicle-like structures, which can be seen under suitable microscopy as “foamy” or “whorled” membranes which may arise by CAD disrupting normal lipid homeostasis. In addition, these agents can accumulate in endosomes and lysosomes where they might directly or indirectly inhibit lipid processing. Modulation of these lipid processing pathways is critical for viral replication as virions usually enter the cell via formation of complexes with membrane lipids. Inhibiting phospholipid production/utilization by any means can stop virus proliferation, and such methods have been shown to be associated with inhibition of coronavirus replication.

The following paragraph is from the authors conclusions in the *Science* article¹ and puts the problems they found in a succinct paragraph.

“These caveats should not obscure the central observation of this study. Many drugs repurposed for antiviral activity against SARS-CoV-2 are cationic amphiphiles, and despite their diverse structures and multiple targets, many likely have their antiviral effects via a single shared mechanism: phospholipidosis. Both because of the side effects with which it is associated, and the limited efficacy to which it leads—rarely better than 100 nM

continued on page 27

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HOT TOPICS IN PHARMACOGNOSY: Revisions of “Repurposing for CoV-2” and Potential Uses of Cationic Peptide Compounds as Antibiotics and Other Diseases

continued from page 26

in vitro—drugs active due to phospholipidosis are unlikely to translate in vivo. Many resources will be saved by counter-screening for phospholipidosis in simple cellular assays, allowing investigators to focus on drugs with genuine promise as antivirals.”

Finally, they comment on the vast numbers of clinical trials that still appear to be in use, or in some cases might just have been “finished or terminated,” and I have also put the paragraph in unedited except for removal of the embedded citation numbers.

“The cost to the community of investments in what appears to be a confound merits consideration for future pandemics. According to the DrugBank COVID-19 dashboard, which draws from US and international clinical tri-

als, putatively antiviral CADs have been promoted into an astonishing 316 Phase I to Phase III clinical trials against COVID-19. While 57% of these trials study the phospholipidosis-inducing CADs hydroxychloroquine or chloroquine, that still leaves 136 trials across 33 other predicted or known phospholipidosis-inducers. Using conservative estimates the expense of the clinical trials component alone, over the last year, for phospholipidosis-inducing CADs may be over \$6 billion US dollars.”

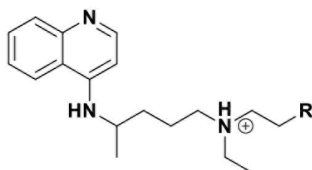
CATIONIC PEPTIDES AS POTENTIAL ANTIBIOTICS

In a paper published in 2020 in *ACS Infectious Diseases*, Hussein et al.² reported synergistic effects between the

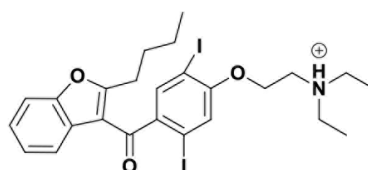
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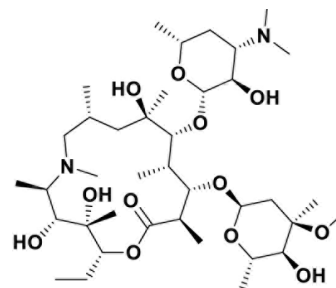
Structures



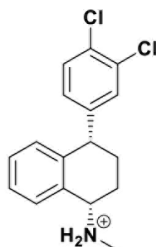
Chloroquine R = H
Hydroxychloroquine R = OH



Amiodarone



Azithromycin



Sertraline

HOT TOPICS IN PHARMACOGNOSY: Revisions of “Repurposing for CoV-2” and Potential Uses of Cationic Peptide Compounds as Antibiotics and Other Diseases

continued from page 27

cationic antibiotic polymyxin B (which used to be discarded if discovered in screens in the 1970s) and the serotonin uptake inhibitor sertraline when used against the Gram-negative polymyxin resistant microbes *A. baumannii*, *K. pneumoniae* and *P. aeruginosa*.

The authors then followed up the effects on the resistant *P. aeruginosa* strain using metabolomics. Unfortunately, even though the mixture was synergistic, the metabolomics work demonstrated that the mixture demonstrated that the major effects were upon the lipid and fatty acid metabolic processes due to the sertraline (Figure 1). Now if this work had been sent for reviewing after the publishing of the CoV-2 paper above, it would probably never have seen the “light of day” as sertraline was one of the “problem children” identified as causing problems with cationic compounds.

SYNTHESIS AND USES OF PEPTIDIC AGENTS

However, all is not lost in terms of peptidic antibiotics and other pharmacological areas where they might be of utility. In a very recent review in *iScience*, a group from CNPD3 at the University of Florida³ published an open access review demonstrating how both chemical and biochemical approaches can lead to a cornucopia of novel structures based upon peptide chemistry. In this they demonstrated how NPRS and RiPPS processes can be used to produce novel agents that can then be tested in a variety of assays, not the least, those directed towards pathogenic microbes.

This is a paper that could be used as a primer for undergraduates / early postgrads and even for those of us, like the author, who are “longer in the tooth!” ■

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Natural Products in the World of Vaccines: Saponin Adjuvants

By Ray Cooper, PhD

There are not any approved natural products cures for COVID-19, nor will you find any suggestion or recommendation presented herein. However, remarkably, a group of natural products, the saponins, is key to a vaccine's success.

Saponins, triterpene or steroid glycosides, are contained in many plants. These compounds are widely used as food additives and possess a foamy quality due to their amphipathic nature. Even more critically, at present, saponins are also of value in the production of vaccines.

Little has been written about their application, specifically in relation to the new vaccines for COVID-19. However, in an article in the popular magazine *The Atlantic*,¹ the history and discovery of adjuvants is nicely presented together with the

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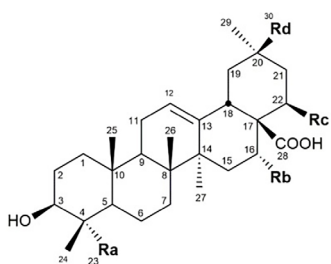
best sources of saponins and critical factors of sustainable harvesting due to vast quantities needed for the current vaccines. Herein, the chemistry and selection of FDA approved adjuvants are reviewed.

SAPONIN SOURCES

Two species endemic to the Andean region of South America, *Quillaja saponaria* and *Quillaja brasiliensis* are important sources of the saponins. The saponins are found in the inner bark of the Chilean soapbark and their chemical structures are shown in **Figures 1-2** below.

Local people used this tree bark plant for hundreds of years by grinding the bark and mixing it with water to make soap. On a large-scale extraction this process is also applied. When the bark is pulverized and soaked in water, the resulting brown fluid provides the starting material, and further enrichment of saponins is generated through filtration over activated charcoal.

continued on page 30



Triterpene	Abbreviations	Ra	Rb	Rc	Rd
Quillaic acid	Q	CHO	OH	H	CH ₃
Quillaic acid, 22β-OH	Q-OH	CHO	OH	OH	CH ₃
Gypsogenin	G	CHO	H	H	CH ₃
Phytolaccinic acid	P	CH ₂ OH	H	H	COOCH ₃
Phytolaccinic acid, 23-O-Ac	P-Ac	CH ₂ OCOCH ₃	H	H	COOCH ₃
Echinocystic acid	E	CH ₃	OH	H	CH ₃

FIGURE 1

Triterpene aglycones in *Quillaja saponaria* and/or *Q. brasiliensis* saponins
(figure reproduced from Fleck et al., 2019).²

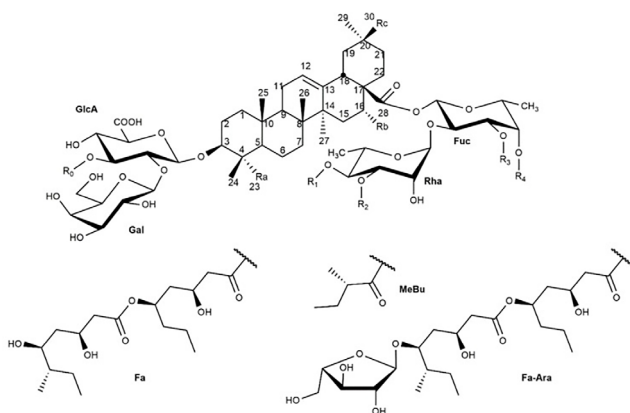


FIGURE 2

General structural features of *Q. saponaria* and *Q. brasiliensis* saponins
(figure reproduced from Fleck et al., 2019).²

Natural Products in the World of Vaccines: Saponin Adjuvants

continued from page 29

SAPONIN SEPARATION AND SELECTION OF QS-21

Research by Kensil (1990)³ resulted in the separation of over 50 saponins found in *Q. saponaria* extract. Each one was tested especially with emphasis on toxicity. Although several individual saponins showed promise, firstly in toxicity studies in mice, only one of the saponins was deemed to have a sufficiently safe profile to be taken forward into humans. This saponin is now named QS-21 shown in **Figure 3** and approved by the FDA. QS-21 costs over \$100,000/gram, or about \$5/dose. The chemical structure of QS-21 consists of a quillaic acid triterpene substituted with a branched trisaccharide and a linear tetrasaccharide, which, in turn, is connected to an acyl chain via a hydrolytically labile ester. QS-21 is in fact a 65: 35 mixture of the apiose- and the xylose-substituted variants of the molecule.

VALUE OF ADJUVANTS

Adjuvants have the effect of improving a “weak” vaccine into an effective one. It should be noted that not all vaccines require an adjuvant; however, of an estimated 200 vaccines about 40% are protein-

continued on page 31



Above: A soapbark tree in the University of California Botanical Garden, Berkeley. Right above: The flowers of *Quillaja saponaria*

PHOTOS, ABOVE AND BELOW: NANCY NOVICK

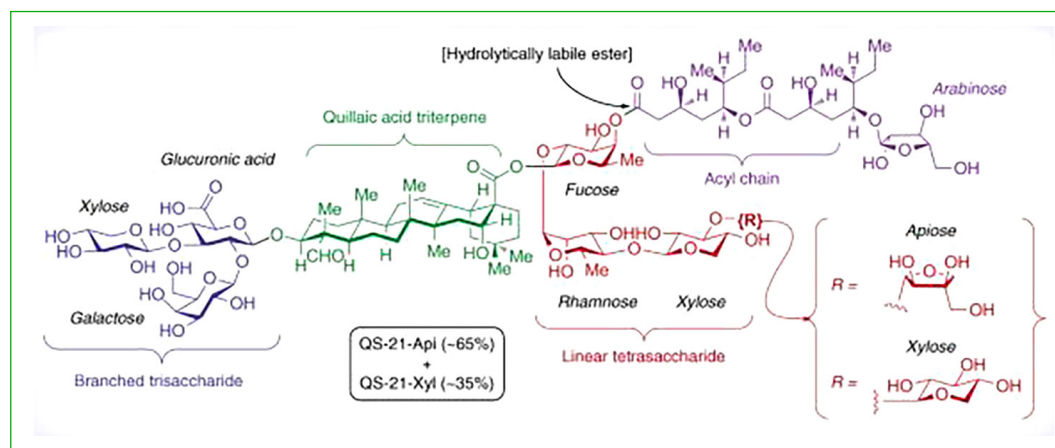


FIGURE 3

Basic structure of QS-21, consisting of a quillaic acid triterpene (green) and sugar moieties (figure reproduced from Ragupathi et al., 2014).⁴

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Right: Soapbark tree bark



Natural Products in the World of Vaccines: Saponin Adjuvants

continued from page 30

based and these vaccines are found ineffective without an adjuvant.⁶

CURRENT USE OF ADJUVANTS

The pharmaceutical company GlaxoSmithKline (GSK) obtained the rights to QS-21. By combining QS-21 with a second adjuvant, a fatty substance derived from a *Salmonella* bacterium, the combination was successfully used in their shingles vaccine. This vaccine called *Shingrix* confers immunity on 90% of people over 70 years old. This same combination of adjuvants is also used in the GSK malaria vaccine, *Mosquirix*, and is being tested in a late-stage-tuberculosis vaccine candidate.

In one example of the development of a COVID-19 vaccine, the company Novavax required the Chilean bark company to increase supply by a hundredfold. Novavax received approximately \$300 million to produce 100 million doses of its COVID-19 vaccine for 2020 and a billion doses by the end of 2021. Since the USA government through Operation Warp Speed was offering financial support for expediting development, Novavax was seeking guarantees of 1,500 pounds of saponin for 2020, and up to three times as much in 2021.

SUSTAINABLE HARVESTING

About 10 years ago, it was already recognized that the supply of high quality *Quillaja* extract would be sufficient only for about 6 million doses of a vaccine. This story parallels the early supply of taxol from the Pacific yew tree. Its bark was the original source of the chemotherapy drug, paclitaxel, which was threatened by large-scale harvesting in the 1980s. Similarly, today there is a risk of over exploitation of Chilean soapbark. Due to the massive increase in need of COVID-19 vaccines, large supplies of Chile soapbark are required. However, a special permit is required to cut down *Quillaja* trees, and the industry is most likely to exceed the limits of sustainable harvest

continued on page 32

Due to the massive increase in need of COVID-19 vaccines, large supplies of Chile soapbark are required. However, a special permit is required to cut down *Quillaja* trees, and the industry is most likely to exceed the limits of sustainable harvest calculated as approximately 27,000 tons.



calculated as approximately 27,000 tons. Harvesters are allowed to prune trees at intervals ranging from 7-20 years, by peeling off all the necessary bark. Chilean landowners are encouraged to plant further native *Quillaja* even replacing eucalyptus and pine.

The leaves do not offer significant amounts; they may account for 30-50 % of the tree's biomass although harvested sustainably.

Since large-scale harvesting is limited, it is critical to identify new sustainable sources. Indeed, the increase of

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Natural Products in the World of Vaccines: Saponin Adjuvants

continued from page 31

adjuvant yield using semi-synthetic methods by a factor of a hundred has been achieved. Cultured plant cells are employed at Phyton Biotech, who used this approach to combat over-exploitation of the Pacific yew for the sourcing of paclitaxel. Secondly, in order to deliver protein-subunit vaccines, companies, such as GSK and Sanofi, are using a less-potent oil-in-water adjuvant, also containing a natural product, an oily compound from shark liver.

In conclusion, no matter how effective COVID-19 vaccines are, they will not be able to dent the pandemic unless they are produced on a massive scale. The adjuvant adds one more link to the global production supply chain. However, it is noteworthy and reassuring that natural products continue to be sources of medicinal compounds of great significance. ■



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- ⁶ covid-19tracker.milkeninstitute.org

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New Members of ASP Fall 2021

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 13 full members and 69 associate members. We look forward to meeting you and learning more about you and your work.



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continued on page 34

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continued from page 33

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continued on page 35

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American Society
of Pharmacognosy

continued from page 34

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University of Lagos
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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.

A number of scientific conferences have been delayed or canceled due to the COVID-19 pandemic.

Please check with conference organizers about the status of any in-person conferences.

2022 ASP Annual Meeting

July 23-28, 2022

Charleston, South Carolina

aspmeetings.pharmacognosy.us

NIH Office of Dietary Supplements Seminar Series

Sept. 15, 2021 – Jan. 12, 2022

Monthly via WebEx Webinars

ods.od.nih.gov/News/Conferences_and_Workshops.aspx

ASP Natural Product Sciences Webinar

Bimonthly Zoom Seminars

Thursdays 4 PM ET / 1 PM PT

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

ODS 25th Anniversary Scientific Symposium

Oct. 25-26, 2021

Virtual Meeting via WebEx

ods.od.nih.gov/About/ODS25thanniversary.aspx

ACS Webinars

Every weekday 2 PM ET / 11 AM PT

<https://www.acs.org/content/acs/en/acs-webinars.html>

Environmental Roles, Biological Targets and Applications Gordon Research Conference: Marine Natural Products

March 6-11, 2022

Ventura, California

www.grc.org/marine-natural-products-conference/2022/

C&EN Webinars

Various Days and Times

<https://cen.acs.org/collections/webinars.html>

Oxford International Conference and the Science of Botanicals (ICSB)

March 28-31, 2022

Oxford, Mississippi

oxfordicsb.org



American Society
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From the Archives: Leonard R. Worthen and Changing *Lloydia* History

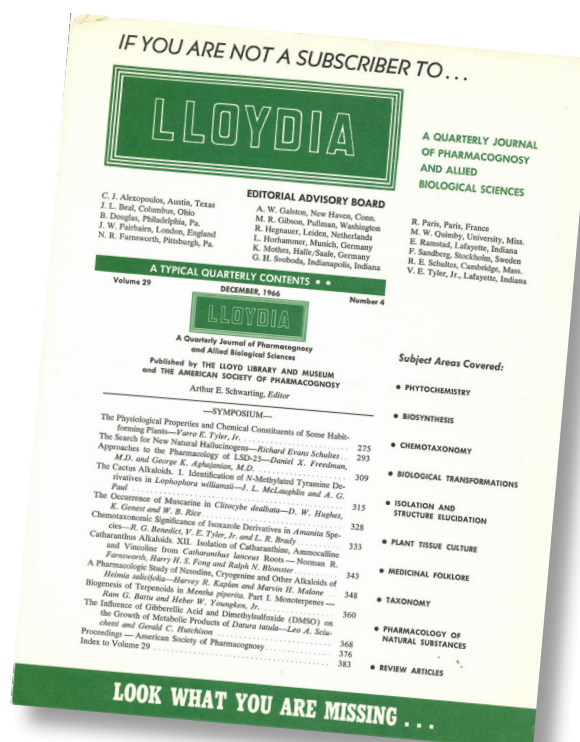
Membership is the heart of any society. It dictates changes for better or worse! Read on to see how past ASP President Leonard R. Worthen propelled changes to the beloved publication, Lloydia, during his tenure as president in 1975.

By Christine Jankowski, MA

January 1, 1961 marked the official start of the American Society of Pharmacognosy's relationship with the Lloyd Library and Museum as they collaborated on the publication *Lloydia*. The journal was first published by the Lloyd Library under brothers and co-founders John Uri Lloyd and Curtis Gates Lloyd. Topics varied from botany to morphology during its original run, and it often was a vehicle for Curtis to publish any new or changed mycological names. The publication continued after the deaths of the brothers. In 1960, following the death of *Lloydia*'s editor Dr. Theodor Just, ASP member Dr. Arthur "Art" Schwarting took over the helm.

The decision for the ASP and the Lloyd Library to join forces on *Lloydia* was signed into recognition by the ASP's then president Dr. W. E. Anderson. His statement included four clauses: the focus of topics published in *Lloydia* (pharmacognosy and botany); rules for selecting the editor and editing board; funding for the publication; and the stipulation that any changes of publication methods or duration would be consented by both the ASP and the Lloyd.¹

Membership and subscriptions to the ASP and *Lloydia* grew throughout the 1960s, but by the early 1970s, there was a significant drop in active and new members. Dr. Leonard R. Worthen had been an ASP member since 1962 and served on the Executive Committee as treasurer from 1967 to 1973 and, for the 1974-1975 tenure, was president. Worthen recognized that *Lloydia*'s costs outweighed the revenue earned from subscriptions to the journal. At the 1974 annual meeting in Chicago, discussion revolved around the drop in both ASP membership and subscriptions to *Lloydia*. The 1974 conference introduced incentives including pushing new ASP members to become subscribers of *Lloydia*. After the annual meeting, Editor Schwarting proposed an increase in the number of issues per year, higher subscription rates, and increased financial contribution from the Lloyd Library and Museum.²



An advertisement for *Lloydia* from 1966, when it was published quarterly.

More changes were required to make the publication profitable. By the spring of 1975, the deficit for producing *Lloydia* Volume 37 was almost \$15,000. The *Lloydia* committee had made some changes that Schwarting proposed, such as increasing publications from quarterly to bimonthly, but now they needed to make drastic ones to cover that cost. In May 1975, Worthen typed a letter, and it was printed in the ASP Newsletter, Volume 12, Number 1. The newsletter begins with the following:

"Open Letter from the President: Dear Member of the ASP: This is probably the first time that any of your presidents has written an open letter to the membership, but under the circumstances, I feel it is imperative to inform you of a problem involving the costs incurred

continued on page 38



From the Archives: Leonard R. Worthen and Changing *Lloydia* History

“This is probably the first time that any of your presidents has written an open letter to the membership ...I feel it is imperative to inform you.”

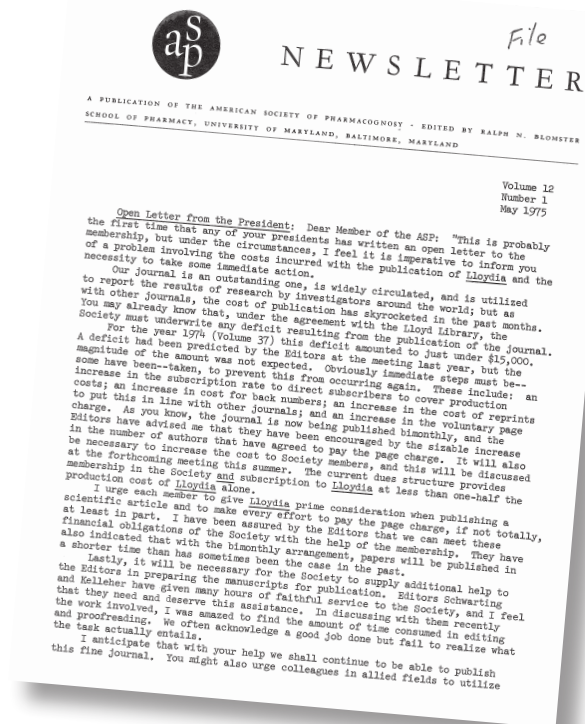
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with the publication of *Lloydia* and the necessity to take some immediate action.”

Worthen goes on to explain the situation and propose immediate changes, “Steps must be —some have been —taken, to prevent this from occurring again. These include: an increase in the subscription rate to direct subscribers to cover production costs; an increase in cost for back members; an increase in the cost of reprints to put this in line with other journals; and an increase in the voluntary page charge.” Changes to subscription costs were to be discussed at the 1975 annual meeting in Storrs, Connecticut. At the closing of his letter, Worthen urged the membership to provide more assistance to the editor in preparing articles for publication. “It will be necessary for the Society to supply additional help to the Editors in preparing the manuscripts for publication...I was amazed to find the amount of time consumed in editing and proofreading. We often acknowledge a good job done but fail to realize what the task actually entails.”

Months later, at the business meeting in Storrs, the following changes were accepted by the ASP Executive Committee: non-member subscribers to *Lloydia* would pay \$35 for a yearly subscription. Reprinted issues increased to \$25 per issue requested. Members would pay \$25 for annual dues including subscriptions to *Lloydia* and the *ASP Newsletter*. Finally, authors who submitted their papers and were accepted for publication would pay a fee per page for their articles, a common practice at that time.

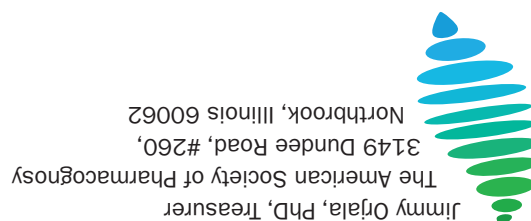
In financial reports from the following years, the changes proposed by Schwarting and pushed by Worthen helped the ASP Readership increased around the world, more authors contributed to the publication, and the publication became profitable. Schwarting retired in 1976 and Dr. Jack Beal was accepted as the new editor in 1977. In 1979, *Lloydia* was renamed the *Journal of Natural Products*. Today it continues to be an official publication of the ASP and is now co-published with the American Chemical Society. ■



Worthen's letter as it appeared in the *ASP Newsletter* from 1975.

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- 2 Letter from Arthur E. Schwarting to Ronald J. Retzler, September 30, 1974. Box 16, Folder 2, The American Society of Pharmacognosy Collection #22, The Lloyd Library and Museum, Cincinnati, Ohio.
- 3 “Report of the Editor of *Lloydia*,” August 1, 1975. Box 1, Folder 11, The American Society of Pharmacognosy Collection #22, The Lloyd Library and Museum, Cincinnati, Ohio.



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