



American Society of Pharmacognosy

Winter 2020

**Discovering
Nature's
Molecular
Potential**

ASP Newsletter: Winter 2020, Volume 56, Issue 4

Georgia's Farewell: A Pioneer's Journey

EDITOR'S NOTE: After more than 13 years writing for the Newsletter, Dr. Georgia Perdue has decided to retire her column "Brief News from Washington." She has been a devoted contributor, who never missed a deadline and expected the highest standards from not only the Newsletter, but herself as well. We thank Georgia for her hard work and dedication, and we wish her good luck in her future endeavors.

By Georgia Perdue, PhD



Georgia Perdue, PhD

This issue of the Newsletter and this column seem an appropriate time and place to briefly tell the story of a woman pioneer in our shared scientific field.

It is the story of a woman's journey in the field of pharmacognosy which began in 1960 when she enrolled in the small, conservative Massachusetts College of Pharmacy (MCP) located on Boston's Longwood Avenue across the street from Harvard Medical/Dental Schools. Many of her male classmates enrolled in one of these schools after graduation from MCP. Fortunately, each had an advantage of having several outstanding MCP classes under their belts. MCP enrolled about 100 students each year with only eight to ten women in each class. The fathers of several young men enrolled in MCP-owned pharmacies. For various reasons it was not uncommon for two or three women to drop out of MCP each year.

In her junior year the pioneer entered a class in pharmacognosy and fell in love with the subject. Dr. Maynard Quimby was the professor who taught the class. By her senior year a decision was reached to continue studies at MCP and obtain a master's degree. Dr. Quimby encouraged her. She inquired of the college dean and two professors about continuing. Shockingly, she was

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Pandemic, Work, Kids and Relationships All in Tight Quarters: Household Implosion

By Melany Puglisi, PhD, Mohd Shahid, PhD, Elsa Góngora-Castillo, PhD, Jessica Carilli, PhD, and Alejandra Prieto-Davó, PhD

A day in the life of a parent during COVID

Science is always full of ups and downs, critical deadlines and the need to continue a high level of self-motivation to stay current and keep meeting the challenges in our career. This has always been a challenge for parents in the best of times. We put in long hours so that we can be there for our families while continuing to build our careers. One parent is

often the go-to parent for the entire family meaning that, regardless of our responsibilities, we drop everything to help everyone else. Since March there have been a number of articles published regarding the difficulty of balancing work and home as school, business and work went remote after the WHO de-

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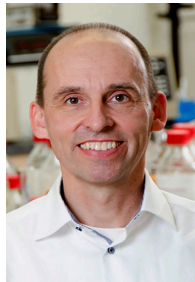
Dr. Georgia Perdue



Dr. Cindy Angerhoffer



Dr. Ted Molinski



Dr. Guido Pauli

Employment Service

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

For more information see the services website.

www.pharmacognosy.us/jobs/

Newsletter Staff

Edward J. Kennelly, PhD

Editor In Chief

Patricia Carver, MA

Copyediting & Proofreading

Nancy Novick, MEd

Design & Production

Gordon Cragg, PhD

Mario Figueroa, PhD

Joshua Kellogg, PhD

Michael Mullowney, PhD

Guido Pauli, PhD

Patricia Van Skaik, MA, MLS

Jaclyn Winter, PhD

ASP Newsletter Committee

Contribution deadlines

Spring: Feb. 15; Summer: May 15

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Please send information to

Edward J. Kennelly, PhD

Editor In Chief, ASP Newsletter

Department of Biological Sciences

Lehman College, CUNY

250 Bedford Park Blvd. West

Bronx, NY 10468

718-960-1105

asp.newsletter@lehman.cuny.edu

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Editor's Corner

American Society of Pharmacognosy

By Edward J. Kennelly, PhD

2020 has been a year full of challenging moments and also a time of hope. In this issue of the *Newsletter*, we cover some additional challenging times in 2020. One of the lead articles is by a group of ASP members that we do not often cover, ASP parents. The pandemic has uncovered many disparities and also blurred the line between the professional and personal, as working from home became the norm and unforeseen issues for parents came to light. It was enlightening to see how many ASP parents have creatively addressed the many challenges of working from home with children.

This year has been a time of grief for many people who have lost family members due to the pandemic. In this issue, we cover the deaths of three ASP members, Bill Keller, Walter Lewis, and Tom McCloud; we learned about the passing of Mahabir Gupta just before we went to press, and his tribute will appear in the next newsletter. We have published extensive tributes to the three in this issue, and I think they each serve as good role models for ASP members. Keller devoted a significant amount of time to ASP as our secretary for decades. McCloud ran a natural product extraction operation for the National Cancer Institute that still provides the starting material for drug discovery programs worldwide. Lewis was an outstanding botanist and mentored several ASP members, including me.

The other lead article in this issue of the *Newsletter* is a farewell from Georgia Perdue, a long-time columnist for this publication and previous editor of her own newsletter, *Washington Insight*. Over the past 13 years, Georgia has unfailingly contributed her column on time and with great care for accuracy and precision. She had a real vision for her column, and I am glad she has been such a loyal contributor. She has not been to an ASP meeting for some time, so newer members may never have had the chance to meet her

in person. I hope you will take the opportunity to read her farewell, which captures what it was like for her being a woman in the field of pharmacognosy when that was a rarity. Georgia, on a personal note, I want to thank you for all you have done for the *Newsletter* and the input you gave me, and I hope through this I have learned from you how to be a better editor. I wish you the best!

ASP Diversity, Equity, and Inclusion Committee has written a thought-provoking article that discusses issues of racial oppression, and specifically how ASP members could help to create inclusive workplaces. Lesley-Ann Giddings provides some concrete ways to try to effect change in the workplace, like the act of speaking up when discrimination is witnessed. I hope you will take the time to read this, as well as the articles from this committee in the past two issues of the *Newsletter*.

ASP welcomes three new fellows, Guido Pauli, Cindy Angerhofer, and Ted Molinski. The fellows are some of the most accomplished members of ASP and are led by Gordon Cragg. ASP Past President Barry O'Keefe made an appearance in a BBC documentary ***Extinction: The Facts***, hosted by Sir David Attenborough. Getting word out about the importance of pharmacognosy research is critical, not only to the scientific community but the popular press as well.

I hope you will also read the other regular columns in the *Newsletter*. Dave Newman offers a fascinating look at the development of dolastatin 10, which involved a number of ASP members, stemming from work conducted originally in the laboratory of ASP Fellow Dr. Bob Pettit.

I hope you have a wonderful holiday, and may 2021 bring you joy and success. ■

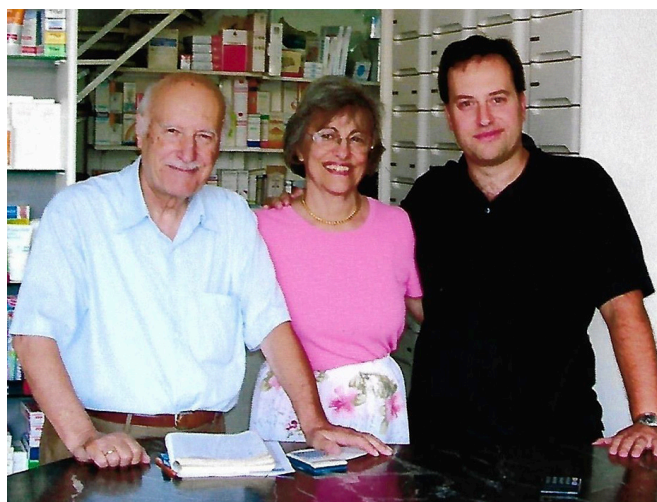
Georgia's Farewell: A Pioneer's Journey

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discouraged from doing so. "Some girls enroll in a master's degree program only to never finish," the dean declared. In defense she replied that at least one girl had finished and continued, "I am serious and will not drop out." For the time being the three rule makers conceded, but then informed her that she would have to take French and German classes taught by one of the professors. "Why? I already took those language classes in order to enter MCP?" came the response. Given no choice, she yielded and completed the two requirements in the first year toward the master's degree. At this point Dr. Quimby had become her advisor and was a great encourager.

The times produced another obstacle. What plant or plants should she study? As it turned out, Dr. Stanley Diamond had given MCP over 47 species of plants collected in Jos, Nigeria. So, the young woman agreed to study several plants for her master's thesis. She applied to NIH for a travel grant to travel to Africa with two professors on her committee to obtain plant

"We are very sorry but we cannot fund this grant because we do not agree that it is correct for a young woman to go together with two male professors to Nigeria."



Athens Greece in the 1990s. Bob Perdue, my husband, and I were visiting my relatives. Left, my cousin who owned the pharmacy, Right, his son, my nephew and current owner. The original owner was my mother's oldest brother; here are his son and grandson. Yes, I am fluent in Greek... have been all my life!!!

details. All was well until the NIH reviewer replied, "We are very sorry but we cannot fund this grant because we do not agree that it is correct for a young woman to go together with two male professors to Nigeria."

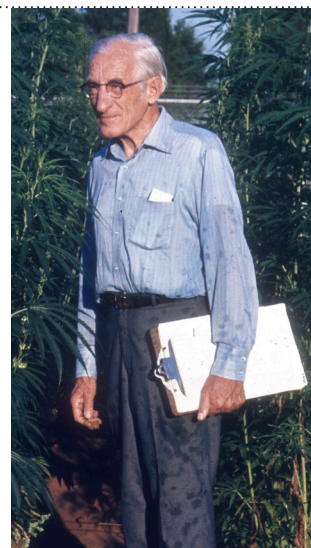
Greatly disappointed with the turn down, she decided to go to Greece for a few weeks and finally meet her relatives. An uncle (her mother's brother) was a pharmacist and owned a pharmacy. His son, her cousin, was also a pharmacist. She had a fabulous time with all her relatives and returned to America refreshed and happy. She completed all requirements for her master's degree.

The young woman had given serious thought to pursuing a PhD. When she mentioned the subject to the dean, the answer again was "No" because another girl started but did not finish. Again, she firmly answered she would, indeed, finish. Finally, they caved. She began her last four years of study. However, a couple classes were not offered at MCP and she had to attend Harvard University. She did not blink. The university was close by and the two professors were both well known in the field. One was the late Dr. Richard Schultes, "father of modern ethnobotany." He frequently went to the Amazon areas where he gathered first hand information on native use of plants.

However, there was still one more requirement, but it, too, had a happy ending. Dr. Norman Farnsworth, an MCP graduate and at the time a professor at the University Pittsburgh, asked to be on her committee. In that position he recommended she spend six weeks that summer at the university to learn everything about Thin Layer Chromatography, a new research tool. She complied, staying at the women's dorm, endured the hot weather, "survived" and learned a great deal.

The day came in 1966 to defend her doctoral thesis on Nigerian plants, with emphasis on *Lophira lanceolata*, before the committee. When time came to enter the examination room, Dr. Farnsworth said, "You are not going in. You stay here, outside the room, because I know the three who will try to axe you! I know things about each one,

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Quimby moved to University of Mississippi in 1967, where he developed an economic plant garden that is now named in his honor.

Georgia's Farewell: A Pioneer's Journey

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THE BIG DAY: Getting ready to leave for graduation in Boston and be the first woman to get the PhD degree from MCP. With proud parents before departure.

After all the roadblocks, hard work and harassments, graduation day in June 1966 arrived. She was the sole PhD graduate in the ceremony, and the first woman to graduate with the degree from MCP.

so they will not say anything negative in my presence!" After a short time, Dr. Farnsworth came out smiling, saying, "You made it."

After all the roadblocks, hard work and harassments, graduation day in June 1966 arrived. She was the sole PhD graduate in the ceremony, and the first woman to graduate with the degree from MCP. She remembers saying to herself as she walked across the stage, "Yes, we did it," looking at her parents, brother and his family.

The young woman leaned in the direction of teaching at a university and to that end had a couple interviews. While still considering her future, a letter from someone she did not know arrived in the mail offering her a job as laboratory director in a newly formed Maryland company, The Natural Products Research Laboratory (NPRL). It was part of the parent company, Amazon Natural Products Drug Company (ANDCO). She was intrigued. After much consideration she decided to take the

Dr. Perdue in the lab —as pictured in the book *Green Medicine*

train to Maryland for an interview. She was impressed with what she saw and heard. After much thought and prayer, she agreed to take the position in September. But she was puzzled as to who recommended her. A few years later she learned it was Margaret B. Kreig, author of the book **GREEN MEDICINE: The Search for Plants that Heal**, who had recommended her. The young woman's picture is in the book along with a short story about her. Several ASP members were also mentioned. Later, the American Society of Pharmacognosy paid a big tribute to Margaret (Peggy).

During her first year as director of NPRL in Rockville, MD, a small consulting group was put together including Drs. Norman Farnsworth and Ralph Blomster. It met quarterly. By this time a pharmacology lab had been set up on the same floor as her office. One thing she had not expected was to travel to the Amazon area near Iquitos, Peru at least twice a year! The parent company had an office in Iquitos responsible for collecting the plants in those areas! It was a treat to travel on the company-owned boat along the Amazon river!!!

It was during these years in the late 1960s that the ASP was being formed with only a handful of women members. It was a grand experience for the woman to be part of the Society's birth. Norman Farnsworth, the force behind it, called on her to serve in different capacities, which she enjoyed. They were all very proud of what they had begun!

Five years later the woman met and married a pediatrician, Dr. Roger Bergstrom, whose office was on the same floor as the lab. And, the ANDCO boss had decided that the Rockville, Maryland lab would be closed. It was about the time that drug use by young kids, 10-12 years old, was just beginning. Her husband asked if they could have the lab to begin testing

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One thing she had not expected was to travel to the Amazon area near Iquitos, Peru at least twice a year! The parent company had an office in Iquitos responsible for collecting the plants in those areas!



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his patients who were just starting to use drugs. The lab was turned over to them and was renamed The Bergstrom Toxicology Lab. But three years later her husband was killed in an accident. She was ready to close down the lab when Montgomery County contacted her because it needed lab testing for young people who were taking drugs. So, the widow agreed to the county's contract for a while.

In 1975, when the widow and her late husband's four boys, whom she adopted, were getting ready to move to a new house, she received a phone call from the world renowned botanist, Dr. Robert E. Perdue, Jr., who worked at USDA. He had no clue of her marital status. They had met at the Society for Economic Botany meetings. He asked her to go to dinner. She agreed. The rest is history. In 1975 they married and it was not long to realize what a famous botanist she had married. And, she learned of his magnificent contributions to new drugs from plants collected before her marriage. She shared the work of obtaining plants from several parts of the world which led to new drugs, especially cancer drugs which have already been referenced to in the column, "*Brief News from Washington*."

Bob encouraged his wife to pursue her idea of a newsletter for the pharmacognosy community, called *Washington Insight* (1988-2000). It was a success. She attended Senate and House hearings and interviewed select Senators and House members. She was happiest when she succeeded in getting the word "pharmacognosy" into the *Congressional Record*! She also attended select council meetings at

NIH. Professional colleagues at universities asked her to give lectures on her work. She fulfilled some of the requests.



She also realized she had married a highly decorated first lieutenant.

Bob served in WWII and was humble about his decorations. He had received two purple hearts and a Bronze star, among others. He wrote his highly received story in the magazine, *After the Battle*. He also wrote a highly well-received book, *Behind the Lines in Greece, The Story of OSS Operational Group II*. It was a BIG hit with Greeks and others all over the country. His wife's fluency in Greek helped, especially on the trips to Greece to obtain facts. The book triggered the Greek Embassy in Washington, DC to have a big banquet attended by living OSS fighters. Later, Bob received an invitation to speak before 1,000 troops at Ft. Stewart, Georgia, divided into two groups of 500 each. Standing ovations were tear jerkers.

Six years after Dr. Robert Perdue, Jr. died suddenly of a stroke in 2011, his widow got to know someone at their church, Fourth Presbyterian Church, Bethesda, MD, Dr. and Col. Donald J. Evans (USA, Ret.) They chatted after church services. Sometimes the fellowship became dinner. Well, it turned serious. Four years ago, they married. Each recognized God's providence in it all.

So now you know the identity of the young woman pharmacognosist, Dr. Georgia Perdue Evans. Her column was "*Brief News from Washington*." She bids farewell to the column and wishes all of you many blessings. A most heartfelt thanks to the "sister" I gained in MCP, Jean Kalil, and special thanks to Editor Dr. Edward Kennelly for his confidence in me. Remember, readers, you are in a unique field of study. I truly hope partisan politics do not overrun either the field nor the Newsletter! ■

Her column was "*Brief News from Washington*." Dr. Perdue bids farewell to the column and wishes all of you many blessings.



Pandemic, Work, Kids and Relationships All in Tight Quarters: Household Implosion

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clared COVID-19 a pandemic (Kramer, 2020, *New York Times*; Nam, 2020, National Public Radio; Kreeger et. al., 2020).

We find ourselves in the new normal time. We welcomed the initial relief of not having to run kids from activity to activity and the ability to clear the social calendar so that we can relax on weekends and talk to our spouses and children. For many of us this new uninterrupted family time is precious. However, three weeks into the pandemic, the ex-

However, three weeks into the pandemic, the extended spring break was over for academics and children.

tended spring break was over for academics and children. Now there were new challenges. We went back to work with modified daily schedules and responsibilities. We switched to teaching on an online platform – new for so many of us and our students. The labs were closed and, for many of us, much was lost when the freezers went down, the backup generator failed and no one was notified. The critical deadlines were still there: student projects and theses, grant submission, progress reports, grant and manuscript reviews, study sections, manuscript submissions, and others. The responsibilities are different for all of us, but the time commitment is the same. We began to realize the impact of the loss of childcare, after school activities and those precious hours of quiet in our offices and laboratories where we can concentrate on meeting those critical deadlines.

I have never known this kind of exhaustion.

Melany P. Puglisi,

College of Pharmacy at Chicago State University

I find myself in an unfamiliar situation. As a working parent I have relied on neighbors and friends to help out with the kids after school. I have outside help with the house. I am also the parent in the house that everyone relies on for most things. Now because I can work from home, I am the caregiver of children of friends who are essential workers on the front lines of the pandemic. On a typical day, I get up early to get a few things done before 7:00 a.m. in the home office. Then I make breakfast for anywhere from three to six children (I have two!). I get them all settled in separate spaces for school and then go to my office for the only two uninterrupted hours of daylight. Then begins the rolling lunch hours – why would they all have lunch at the same time? But that is not the real challenge. The challenge is that almost all of them are picky eaters or have dietary restrictions. This part can be handled with a little bit of planning.

Then, the end of the school day hits. Everyone is starving. I really thought I fed them two meals today! The emails come flying from their schools and the other parents regarding the work that was not completed. The younger children need help completing their asynchronous assignments; the older children glare at me because I said no video games until their work is done. The next thing I know it is 5:00 p.m., and the only reason I know that is because people are picking up their children. I have managed to fit in several meetings and most of the important e-mail into this chaos. I fit in what used to be after-work chores as well as dinner, and around 7:30 - 8:00 p.m. I make it back into the home office to meet with students for classes, research and support during this difficult time. I try to get a few more things done before I get ready for the next day.

This chaos is now a routine, but just last week THIS HAPPENED! I walked upstairs to hear the cacophony of “The internet went out!” from all corners of the house as we all tried to log in for our virtual day at school and work. The range of reactions was tears from the younger children to pure elation from the teenager who thought it would be a day off. But that would not do! I had important meetings, my spouse had classes to teach, and none of us could work without internet access. We loaded the kids up in two cars and headed to a friend’s house where they weren’t doing electrical work on the roads (two days and did not notify the residents!). Everyone was back on the internet in 30 minutes. The best part of the day was amid the stress of keeping everyone on track, someone made my lunch, entertained the kids after school and gave me a brief reprieve from my daily concerns. Thank you to those wonderful people in my COVID bubble that provide relief during these crazy times.

It would have been a relief to tell everyone to take the day off, but I worry for the children. I never hesitate to drop what I am doing to help them with school and to deal with the isolation from their friends. I have remodeled the house to make better learning and work spaces. I worry for my students as well, working with them to meet deadlines and adapt to the remote platform.

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I make it back into the home office to meet with students for classes, research and support during this difficult time.

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Pandemic, Work, Kids and Relationships All in Tight Quarters: Household Implosion

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Last Tuesday I almost crashed.

Alejandra Prieto-Davó,

School of Chemistry, UNAM, México

So, I have been trying to do the best I can during this time, a single mom of two kids (5 and 9 years old) and, of course, two dogs. I have no help at home since the helper sent a message saying she had a cough, so there goes any help for the next two weeks. Since the week before we had a hurricane scare, I had to prepare for it, and so I had little time to do any work. I have to help both of the kids during their asynchronous sessions since they are not old enough to focus on their own. Also, I teach two undergraduate classes and one graduate class. I had not had time to prepare for a lesson I had to give the next morning; I was just completely overwhelmed. And this is from someone who has a secure job, enough salary to pay her debts and lives in an enclosed complex so we can go out safely to walk and play. Our confinement has definitely been eased by some neighbors who have same-age kids and who have been part of our lockdown bubble.

That Tuesday I just gave up. I sat down and decided I needed a break from my screen. You see, now we are always looking at a computer screen at all times, whether it is to talk to someone, watch a movie (in my case), work, read a paper, etc. When I go to work, I come back and really do not have much time to sit and work in the afternoon. I am always driving

Basically, I do not rest; my mind always reminds me of something that I know I should be doing, but it is impossible for me to do.

around taking kids to extracurricular activities or running errands and, sometimes, out to see friends. But now my screen is always here reminding me that I have to finish that review, I have to write that paper, I have to prepare that lesson. Also, I have to upload my children's homework, make sure they go over their lessons, cook and clean the house and kitchen. Basically, I do not rest; my mind always reminds me of something that I know I should be doing, but it is impossible for me to do. Then there is the fact that I actually run a lab and scientific projects, and we are not yet allowed to go work full time. I have to keep in touch with all of my students and postdocs by Zoom or another platform. This means that, when I am not helping the kids go over their lessons, homework or studying for tests, I am in a Zoom meeting with someone.

I am also always worried about my future evaluation coming up soon. In UNAM we have an evaluation every four years; part of our salary (almost 1/3) comes from that evaluation. We also have an extra part of our salary coming from the governmental support agency SNI (National System of Researchers), and I have to show that



Góngora-Castillo helping her 7-year-old son with homework while attending a webinar in the smaller computer.

I have written papers and taught classes during the past four years. I do not know if I will make the cut next year to keep my appointments and my same salary after this year. I cannot even think about how people with no secure jobs are doing it. I have no idea what they might be going through. I also do not know how much harder or easier it is to have a partner at home.

The “new normal” is not normal.

Elsa Góngora-Castillo,

CONACYT-Biotechnology Unit, CICY, Yucatán, México

The health crisis due to the COVID-19 pandemic has widely exposed the gender bias and inequity in academia which is echoed by the brutal number of women dropping out of the wider workforce to attend to family needs (Connley, 2020, CNBC). The fact is that work in science is not very family friendly. The long working hours that include a number of activities such as laboratory work, competition for funding, writing scientific publications, management of graduate students, preparation for classes and a very long list of other duties, leave a very narrow window for family time.

Now in this pandemic, the long working hours have become endless along with the home responsibilities. There is no day that lasts long enough, nor a body that can endure it. As a woman in science I have dealt many times with gender bias and discrimination. I earned my PhD eight years ago, and for four years I have been in a tenure-track position as a PI in a research center in southeast Mexico. I am a mom of a 4-year-old girl and a 7-year-old boy, and for the past seven months I have tried really hard to keep working in science.

“Do you have meetings tomorrow? What time?” – this is how the conversation usually starts at the dinner table

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with my husband trying to find time when the two of us can work. “I have several meetings in the morning, but I will take care of the school assignments in the evening,” my husband answers. “Ok, I will do the online classes with the kids, but I will be teaching bioinformatics from 3 to 5 p.m. So, please do not schedule anything during that time so you can watch the kids,” I reply. And this is how the days, weeks and months have passed, trying to find some balance at home in order to attend the needs and responsibilities of all family members.

At the beginning of the confinement my days began before seeing the sun trying to get a little work done before break-

The fact is that work in science is not very family friendly.

fast. Mornings fade away between breakfast, online classes for kids, lunch and housework. My first shift starts around 3:00 p.m. and lasts only a couple of hours. Sometimes I manage to work around the online classes schedule and set up a meeting at noon. At 5:00 p.m. it is time for dinner, baths, pending tasks and the kids’ bedtime. My second shift starts at 10:00 p.m. and ends at 1:00 or 2:00 a.m. This is the period of time I get to work without interruptions, but also it is the time my body begs for rest. I have to prepare the next day’s classes. There is no truce – I make the second or third round of coffee wishing that Google classroom will be intuitive enough to create a quiz and that I can avoid watching a tutorial. After several months, this “routine” has become unsustainable. Waking up before sunrise or working late at night is not that easy anymore. My enthusiasm and patience for my kids’ online classes are not the same either; any suggestion coming from my kids’ teachers irritates me; my anxiety and frustration levels are sky-high because I cannot get anything done at the same pace that I used to do. Unfortunately, the pandemic in Mexico is far from being controlled, and therefore, the schools will remain closed.

There is nothing normal with the “new normal.” The physical fatigue is more than evident, and the emotional fatigue is indescribable. Adding to the endless daily routine are the claims and demands of my employer and a tenure-track faculty annual evaluation. It has been a huge challenge having a “good” performance when we have been limited in time, resources and space. During this year’s evaluation, someone told me that now is the time to get the papers written because I will be at home all the time and the pandemic situation should not be an excuse for my productivity. Most of these comments come from male colleagues that are not able to see that right now I am a faculty member and also a kindergarten and first grade teacher. Moving from tenure-track to

tenured position looks more and more difficult; the economic situation in Mexico has all these positions on hold, not to mention that politics in the country is not friendly towards science and its researchers (yes, in the middle of a pandemic!). If the evaluation criteria for next year does not consider the current conditions, the productivity of many women in academia will be compromised and our jobs’ positions at risk. And yes, it worries me not being able to hold my job.

There are many resilient women in academia struggling every day against an avalanche of responsibilities, endless work hours and lack of institutional empathy. The “new normal” will never be normal, and the dropping out of women from academia will continue to increase as long as this pandemic lasts if the working conditions during the pandemic and post-pandemic do not change to a system that is more family friendly.

Who is “in charge” right now?

Jessica Carilli,

Navy Scientist, USA

I really thought life was hectic before COVID: my partner and I both work full time and we have two little kids, now 5 and 9 years old. Most days I barely had a moment to relax and felt I was constantly either working, commuting, dealing with meals and laundry or trying to appreciate a few calm minutes with the kids before collapsing into bed. At the beginning of the stay-at-home order, which we thought was temporary, I was frantic about how I would possibly stay on top of work. My partner made the incredibly helpful observation that we needed instead to try our hardest to appreciate this new forced time together and pay attention

Then school started again, virtually at first, with crazy-complex Zoom schedules that did not match up and made the daily schedule-Tetris® break my skull.

to the kids. We evenly divided time every day to make sure we each had uninterrupted work time and non-work time when we were “in charge” of the kids and agreed that we would actively do things with them, not just let them watch TV while we continued to work. This perspective helped, and it was helpful as well that the world had to sort of pause and take a breath. We used a shared Google calendar to try to avoid scheduling meetings at the same time. Then each morning, we would review and plan the day; usually it was crazy, fragmented with chunks of work and kid-stuff interwoven. But we hung on, focusing on things that we would push down on the work to-do list because field and lab work was paused.

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As the weeks wore on, we were also able to get a little help in the form of a few hours a week of kid-watching from in-town grandparents and an hour or two a day of Zoom with their far-away grandma who reads books and plays games with the kids. (They are on the 23rd Wizard of Oz book!) This helped so much but also increased the schedule complexity, taking into account the grandparents' schedules, too. Then school started again, virtually at first, with crazy-complex Zoom schedules that did not match up and made the daily schedule-Tetris® break my skull. I had to add in a spreadsheet to keep track of it all. Finally, about six months in, we got a break and our kids started back at school for two six-hour days a week. By getting up at 5:00 am, I have nine kid-free hours, ALL IN A ROW, to work (and my partner gets the same trailing into the evening). It is unbelievable how much better my brain works and how productive I can be when I am not having to pivot between analyzing data, explaining how to spell "went," and writing reports 20 times a day. (I also got to trash the schedule spreadsheet because home-days now are self-paced, the local grandparents cannot help for fear of vectoring the virus to them, and school days are just so much easier!) We've now had a total of six days of kids physically in school, and I am desperately hoping we can keep this going.

Congratulations! New grant! New baby makes three! All in the wake of a pandemic.

Mohd Shahid

College of Pharmacy at Chicago State University

March of 2020 finally brings a piece of long-overdue good news that I have been waiting for over a year, the National Institute of Health (NIH) is funding my grant that I submitted in January 2019. All the hard work for several months and many sleepless nights was finally all going to be worth it. Writing an NIH proposal for funding is an incredibly difficult and exhaustive task at a teaching-heavy institution. Chicago State University is an institution that serves the underserved and underrepresented minorities, and much of our attention is focused on the success of our students. In the midst of midterms and the warning of a potential pandemic, I was beginning the process of hiring laboratory technicians and kicking off an exciting summer of research with my students.

Then, during spring break in March, Chicago was hit hard by the COVID-19 pandemic. CSU, like many other institutions in the country, decided to shut down due to COVID-19, extending spring break an extra week. The course coordinators were asked to transition to an e-learning platform post-spring break, with which most of us had very little prior experience or none at all. The bottom line was that my labo-



Shahid, balancing a new baby and a new grant.

To date, we have not been able to make significant progress on my NIH research project. I have been seriously anxious as to what I would write in my progress report to NIH which is due very soon.

ratory, like others, was closed for an indefinite period until further notice. The pandemic continued and worsened with time, and the lockdown, consequently, remained in place. To date, we have not been able to make significant progress on my NIH research project. I have been seriously anxious as to what I would write in my progress report to NIH which is due very soon.

Meanwhile at home, we were expecting our third child, and my wife was in the first trimester when the pandemic began. At the beginning of the second trimester, my wife developed pemphigoid gestationis, a rare skin disease that manifests as fluid-filled blisters all over the body with severe skin inflammation and itching. This changed her pregnancy to high-risk, requiring several visits a week to different hospitals and careful monitoring of her diet and medications. In the absence of any family support (our families live back in India), I initially saw a silver lining in the e-learning environment due to COVID-19 lockdown, as I could potentially stay at home and take care of my wife. However, this thought disappeared very quickly after spring break was over.

It turned out that e-learning required more office hours, more planning for online lectures, quizzes, and administra-

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tion of examinations, and multiple meetings with students to address their newly found issues (technical and/or academic). In addition, being a part of several colleges and university-wide committees stipulates me to attend or coordinate meetings almost every day. Due to the nature of online meetings, they were longer and more frequent now than they would have been otherwise. Now, due to the changes in the testing format, there were more accommodation requests, more exams per course, more exam reviews, more exam question challenges, etc. To prevent impairment in students' learning, I worked around the clock to immediately address any issue or challenge whether it was related to

This is not just my story. I have witnessed many of my colleagues going through the same experiences. We have been stressed since spring break, not for our sake but because we truly care about our students.

the course material, assessment, online proctoring requirement, or technical issue that our students were facing due to COVID-19. All of a sudden, my office hours have changed from one hour to 15-16 hours a day. Amidst all this, I have two other small children at home that I have to share responsibility for with my wife.

This is not just my story. I have witnessed many of my colleagues going through the same experiences. We have been stressed since spring break, not for our sake but because we truly care about our students. However, it has taken a toll on us and our families. We are not able to give enough time and support to our spouse and kids, especially when they need that most.

The end of the day

At the end of each day, it is true to say that we all feel the same type of exhaustion as if driving a car for 12 hours. With the exception of moving from room to room, we reach our mental capacity trying to manage our work and home responsibilities. In these uncertain times, what we find ourselves doing is working 24/7 to fit in all the demands of parenting, teaching and science. The order of those words changes daily in terms of priority. At times, the commitment at home does not allow us to get anything done as we used to, when our minds cannot focus because we have multiple overlapping schedules to remember. Keep in mind, everything we do right now, we do in front of our children, families and friends. They see us persevere through these challenging times. They see our successes and our sacrifices. They will look back on these days and see us for the strong parents that we are.

We all wonder how our careers will suffer, and, when our family life gets tested by extra loads of stress from managing new responsibilities, we wonder if we are doing all the right things for our families. We imagine that everyone who is reading this article has experienced their own challenges and have their own sets of worries. We will not be able to maintain this 24/7 schedule for another six months, never mind how long it will take to distribute a working vaccine. We need to take care of ourselves while we pursue our careers in these interesting times. ■

We all wonder how our careers will suffer, and, when our family life gets tested by extra loads of stress from managing new responsibilities, we wonder if we are doing all the right things for our families.

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Taking Action: Intentional Inclusivity

By Lesley-Ann Giddings, PhD

Since the beginning of the pandemic, many of us have spent more time at home. It has been a time for us to reflect upon our careers and families, mourn old routines, and dream of what we will do once the pandemic is over. It was during this time that the horrendous murders of Ahmaud Arbery, George Floyd, Breonna Taylor, and countless other Black citizens took place, causing an international reckoning with the daily racial oppression faced by many within Black and Brown communities. Even though countless other murders have been captured on video and circulated for years, people finally had the time to watch the videos and reflect.

It became apparent that concrete structural changes had to be made. Many people took to the streets to protest, while others urged their organizations and institutions to not only make statements but make systemic changes to dismantle racism. We are now at the point where *diversity* is teetering at a point of being more than just a buzzword. Many now recognize that creating inclusive and equitable environments is necessary. People are finally willing to dedicate significant resources and time to this cause.

Members of the ASP Diversity, Equity, and Inclusion Committee recently [polled](#) the ASP community to determine what our membership is interested in reading about. To date, of the 178 people who responded, most would like to know more about how to create inclusive workplaces where people truly feel comfortable being themselves. There is a sense of urgency to do this work; however, many do not know where to start. Simply tweeting about the importance of diversity initiatives is not enough. Hiring someone from a marginalized group because that is the current trend without providing the support a candidate needs to ensure their success is not enough. Proposing to do a two-day science workshop involving Black and Brown children for outreach in your next grant application is

not enough. While these gestures are important first steps, they are not sufficient to eradicate racial inequality in our country. We need cultural and structural changes that focus on inclusion and prioritize antiracist practices.

We ultimately want to build a strong pipeline that recruits and retains students from all backgrounds in science, technology, engineering, and mathematics (STEM). The American Chemical Society (ACS) recently published data showing that the chemistry pipeline is broken at the undergraduate level.¹ For example, we lose many Black undergraduates in introductory chemistry courses^{2,3} and fewer Black chemistry majors continue to graduate school compared to other racial and ethnic groups.¹ In 2018, only 4.5% of all chemistry PhDs were awarded to Black graduate students.⁴ If these graduates persist to become postdoctoral fellows, few continue on to secure academic jobs.⁴ The ACS recently reported that at 50 doctorate-granting institutions in the United States that spend the most on chemistry research, the racial and ethnic diversity of chemistry faculty has changed by less than 1% since 2011.⁴ The percentages of racially and ethnically diverse faculty are abysmal, a mere 5.2% in 2018 compared to 4.4% in 2011.⁴ What is worse is that these numbers include all faculty from underrepresented groups, including American Indian/Alaskan Native, Black, Latinx, and multiracial, which make up more than one-third of the United States population.⁵ To correct this inequity, graduating more chemistry majors from underrepresented backgrounds would increase their representation in graduate school as well as in positions in higher education and industry. Increasing graduation rates is the first step, but creating inclusive environments is paramount to increasing representation in lifelong careers in science.

To increase the diversity in our labs and work environments
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Taking Action: **Intentional Inclusivity**

We ultimately want to build a strong pipeline that recruits and retains students from all backgrounds in science, technology, engineering, and mathematics (STEM).

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ments long-term, we have to practice the act of inclusion. Diversity and inclusion go hand in hand; inclusion creates the space for others to feel comfortable being themselves and diversity is the result. Some may say they do not mind having diversity initiatives in the workplace. However, “not minding” is the same as tolerating, maintaining the status quo. To be inclusive means to constantly challenge stereotypes and assumptions, listen to others, speak up when you witness discrimination, be open-minded, initiate uncomfortable conversations, think about why certain issues make you feel uncomfortable, recognize your privilege, and work to educate yourself. The act of inclusion is about being more intentional, self-aware, and aware of others. It requires having compassion for other journeys traveled and consistently advocating for others who are not in positions of power to make sure they have a seat at the table. Sometimes the act of inclusion also requires courage, and those in positions of privilege should exercise their power to act. Inclusion is about making sure that everyone feels valued.

We often surround ourselves with individuals in which we share commonalities, such as behavioral, cultural, and moral standards, and forget to consider those who are not in our social circles. It is from these circles that we define ourselves and gain confidence in who we are. Individuals on the fringes of those circles looking in likely feel uncomfortable in that space. To enter these spaces, there are certain social codes one has to know. For those on the outside, it can be exhausting trying to code-switch to be accepted. For example, some people feel excluded when attending conferences and realizing a significant portion of the social capital in science

is built around drinking at bars after conference sessions. If you do not drink alcohol, you are not going to enjoy or participate in these activities. Thus, we need to organize a variety of workplace or conference activities to give everyone an opportunity to participate. This is why we also need organizing committees and labs composed of people from diverse backgrounds to think of new ways of engaging everyone. We all have unconscious biases or blind spots, but just like when driving, we need to continuously check them so we do not hurt anyone or ourselves.

We need to create safe work environments that celebrate all people. To do so, we can start by assessing our laboratory cultures, identifying different ways of supporting all laboratory members, seeking out additional mentoring for those who might be struggling, and discussing strategies to minimize those who may feel excluded and unsafe in the lab environment. The act of inclusion is iterative and must be reassessed to ensure a productive work environment. For those of you running labs with students or postdoctoral fellows from underrepresented backgrounds, you have a huge opportunity to make a difference by creating a supportive environment that ensures their success and encourages them to persist toward careers in chemistry. If you have a colleague who is an untenured faculty member from a racial and ethnic group underrepresented in STEM, reach out to them and see how you can support them and their scholarship through tenure. Many of these underrepresented scientists are code-switching to be a part of predominantly white institutions, where they lack role models or people in positions of power

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Taking Action: **Intentional Inclusivity**

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who look like them. It is such an excluding experience and the reason why the act of inclusion is critical for our persistence.

In the introductory chemistry laboratory courses at Smith College, we spend the first lab discussing group norms and usually learn that many students dislike working in groups. We ask the students to share 1) the strengths they bring to the group and 2) what they hope to get from the group. From these discussions, it becomes apparent why students dislike working in groups. Almost all of the students say they want a group that respects, values, and supports them. They want groups that communicate well, do not dwell on their weaknesses, check in on them, are open-minded, collaborative,

reliable, welcoming, and promote positivity. We try to establish group norms early in students' scientific careers and keep checking in with students during the semester to remind them of how they want to be treated. However, while we try to instill these values within our students early on in their scientific training, we, the educators and scientists, need to practice what we preach. It is time that group norms are discussed and implemented in the workplace to set the tone and encourage a greater sense of belonging. To learn more about inclusion, please read references 6–8. These simple acts of kindness make people feel appreciated and valued and will help recruit and retain all students. Because at the end of the day, we *all* want to feel respected and valued. ■

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In Memoriam: William J. Keller

By A. Douglas Kinghorn, PhD

It is with a feeling of profound sadness to have to report that the long-term ASP Secretary and Honorary Member Dr. William J. Keller died on October 29, 2020, due to severe back problems, which were aggravated by a serious fall in late 2019. He began his duties as ASP secretary in 1985 and conducted these with great efficiency and reliability for some 30 years. In addition to being a bastion of our Society for so long, and a person who was approachable to young and old colleagues alike, Keller was also an excellent natural products scientist, who had highly successful portions of his career in both academia and the dietary supplements industry.

Keller received his first two academic degrees from Idaho State University, namely a BS in pharmacy (1966) and MS in pharmacognosy (1969), and then earned his PhD degree in pharmacognosy from the University of Washington in 1972. He was appointed shortly thereafter to the faculty of the School of Pharmacy at Northeast Louisiana University (now the University of Louisiana at Monroe), Monroe, LA, where he was employed for over 20 years. He became head of the Division of Pharmaceutics and Medicinal Chemistry in 1978 and was named Clarke Williams Distinguished Professor in 1989. Keller then moved in 1995 to the McWhorter School of Pharmacy, Samford University, Birmingham,



Dr. Keller and his wife Tram

AL, as professor and chair of the Department of Pharmaceutical Sciences.

ASP President Dr. Nick Oberlies reflected, “Bill was one of those bedrock members of the ASP, and by that I mean solid and long lasting. I recall being in an Executive Committee meeting many years ago, and when a question would arise about how we, the Society, handled some endeavor, he was always a fountain of knowledge on the historical perspective of why certain decisions were made. Bill took his role as secretary quite seriously and was always

well organized. But, what I remember the most was that he was simply a nice guy, who was always happy to reconnect with friends and colleagues, and always willing to offer words of encouragement.”

In April 2001, Keller transitioned from academia to working at a major botanicals company, when he became vice president of Health Sciences and Educational Services and chief scientific resource officer at Nature's Sunshine Products, Inc. (NSP), Spanish Fork, UT. During the industrial component of his career, Keller worked initially for several years with Dr. Jerry McLaughlin, former ASP president and former professor of pharmacognosy at Purdue University. Earlier, McLaughlin served as his PhD dissertation advisor at the University of

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—Dr. Nick Oberlies

“My admiration for his character and career motivated me to join a collaborative research program on botanical dietary supplements ‘on the side’ from my doctoral thesis work. Even through his emeritus years, Bill remained involved in and encouraging of rigorous and meaningful scientific discovery and dissemination. Bill was an inspirational scientist and leader, and he will be missed.”

—Dr. Ben Naman

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Washington, on research concerning the investigation of cactus alkaloids. Keller was highly regarded by the senior management of his company and was appointed to the Nature's Sunshine Products Medical and Scientific Advisory Board in 2014. While formally retiring in 2015, he remained in this advisory board position for some time thereafter.

In addition to being secretary of ASP, Keller was a member of the Board of Trustees for the American Herbal Products Association and was on the dean's advisory board for both the Colleges of Pharmacy of Idaho State University and Texas A&M University. While in academia, he served on several NIH grant review panels and was a frequent journal manuscript referee. He published about 100 journal articles and made approximately 200 scientific addresses both in the United States and internationally. In the 1990s, Keller spent a sabbatical period as a guest professor at the Department of Pharmacy of the Swiss Federal Institute of Technology (ETH-Zurich), Zurich, Switzerland, where he worked with ASP Honorary Member Prof. Dr. Otto Stichler. Keller became an honorary member of ASP himself in 2010 at the annual meeting held in St. Petersburg, FL.

Since we were both long-term members of the ASP Executive Committee, he and I would frequently share a room for each annual meeting. At the meeting in New Brunswick, NJ, held in 2002, he approached me about performing some phytochemical and biological testing laboratory support work on selected botanical dietary supplements. We started off by looking at noni, but over the years my group members went on to investigate also açai, black chokeberry, goji berry, mangosteen, licorice, and maqui berry. This collaborative work with my group at Ohio State University (OSU) eventually led to

11 journal articles and 18 meeting presentations on these topics.

This gave an opportunity for several of my former graduate students at OSU to perform in-depth research on dietary supplements, including Drs. Jie Li and Ben Naman, who are both now university faculty members. Naman recalled, “My admiration for his character and career motivated me to join a collaborative research program on botanical dietary supplements ‘on the side’ from my doctoral thesis work. Even through his emeritus years, Bill remained involved in and encouraging of rigorous and meaningful scientific discovery and dissemination. Bill was an inspirational scientist and leader, and he will be missed.” Li added, “Dr. Keller definitely played a very important, positive role in my career. When I was at OSU, the entire first four years of my PhD study was focused on dietary supplements, and the raw materials were all from Nature's Sunshine under Dr. Keller's coordination. I still remember the occasions I talked to him in ASP meetings: he was a very nice and helpful gentleman.”

In an e-mail message on September 27, 2017, Keller stated: “Yes, I remember the meeting in New Jersey well. That's when liquid noni was a hot product for NSP and I was just starting out with the company. As you pointed out, I asked the question about Noni and sent some material when I returned to Utah. And that was the start of a great collaboration.” By having a research program on botanical dietary supplements, this gave me a very useful insight for teaching professional pharmacy students. Even to the present day, I assist my colleague Dr. Esperanza Carcache de Blanco in the instruction of our first-year PharmD students at OSU for a course module on this topic, and often

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“He was a modest but great scientist with a boundless heart. He was a strong supporter of natural product research.”

—Dr. Esperanza Carcache de Blanco

In Memoriam: William J. Keller

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utilize our previous research insight gained. Carcache de Blanco noted, “I had the opportunity to know Dr. William J. Keller for several years. He was a modest but great scientist with a boundless heart. He was a strong supporter of natural product research. Bill also supported the development of junior faculty from diverse backgrounds and was always approachable. I am sure his legacy will live on through the great work he did when he was alive.”

As ASP secretary, Keller was known by all those in attendance at each annual meeting for shipping a large box to his hotel room containing about 100 copies of the minutes for the previous business meeting, as well as circa 30 copies of an even more detailed report dealing with the minutes of the Executive Committee meeting from the year before, along with copies of the Teller’s Report. Each major report required many hours to compile and accurately documented the important affairs of the Society from the previous year. At the business meeting for each annual meeting, he would sit at the table at the front of the meeting room along with the outgoing president and was always a voice of calm on these occasions. From the point of view of the Society, he had a great stabilizing influence over the years and an excellent recall of former members and past events. For an article written to mark his retirement as long-term secretary of ASP (*ASP Newsletter*, Winter 2015, vol. 51, issue 4, pp 15-16), he made several comments about his early experiences in this role, including: “I remember that the process of minute preparation was completed in the days before computers and word processors. We did not have e-mail or all of the sophisticated mechanisms of tracking revisions back in the late 80s.” He also stated: “I could mention many other memorable experiences involving events such as international travel to joint meetings, interacting with icons of the Society, and the close association that was built with colleagues who served with me as officers. Particularly the presidents and those Society members who were great personalities with a résumé that reflected their outstanding scientific contributions to the field of pharmacognosy.”

A number of his former colleagues who attended ASP meetings with him over the years have kindly provided comments on his passing, which are compiled following.

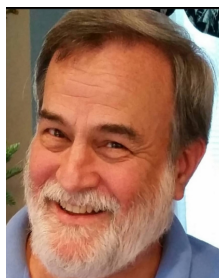


PHOTO: BERNADETTE CARDELLINA

John H. Cardellina II, PhD
(ASP Past President;
Honorary Member;
ASP Foundation Chair).

“Bill Keller, like David Slatkin, was a living legend in the ASP, with both serving for decades as Secretary and Treasurer, respectively. Bill was a quiet, unassuming, non-egotistical man, but a focused, dedicat-

ed officer of the ASP who vigorously defended his carefully construed positions on matters before the Executive Committee. It is difficult to imagine how he, with serious and chronic back issues, managed to transport and distribute the considerable piles of reports and other documents that had to be printed for both the Executive Committee and member business meetings in the pre-electronic report days, yet I never heard him complain. His elevation to Honorary Member status was a well-deserved recognition of his long, extraordinary service to the ASP.”



PHOTO: LIFETOUCH, INC.

Gordon M. Cragg, PhD
(ASP Past President;
Honorary Member;
Chair, ASP Fellows Group).

“I was greatly saddened by the news of the passing of Bill Keller. Bill’s knowledge of Society history, protocols and procedures was legendary, and his advice and wisdom greatly helped me cope with the issues confronting the Society as we approached the new millennium during my period as president in 1999-2000. It was a pleasure and privilege to be associated with Bill as a friend and colleague for over 30 years, and I will always remember his gracious and ever-helpful manner. My sincere condolences go out to his widow, Tram.”

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In Memoriam: William J. Keller

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PHOTO: APRIL DOW

David G.I. Kingston, PhD (ASP Past President).

"Bill Keller was the model of what the secretary of a scientific society should be. He was regular in his attendance at Society meetings; he was faithful in taking accurate minutes of the Executive Committee and annual meetings, and he was a trusted member who

was involved in many of the key decisions that have made the ASP the strong society it is today. And he did all this and much else in a kind and gentle way; he was the embodiment of a gentleman scholar."



PHOTO: WILLIAM BITZINGER, FSU

Robert J. Krueger, PhD (ASP Honorary Member; Treasurer, ASP Foundation).

"I have known Bill for over three decades as a colleague in ASP/ASPF. In his capacity as secretary to both, I often corresponded with him to check on items from the board meetings of these two entities that Bill had includ-

ed in his minutes. But he was also a mentor and a good friend. Over many a beer we discovered that we had a connection through a small restaurant in a small town in Wisconsin (Menominee Falls). We both shared an interest in dietary supplements, and Bill was a great mentor to me in that area. He was also responsible for convincing his employer for many years to sponsor an ASPF student travel award for undergraduates to attend our ASP meeting. We laughed together, had dinners with our wives together, 'plotted and schemed' together, and shared his love for our science and helping the ASP in whatever way he could. The latter was the best lesson Bill nurtured in me. He will be missed."



Rachel Mata, PhD (ASP Fellow; Chair, ASP Norman R. Farnsworth Research Achievement and Matt Suffness Young Investigator's Award Committee).

"In 1976, I was a student attending my first ever ASP meeting at Telemark, Wisconsin. It was then that Dr. Jerry McLaughlin, our common mentor, introduced me to Bill. Since then, it was always a pleasure to meet him in our annual meetings. He was very affectionate, still finding a moment to catch up about our personal and academic affairs. I really enjoyed these annual conversations. He was very proud of pharmacognosy and our society, which has now lost one of its pioneers. As I express my condolences to his family and friends, I remember his cordial presence. I will miss him."



PHOTO: CHUCK FRANCE,
UNIVERSITY OF KANSAS

Barbara H. Timmermann, PhD (ASP Past President; Honorary Member).

"I'm very fortunate and grateful for having crossed paths with Bill early in my professional life when I started learning how to navigate across the complex academic and grant-funding worlds. I learned a great deal from him, particularly during the discussions at the NIH study sections we both served on. I will remember Bill for his true friendship when I looked forward to our next meeting to catch-up or just to have a good chat.

Years later, working with Bill while I was president of ASP and throughout our many years together in the ASP continued to be a true joy. I remember Bill as the consummate professional when it came to recording the Executive Committee Meeting of the Society.

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**He was a very special person and an outstanding individual who
was unusual in caring more about the welfare of others than of himself.
Bill Keller was the epitome of being a truly Honorable
Member of our Society.**

From the point of view of the Society, he had a great stabilizing influence over the years and an excellent recall of former members and past events.

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He was a meticulous writer, very attentive to detail, and the Society benefited greatly from his dedication. My respect and appreciation for all he did for the Society grew with time. Bill will always be remembered by the ASP community for his contributions to and insights into the workings of this organization.

He was very fond of his last job and made many friends in the botanical supplements industry. His expertise and experience in pharmacognosy and natural products chemistry, coupled with his pharmacy training, contributed greatly to our ability to assess new ideas and innovate them into new products, especially in the area of nutrition and phytochemicals.

Bill was a true gentleman and was admired and respected by everyone who knew him. His passing is a loss to all of us. I will always remember the wonderful friend that Bill was to me."



It was very unfortunate that ill health caused Bill to have to resign in 2015 from both his industrial job as well as his position of secretary of ASP. In an e-mail message to me dated April 15, 2017, he mentioned, "I miss the academic life as well as the life in the nutritional supplement arena. Although it was hectic at times, I wish that I had not retired. Although I keep busy, it's just not the same as having a full-time job. Oh well!" However, all of us who met Bill annually at ASP meetings feel that we were very fortunate indeed to know him for as long as we did. He was a very special person and an outstanding individual who was unusual in caring more about the welfare of others than of himself. Bill Keller was the epitome of being a truly Honorable Member of our Society. We send our deepest commiserations to his widow, Tram, at this most difficult time. ■

Keller served as ASP secretary for 30 years, a fixture at the annual meetings. He provided copies of numerous reports to both the Executive Committee and the Business meetings, involving considerable amounts of time to assemble.

DR. MANSOOR KHAN

He was a very special person and an outstanding individual who was unusual in caring more about the welfare of others than of himself. Bill Keller was the epitome of being a truly Honorable Member of our Society.

In Memoriam: Thomas G. McCloud

By John Cardellina, PhD, Gordon Cragg, PhD, John Beutler, PhD, Barry O'Keefe, PhD, Nicholas Oberlies, PhD, Suzanne Shipley, PhD, Matthew Harris, PhD, and John Britt, PhD

Long-time ASP member Thomas G. McCloud passed away unexpectedly on Saturday, October 3, 2020 at the age of 76. He was a well-respected and successful scientist and researcher with the National Cancer Institute (NCI), where he played a crucial role in natural products extraction.

McCloud was born 23 August 1944 in Akron, Ohio to George and Doris McCloud; he grew up in Massillon, Ohio, which named him a Distinguished Citizen in 2008. Following undergraduate studies at Ohio State University, McCloud earned an MS in chemistry at North Carolina State University, after which he was drafted into the US Army, serving at Walter Reed Hospital. Upon completing his military service, he undertook PhD studies at Purdue University under the mentorship of Drs. Jerry McLaughlin and John Cassady, both former ASP presidents. There, as current ASP President Nick Oberlies recalled, "Tom quickly became the guy who could fix any instrument, even as he developed his skills as a natural products chemist. He was a legend at Purdue—during a blizzard, when the entire town was shut down for several days, he hiked about 2 miles into campus (with his trusty dog), and camped out in the building for several days, taking care of his own experiments and those of others in the department." Before he could finish writing his dissertation and defend his PhD work, McCloud was recruited to the budding natural products program at the NCI, where he proved to be a pivotal cog in the mammoth battle against cancer and AIDS.

McCloud spent his entire post-graduate career as a contractor at the NCI, where he served as the architect, builder, and manager of the Natural Products Extraction Laboratory (NPEL), which produces the extracts that comprise the NCI's Extract Repository. He proved to be the ideal individual to take on this task, for which he had to be not only a talented



McCloud in his laboratory at NCI, Frederick, Maryland, preparing to grind a specimen.

organic and analytical chemist, but also a designer, engineer, and trouble shooter.

His charge was fraught with challenges. McCloud had to produce hundreds of extracts a week, both organic and aqueous, from plants, marine organisms and microorganisms, yet the extraction process had to be specifically tailored to the organism type and condition. Since marine specimen arrived frozen, they were ground with dry ice and extracted with water; the filtered solids were freeze-dried and then extracted with or

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"Without Tom McCloud's tireless 'in-the-trenches' leadership, coupled with his incredible organizational skills, the NCI Natural Products Repository would have never traversed the complex and uncertain course from concept to reality; researchers worldwide who use the Repository in the search for cures for devastating human diseases are indebted to Tom for his critical role in the creation of this invaluable resource for medical research."

—Dr. Michael Boyd

In Memoriam: Thomas G. McCloud

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ganic solvents. Conversely, plants were field dried, but needed to be ground to powder or small fibers or chips of wood before extraction – first organic, then aqueous. Organic extracts required rotary evaporation for drying, and aqueous extracts needed to be lyophilized. All these operations required specialized equipment, processes needed to flow from one space to another, and all the equipment and working space had to fit into one modest-sized building. Powerful vacuum systems were required to drive a bank of rotary evaporators and all the freeze-driers, and coolant systems were needed for the condensers in the rotary evaporators. Every step in the process was first run on a modest scale, then scaled up to operating levels, permitting adjustments to be made to conditions or equipment. Over time, everything, from grinders to extraction capacity to freeze-drier capacity, was scaled up to industrial proportions.

Since McCloud proved so effective in this role and so adept at adjusting equipment and conditions as problems arose, he was soon called upon to bring his insight and expertise to bear on other challenges. He and his group were called upon repeatedly to aid researchers in reisolatation efforts; examples include silvestrol, schweinfurthins, englerins, brefeldin A, and michellamines. Similarly, he was frequently the go-to guy for synthetic modifications of natural products considered potential development candidates. Likewise, analytical evaluation of other plant parts or related species for a compound of interest often fell to McCloud's group. Later, his group was a major force in developing libraries of pre-fractionated extracts. The many responsibilities that he took on led to the renaming of his laboratory as The Natural Products Support Group (NPSG).

Dr. Michael Boyd, who conceived the idea of the Natural Products Repository as director of the Developmental Therapeutics Program, offered his thoughts, "Without Tom McCloud's tireless 'in-the-trenches' leadership, coupled with



McCloud adding solvent during the extraction process. He helped to build an extract library of more than 200,000 samples that are still used today.

his incredible organizational skills, the NCI Natural Products Repository would have never traversed the complex and uncertain course from concept to reality; researchers worldwide who use the Repository in the search for cures for devastating human diseases are indebted to Tom for his critical role in the creation of this invaluable resource for medical research." Dr. Barry O'Keefe, chief of the Natural Products Branch (NPB, NCI), had a similar reflection, "Tom McCloud had more impact on natural product research in the United States than most people know. His hard work and ingenuity built the NCI Natural Product Extract Library into a resource (>200,000 extracts) that more than 300 laboratories have accessed over the years. Without the NCI Repository, natural product research in the United States would not have had the prominence it has enjoyed. Today, our work in the Natural Products Branch is building upon Tom's legacy to enable another

generation of natural product researchers who, we hope, will remember the name Thomas G. McCloud. I was honored to know Tom for many years; he was an institution at the NCI Frederick campus. He was an excellent scientist, an outstanding canoeist, and a gifted leader of the NPSG. He will be sorely missed by many here at the NCI."

ASP Fellow and Honorary Member Gordon Cragg, chief of the NPB from 1989 till 2005, remembers the tremendous impact that McCloud had on drug discovery worldwide, "The NCI natural products research program involved the collection of plants and marine organisms in over 35 countries worldwide, and the samples were shipped to the NPEL in Frederick, Maryland, where Tom and his team entered detailed collection data in the NCI Natural Products database before proceeding with extractions. The collections were performed in collaboration with scientists in each source country, and NCI entered into benefit-sharing agreements with appropriate au-

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thorities and organizations in the source countries. Officials and scientists from many of these source countries visited the NCI and toured the extraction and cell line screening facilities. All visitors were impressed by Tom's expert knowledge and explanations of the extraction procedures, as well as his skill in demonstrating the efficiency of the natural products database in locating samples collected in their countries. Tom's expertise and transparency helped convince these visitors that their precious natural resources were being handled and processed in the most efficient, productive way possible, and that they could be confident that their countries were being treated in a fair and equitable manner in the collabora-



McCloud, an avid canoeist, enjoying his favorite pastime.

tion with the NCI. Scientists from the source countries were invited by NCI to spend 6 to 12 months working in Tom's labs. Tom provided these visiting scientists with expert training and equipped them with the knowledge and expertise to return to their home countries to establish or improve in-country extraction facilities. Thus, Tom helped promote drug discovery programs in Bangladesh, Brazil, Cameroon, Republic of Korea, Pakistan, Papua New Guinea, Sarawak/Malaysia, South Africa, Tanzania, and Zimbabwe. It was a pleasure and privilege to work with Tom over the years, and I know that the many colleagues from other countries who worked with him will share our sadness at his sudden passing."

Apart from his considerable skills as a chemist and engineer, McCloud was also an accomplished canoeist, building and restoring antique canoes and riding every river he could access. In 1987, he coauthored a book on canoeing in North Carolina (*A Paddler's Guide to Eastern North Carolina*) with Bob Benner; many paddlers consider it the quintessential guide, especially since it was published long before the days of Google Earth and Google Maps. If there was a river near the site of an ASP meeting, he was sure to paddle, usually taking interested meeting attendees with him, even relative novices. Nick and Hollis Oberlies were fortunate enough to

go on an overnight canoe trip with him in the early 2000s, "We were pretty novice campers and had never really been on a canoe trip. Tom loaned us gear, took care of all the logistics, didn't fret once when I ran his boat over the rocks, and kept a watchful eye on us as we travelled some beautiful, but sometimes challenging water. At the end of the trip, one of the other paddlers finally put together that Tom was 'the Tom McCloud' of the paddler's guide, quickly pulled out his dog-eared copy of the book, and asked Tom to sign it. If you knew Tom, you would know that he did not love to draw attention to himself, but he graciously signed the book, noting in his self-deprecating way that it probably needed updat-

Apart from his considerable skills as a chemist and engineer, McCloud was also an accomplished canoeist, building and restoring antique canoes and riding every river he could access. In 1987, he coauthored a book on canoeing in North Carolina (*A Paddler's Guide to Eastern North Carolina*) with Bob Benner; many paddlers consider it the quintessential guide, especially since it was published long before the days of Google Earth and Google Maps.

ing. The funny thing is that I, who had only known Tom as the genius behind the NPSG and the legendary chemist from Purdue, had no idea he was also an author of such a guide!"

Katherine Mull, a friend from Coastal Canoeists, echoed President Oberlies' comments, "I first paddled with Tom more than 20 years ago. At the urging of a mutual friend, I called to sign up for his three-day WV whitewater trip in February of 2000. I'd just gotten a whitewater canoe and was being encouraged to get on harder rivers. Tom seemed a bit dubious of my skills (and rightly so) but I went anyway, knowing I'd better prove myself. We paddled five rivers in three days, most at a higher level of difficulty than I'd run before. But I could not have picked a better trip leader for new challenges. It was a skill-testing weekend that I will never forget; my life had somehow reached another plane. For more years than I can count, Tom's Smokehole Canyon trip on Easter weekends was a regular feature on the paddling club calendars. He also led an annual canoe camper in eastern NC/VA the week before Thanksgiving. Tom was an expert in finding interesting rivers to run, planning trips, organizing groups, and being alert to hazards of exploring new rivers. I always trusted his judgment. I recall a time when a whitewater river in WV was rising and a couple of

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kayakers were keen to have the group put on despite raging waters. I was worried, as no one was saying anything. Tom quietly let them go on for a time and then steered the discussion toward an upper section that was now runnable due to the excess flow. He handled it beautifully and it all worked out. Tom also displayed gorgeous wooden canoes that he painstakingly restored. (By the way, Tom was always partial to open canoes and never much of a fan of plastic kayaks - he called them 'salad spinners.'). I am very grateful for having had the chance to know and paddle with Tom during the past twenty years, including quite a bit in the months before he died. The paddling community has truly lost a legend."

Another of McCloud's unique skills was pig roasts. Predictably, he fashioned his own grill and trailer and hauled it to many a research group picnic, roasting a whole pig Carolina style, which all present would devour with gusto. For many years, he roasted a pig for the Coastal Canoeists' annual fall meeting in Shenandoah, VA. Martha James of the Coastal Canoeists, when apprised of his passing, said, "Tom was the one who always roasted the pig for our annual fall gathering on the Shenandoah River. This year our trip was the weekend after Tom passed. When we stopped for lunch, we all raised a bottle of water in his honor and, from now on, that trip will be known as the Tom McCloud Pig Paddle."

McCloud also participated in backpacking and camping trips associated with the ASP Taxol Historical Marker project in Washington State near Mt. Rainier, and helped in site selection and plaque design for the historical marker along

with Drs. John Beutler, Jim McAlpine, and Nick Oberlies. Dr. John Beutler reflected, "Tom was a highly valued colleague of mine from the time he came to NCI until his retirement, a span of 23 years. We worked for a while in the same building, and he immediately started to build a group and develop the NCI extraction protocols, even before his extraction lab was renovated. We were friends, colleagues, allies, and co-conspirators in re-isolation projects, dereplication, biological testing, and mutual survival within the bureaucracy. I particularly cherish the taxol historical marker project, because it was an opportunity to combine our mutual love of the outdoors and science."

McCloud managed the NPSG from his first to his last day with one eye on meeting objectives and timelines, and the other on the diverse group of individuals who worked with him over the years. The team consisted of people with PhD, masters, bachelors, and associate degrees, and on to youngsters just out of high school looking for a good job. In his own unique style, he nurtured and encouraged them all, expanding their work scope to include more responsibility and training, urging them to further their formal education, and tailoring future work assignments to fit special skills and interests.

McCloud and members of his group were frequent presenters of posters at ASP meetings for nearly three decades. Those of us who worked with him as collaborators quickly realized the intrinsic value of his perspective; he very often provided well-founded alternative approaches to a problem, most of which proved successful and clearly superior to the original plan or proposal. Dr. Suzanne Shipley remembered, "Eighteen years ago, I was interviewed by this rather 'rough around the edges,' mad scientist-looking man named Tom McCloud. He took a chance and hired me to run his fungal lab. Little did I know how this would shape my career, as he taught me to be a better scientist and gave me so many chances to advance. In the lab, he provided guidance and ideas, but also showed me the importance of learning from mistakes and failed experiments. Tom was always ready to help. He would come up with brilliant (and sometimes bizarre) solutions to problems. One day he'd help me run a 50-liter fermenter, and the next day show me how to refinish my kitchen cabinets. After his retirement, we remained good friends. Tom has passed away, and the world has lost an amazing chemist...and I lost an amazing friend and mentor. Rest in peace, friend." ■



Tom McCloud imagined in the 1992 movie poster *Medicine Man*, based on the pursuit of cancer treatments in the Amazonian jungle.

In Memoriam: Walter H. Lewis

By Edward J. Kennelly, PhD

Professor Walter H. Lewis, 90, died on November 17, 2020 due to complications from Alzheimer's disease. Lewis was a world-renowned botanist, noted for the breadth of his research that included the taxonomy of North American roses and the ethnobotany of native peoples of Peru. He is well known for his seminal book, *Medical Botany, Plants Affecting Man's Health*, that he cowrote with his wife of 63 years, Dr. Memory Elvin-Lewis. ASP members warmly recall his pleasant demeanor, amazing tales of botanical adventures, and unfailing personal and professional partnership with his wife.

ASP President Dr. Nick Oberlies commented, "Walter Lewis was a renowned botanist specializing in ethnobotany, a discipline that lays the foundation for many studies conducted in pharmacognosy and natural products. He was known to many ASP members for his classic book on medicinal plants and as a leader of one of the NIH-sponsored International Cooperative Biodiversity Groups projects in Peru. ASP conveys its deepest condolences to his family and friends."

Lewis began his career as a classically trained plant taxonomist, receiving his doctorate in biology at University of Virginia, where he conducted a revision of the genus *Rosa* under Professor Walter Flory. He received the Horsley Research Award from the Virginia Academy of Sciences for his dissertation work in 1957. Late in his career, he returned to his original love for the genus *Rosa*, published several papers on American roses, and was elected "Great Rosarian of the World" in 2013 by GROW, affiliated with the American Rose Society.

After postdocs as a Guggenheim Fellow at the Royal Botanic Gardens, Kew and the Royal Swedish Academy of Sciences, and as a faculty member in biology at Stephen F. Austin State University, he joined Washington University in St. Louis in 1964 where he spent the remainder of his academic career.

His concurrent appointment at the Missouri Botanical Garden as director of the Herbarium (1964-1972) and senior



Walter and Memory Lewis in 2013 at the Hispanic Museum and Library in New York City when he was elected the "Great Rosarian of the World."

PHOTO: DR. EDWARD KENNELLY

botanist led him to projects on neotropical plants, especially in his role as editor of the *Flora of Panama* (1965-1970). His research interests in medical plants and ethnobotany began in the 1970s with work in collaboration with his wife on plants for dental health in Ghana. This resulted in the 1976 publication of their well-regarded book on medical botany, and the second edition followed in 2002.

At Washington University Lewis was held in esteem as an outstanding teacher and scholar with over 320 publications. From his 1976 book, he developed an undergraduate course entitled "Medical Botany," that was extremely popular with Washington University students. Former students vividly recall his stories of Amazonian adventures, and at the end of the semester unexpectedly arriving for lecture dressed in traditional Jivaro clothing toting a dart gun. In 1996 he was given the Interfraternity Council Teaching Excellence Award at Washington University.

Lewis was very active in the Society for Economic Botany; he served as president and was named the society's Dis-

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He was known to many ASP members for his classic book on medicinal plants and as a leader of one of the NIH-sponsored International Cooperative Biodiversity Groups projects in Peru.

In Memoriam: **Walter H. Lewis**

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tinguished Economic Botanist in 2006, along with his wife. ASP Fellow and Editor Emeritus of the *Journal of Natural Products*, Dr. Douglas Kinghorn, remembered Lewis fondly from that period, “I was very saddened to learn of the passing of Walter Lewis, who was a truly outstanding economic botanist. He served as president of the Society for Economic Botany in 1990-1991. I became president myself the following year, and Walter was extremely helpful to me on numerous occasions and provided always excellent advice throughout my term of office. Also, Walter and his wife Memory introduced me to Edward Kennelly, a graduate student at Washington University in St. Louis with an interest in phytochemistry. Ed later became an outstanding postdoctoral fellow in my laboratory, then at the University of Illinois at Chicago, during the period 1993-1996. As a person, Walter was unfailingly courteous and an extremely polished individual. He will be very greatly missed; I send my deepest condolences to Memory.”

Lewis was the principle investigator on an International Cooperative Biodiversity Group (ICBG) project regarding plants used in Andean tropical rainforests of Peru. He, as well as other ICBG PIs, spoke at the ASP annual meeting in Orlando, Florida in 1998; his talk was entitled “Plant Prospecting in Peru Based on the Aguaruna Jivaro Pharmacopeia (ICBG-Peru).” The ICBG program is coordinated by the NIH Fogarty International Center and jointly sponsored by several NIH institutes, including the National Cancer Institute, as well as the National Science Foundation and, in the initial stages, was also supported by the US Agency for International Development. The program is aimed at the discovery of novel bioactive molecules from nature while promoting sustainable biodiversity conservation, and involves the assembly of international research consortia composed of at least one US academic research institution and at least one non-US host organization based in a biodiversity-rich, low- or middle-income nation. Lewis’ ICBG project with Aguaruna peoples was a collaboration with the Universidad San Marcos, the Universidad Peruana

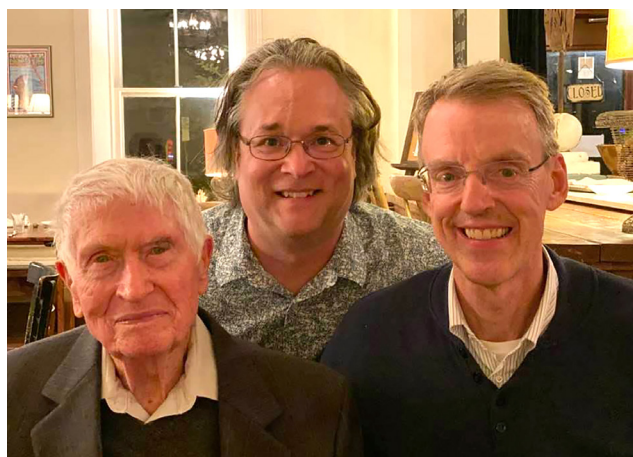
Cayetano-Heredia, and Monsanto-Searle Co., but ran into challenges over informed consent.

Dr. Steven J. Casper, Lewis’s last doctoral student, began in 1997 and conducted his dissertation research as part of the ICBG project. “Dr. Lewis was recommended to me by Dr. Richard Evans Schultes who said that I could find all aspects of my interests in his lab. Although Dr. Lewis was nearing the time of not accepting new graduate students, he was enthusiastic to welcome me to the lab. This enthusiasm was evident in everything that he did, especially when engaging with students. His medical botany class was extremely popular, and the students were fascinated by the course and Dr. Lewis’s amazing stories of his travels and research. He was always willing to talk with, help, and guide students. He was one of the rare gentleman scholars and is greatly missed.”

ASP Fellow Dr. David Kingston, who led an ICBG project in Madagascar, wrote, “Walter Lewis was a towering figure in the ethnomedicine area and had an enormous impact on the field. He was the recipient of one of the first International Cooperative Biodiversity Group awards for research on the ethnomedicines of Peru and put together an exemplary benefit-sharing agreement for this work.”

ASP Fellow Dr. Gordon Cragg also got to know Lewis in the early 1990s through the ICBG Program. He commented, “Walter Lewis assembled a distinguished group of multidisciplinary and international scientists, including Drs. Abraham Vaisberg (Universidad Peruana Cayetano Heredia) and Gerardo Lamas (Universidad Nacional Mayor de San Marcos), with the goal of conducting an ethnobotanical study of plants used by the Aguaruna people of the Peruvian Amazon forest. The ethnobotanical focus of his project led to the negotiation of pioneering legal agreements with the Aguaruna communities, which are regarded as models for collaborative drug discovery programs involving indigenous peoples.¹ Almost 4000 plant species were collected, including a large number prescreened for human use by the Aguaruna themselves, and it is significant that these provided higher

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Lewis with his former doctoral students Steve Casper and Ed Kennelly in Guelph, Canada, 2019.

PHOTO COURTESY: DR. EDWARD KENNELLY

In Memoriam: Walter H. Lewis

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frequencies of bioactive secondary metabolites than those found in the flora as a whole. Since the cessation of Walter's ICBG grant support in the early 2000s, this invaluable plant collection has continued to be studied by most of the original team members, and has been the source of a range of potential new anticancer, anti-infective, and wound-healing agents.²

I was a doctoral student with Walter Lewis from 1987-1993, and it was a great pleasure working with him and Memory. I remember when I started my studies, he immediately invited me to join him on a month-long National Geographic-sponsored field trip to Ecuador in the summer of 1988 to study the ethnobotany of the Achuar people. I was thrilled, and never imagined traveling to such a remote area for research. Memories from that trip to the Amazonian headwaters include helicopter rides to isolated villages with an old German pilot, Walter drinking a ceremonial fermented beverage with the village leaders, and being locked down in a small village until our interpreter could get the proper government permissions. From lab work, in collaboration with his wife and Dr. Rudolph Winter (University of Missouri, St. Louis), to field work, it was a wonderful experience for me to learn so much from him.

I also felt like part of his extended family and remember frequently going to his beautiful home near the university where he had extensive gardens, and most importantly, especially during the hot and humid St. Louis summers,



Lewis, sporting a cap given by his daughter Memoria, on a trip to Guelph over Canadian Thanksgiving, 2019.

PHOTO: DR. EDWARD KENNELLY

a magnificent swimming pool. I enjoyed spending time in this little paradise with other students, like Oliver Phillips, Dennis Milanowski, Bin Moy, and Kate Johnson. House-sitting for the Lewises was a plum gig, and I felt fortunate to do this on several occasions. Walter was charming and a wonderful boss, but he also had high standards that we knew to take them seriously. He did not suffer fools.

My last meeting with Walter was traveling to Guelph, Ontario over Canadian Thanksgiving in 2019 to celebrate his wife being recognized as a leading woman Canadian scientist. Although his mind was clearly impacted by the onset of Alzheimer's disease, he was a perfect gentleman and outgoing and polite to everyone he met. Memory later commented to me that she thought his greatest accomplishment was being able to work in botany until he was 87 years

old, having to stop only because of Alzheimer's disease.

Lewis is survived by his wife, Memory Elvin-Lewis, and his children Memoria and Walter Jr. He will be greatly missed. His work on medicinal plants and ethnobotany, and botany in general, are his great legacy. In a satirical video tribute to their father in 2011, his children fondly remember their father's enthusiasm for all things botanical, even on family vacations when they were young. That same enthusiasm was evident to the end of his life as he would show visitors his wild rose collection in his home garden. The family is planning a celebration of his life in June 2021, when the wild roses in his garden will be in full bloom. ■

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ASP's New Fellows

**Their role is to help advance natural product sciences
by advising on science and professional matters within the ASP.**

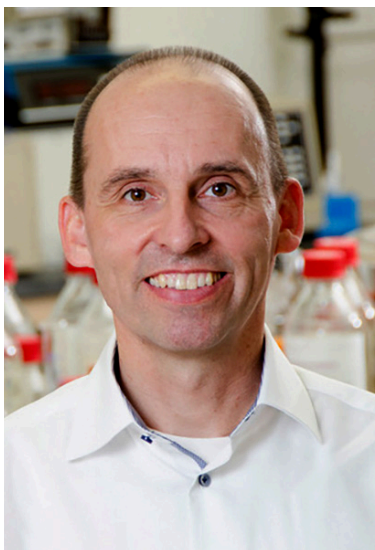
By Vanessa Nepomuceno, PhD

The ASP would like to congratulate and celebrate the addition of three new ASP Fellows: Drs. Guido Pauli, Cindy Angerhofer, and Tadeusz Molinski. In the field of pharmacognosy, selection as an ASP Fellow is one of the highest honors that the ASP can bestow upon a research scientist. Distinguished by their continued achievements and contributions to the field, the Fellows serve as global advocates for the society. Candidates for Fellowship are nominated and elected by the existing Fellows and are ratified by the Executive Committee. Their role is to help advance natural product sciences by advising on science and professional matters within the ASP. Herein, as an annual tradition, the ASP recognizes and commemorates the incoming Fellows.

GUIDO F. PAULI

Dr. Guido Pauli is the Norman R. Farnsworth Professor of Pharmacognosy in the Department of Pharmaceutical Sciences at the University of Illinois at Chicago. Dr. Pauli is also the associate director of the Institute for Tuberculosis Research and director of the Program for Collaborative Research in the Pharmaceutical Sciences. In July 2019, he was appointed as a distinguished professor. Dr. Pauli's research focuses on metabolomic analysis of natural health products, botanicals, and anti-tuberculosis drug lead discovery. Dr. Pauli seeks to address challenges posed by the metabolomic variation in nature and enhance the understanding of natural products as health products and sources of new drugs. His publication record consists of over 180 peer-reviewed journal articles. Dr. Pauli has mentored and trained 18 PhD students, 20 postdoctoral researchers, and several visiting professors and scientists.

Dr. Pauli has established himself as an expert in the



Guido F. Pauli PHOTO: JOSHUA CLARK, UIC

expansion and innovation of analytical approaches. ASP Fellow Chair Dr. Gordon Cragg notes that Dr. Pauli "is internationally recognized for his research in advancing the development of high-resolution countercurrent separation and partition chromatography, and his pioneering research in the development of quantitative NMR and its application to natural product analysis." In 2018, Dr. Pauli was awarded the Varro E. Tyler Prize in recognition of his contributions to the metabolomic analysis of natural health botanical products. The award winner commented: "Being elected as an ASP Fellow is very humbling – and a great motivation to help foster high-quality science within the ASP community in the future. The ASP Fellow role allows me to share my excitement for natural products research in new ways and such that coming generations of pharmacognosists can hopefully benefit from the many innovative opportunities in our field."

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**Dr. Pauli seeks to address challenges posed by the metabolomic
variation in nature and enhance the understanding of natural products
as health products and sources of new drugs.**

ASP's New Fellows

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CINDY ANGERHOFFER

Dr. Cindy Angerhofer serves as the executive director of botanical research at Aveda. Dr. Angerhofer's research focuses on exploring the chemistry and biology of botanical ingredients to produce plant-based personal care products. In particular, her work emphasizes phytochemical analysis, bioassays, and sustainable sourcing. Dr. Angerhofer earned her PhD in Pharmacognosy from the University of Minnesota. As an assistant professor, she taught medicinal and biological chemistry of natural substances at the University of Illinois at Chicago. Dr. Angerhofer directed research and product development for Tom's of Maine, Inc. for five years before joining Aveda in 2003. In addition, she is a former president of the ASP (2016-2017), and on the advisory board for the American Botanical Council. She has authored more than 45 peer-reviewed publications.

From her early work in academia to Aveda, Dr. Angerhofer exhibits a wide range of research topics and career successes. Dr. Cragg comments that Dr. Angerhofer "has over 25 years of experience in the development of plant-based personal care products. In 2015, she was awarded the Varro E. Tyler Prize in recognition of her scientific contributions to the field of botanical healthcare products." Dr. Angerhofer tells the *ASP Newsletter* that she is "honored and humbled to be invited to join this esteemed group of scientists, many whom have been mentors to me over the years. I look forward to participating in the Fellows community, continuing to advocate for ASP and natural products research."



Above: Cindy Angerhofer

Below: Tadeusz Ted Molinski



Tadeusz Molinski PHOTO: JANUSZ MOLINSKI

TADEUSZ TED MOLINSKI

Dr. Tadeusz Molinski is a professor of chemistry and biochemistry at the Skaggs School of Pharmacy and Pharmaceutical Sciences and of the Center of Marine Biotechnology and Biomedicine at the Scripps Institution of Oceanography. His primary research interest is the investigation of the structure, synthesis and biological properties of marine natural products. Dr. Molinski utilizes various analytical techniques for the chemical investigation of minute quantities of natural products, termed "nanomole scale." Dr. Molinski and his team advanced the development and use of new chiroptical methods for defining the structure and absolute configuration of challenging compounds. In addition, he has also been active in synthetic chemistry efforts.

Dr. Molinski's research demonstrates his mastery of natural products, analytical chemistry methods and synthetic organic chemistry. According to ASP Fellow Chair Dr. Cragg, Dr. Molinski received the prestigious Ernest Guenther Award for the Chemistry of Natural Products from the American Chemical Society and is the first active UC San Diego academic awardee. Additionally, he served as ASP president from 2009-10. Dr. Molinski tells the ASP, "I was surprised and deeply honor to hear from Gordon and Jon, earlier this year, that I'd been named an ASP Fellow. I've been a member for 31 years and like to think of myself as 'active' in ASP's affairs, including former president of the ASP. I was most proud to have organized ASP's 2003 Symposium in honor of the late D. John Faulkner, who passed away before he could accept the Norman Farnsworth Award, and to have helped establish and support the ASP D. John Faulkner Award." ■

The ASP bestows its warmest congratulations to the three new ASP Fellows, along with many thanks for their past and continuing efforts in supporting many ASP initiatives. We look forward to their future contributions as Fellows.

The Case for Development of Natural Product Drugs: Back to the Future?

By James D. McChesney, PhD

INTRODUCTION

Chemicals derived from natural product preparations, especially higher plants, have played a central role in the history of humankind. The utilization of plant-derived starches, fats, and proteins as a major source of food materials cannot be contested. Similarly, the importance of fibers derived from plants for the preparation of clothing and building materials is well recognized. The Age of Discovery, which brought Western civilization out of the so-called “dark

Until the early 1900s plant-derived pharmaceuticals, primarily as preparations of mixtures derived directly from plant material, represented the major source of pharmaceuticals throughout the world.

ages,” was stimulated by the desire to discover cost-efficient sea routes to Asia for the procurement of plant-derived substances: spices, fragrant oils, etc. The fortuitous discovery of the Americas as a consequence of the effort to find a shorter and more direct sea route to Asia brought about a rapid expansion of Western civilization and, more importantly, the opportunity for the expansion of world economies by the exploitation of the huge resources of the undeveloped western hemisphere. The significance of these events is self-evident. The importance of plant-derived chemicals as the underlying stimulus to cause these events may not be as widely recognized.

Plants for millennia have provided the major source of the medicinal compounds used to treat our illnesses. Until the early 1900s plant-derived pharmaceuticals, primarily as preparations of mixtures derived directly from plant material, represented the major source of pharmaceuticals throughout the world. Even today, according to the World Health Organization (WHO), roughly two-thirds to three-quarters of the world's population relies upon medicinal plant preparations for their primary health care needs. The recognition of the importance of active ingredients in these complex mixtures fostered the development of organic chemistry, physiology, and pharmacology as important contributors to the practice of medicine. With the isolation and characterization of the structures of select natural products, synthetic organic chemistry became an important contributor to pharmaceuticals, and a number of important pharmaceuticals modeled upon natural products be-

gan to be developed. The development of aspirin based upon the salicylic acid of willow bark is a classic example. Testing of numerous chemical compounds against an important parasitic disease and observation of efficacy led Paul Ehrlich to postulate “the magic bullet” concept in the early twentieth century (Schwartz, 2004; Strebhardt and Ullrich, 2008).

In the 1930s, the observation that microorganisms produced substances which inhibited the growth and development of other microorganisms triggered the “Age of Antibiotics” and their use in medicine (Aminov, 2010). These naturally occurring substances had a profound impact upon humankind through the adequate treatment of infectious diseases, formerly a major cause of early mortality in humans. Consequently, significant increases in life span have occurred over the last 100 years. The efficacy and safety of these newly discovered medications further solidified our belief in the magic bullet paradigm (Bosch and Rosich, 2008). The utilization of microorganism fermentation to produce natural products for application in medicine and the growing sophistication of synthetic organic chemistry largely displaced interest in plant-derived substances as pharmaceuticals in the 1940s through the 1980s. Then the recognition that marine environments represent more than 70% of the earth's surface has led to an explosive expansion

The recognition of the importance of active ingredients in these complex mixtures fostered the development of organic chemistry, physiology, and pharmacology as important contributors to the practice of medicine.

of examination of marine organisms as sources of new biologically natural products which continues as a focus till today.

Importantly, the ease of standardization of single chemical entities into dosage forms, thereby allowing predictable outcomes of dosing, further supported the move to such pharmaceutical preparations. Even so, the importance of naturally derived substances for drug discovery and development was still strongly evidenced by the analysis published by Newman and Cragg in 2012.

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The Case for Development of Natural Product Drugs: Back to the Future?

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Interest in the study of natural products was relegated to the academic community. However, the National Cancer Institute of the United States retained a core program of research on natural products for the discovery and development of anti-cancer pharmaceuticals. The discovery and development of Taxol (paclitaxel) in the decades of 1960s-1990s, as the most successful anti-cancer agent ever, caused a momentary resurgence of interest in natural products for drug discovery (Wani and Horwitz, 2014). This interest has once more been replaced by a focus on new approaches to drug discovery, such as combinational chemistry and computer-based molecular modeling coupled to high-throughput screening of biomolecu-

This interest has once more been replaced by a focus on new approaches to drug discovery, such as combinational chemistry and computer-based molecular modeling coupled to high-throughput screening of biomolecular models (receptors, enzymes, etc.) and most recently by our increased understanding of molecular genetics and immunology.

lar models (receptors, enzymes, etc.) and most recently by our increased understanding of molecular genetics and immunology. The importance of natural products within the pharmaceutical industry has waned significantly over the decades from the discovery of antibiotics and has practically disappeared today.

The emergence of resistance to single chemical entity agent materials, whether a pharmaceutical (antibiotic-resistant infections, drug-resistant malaria, drug-resistant tuberculosis, numerous others), insecticide (insecticide-resistant mosquitoes and crop pests), or herbicide (herbicide-resistant weeds in our crops), has or is bringing the magic bullet paradigm into question (Ventola, 2015). There is an urgent need to identify novel active leads for the development of a new strategy to overcome the emergence of resistance. As was dramatically illustrated by the discovery of the “wonder” antibiotics of the 1940s and 1950s and the anticancer agent paclitaxel and others in the 1950s through the 1970s, nature is the prime source of such unique, novel lead discoveries. As emphasized by the late Dr. Norman Farnsworth, a leading world-renowned natural product researcher, “The World of Plants, and indeed all-natural sources, represents a virtually untapped reservoir of novel drugs awaiting imaginative progressive companies.”

The role of natural products in the discovery of prototype pharmaceuticals arises from the observation that organisms

interact with their environment by chemical means. Plants protect themselves; they attract pollinators, etc. by means of chemical substances. Soil microorganisms carve out their niche by secreting inhibitory substances to suppress the growth of competing microorganisms. Similarly marine organisms protect themselves from predation with toxic substances. Those interactions are very effective. Since plants are rooted in place, they have evolved mechanisms to protect themselves by producing chemical defense substances. The function of these chemicals is to enhance the competitiveness of the plant in its environment, making it more successful, in turn creating the opportunity for it to propagate offspring. Because there are hundreds of thousands or even millions of species all producing large numbers of discrete chemical defense substances and chemical signaling for mutual cooperativity among neighboring organisms, thus there are literally millions of chemical structure types to select from for evaluation for pharmaceutical application. It may also be argued that these substances represent “nature’s combinational chemicals” and that they have the advantage of already having been screened evolutionarily for pharmacological utility. The following three compounds are recent important examples of plant-derived natural products which have defined new pharmaceuticals.

Paclitaxel, a diterpene isolated from the stem bark of the western yew, *Taxus brevifolia*, is the most significant anticancer agent developed in the last several decades. It is unique among currently available antitumor agents in that it enhances tubulin polymerization, acting via that mechanism as a mitotic poison. **Topotecan**, a more recently approved anticancer agent, is a derivative of the natural product camptothecin, an alkaloid isolated from *Camptotheca accuminata*. It also has a unique mechanism of action, functioning as an inhibitor of topoisomerase I.

There is an urgent need to identify novel active leads for the development of a new strategy to overcome the emergence of resistance.

Drug-resistant strains of malaria claim hundreds of thousands of lives worldwide each year. Significant effort continues for the development of new, safer agents effective against drug-resistant malaria. For this, researchers have turned once again to a plant-derived natural product. For centuries, extracts of the plant known as qinghao (*Artemisia annua*) were used in traditional Chinese medicine for the treatment of malaria, including cerebral malaria. Chinese investigators reported the isolation and identification of the active constituent of qinghao as the unusual sesquiterpene endoperoxide, artemisinin. Semi-

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The Case for Development of Natural Product Drugs: Back to the Future?

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synthetic derivatives of artemisinin have now been approved in several countries and represent current drugs of choice for treatment of chloroquine-resistant malaria.

As might be expected, we are seeing the development of resistance to these crucial agents. An important element of the development of resistance is the reliance on single chemical entity agents. Nature is communicating a strong message to us when we examine the composition of natural product preparations. These are mixtures of many compounds, often closely related to what we perceive as the “active principal.” The accepted role of these natural products as protective from pathogens and consumers/predators and the lack of resistance development by the target organisms should clue us that mixtures make an important contribution to prevent resistance development.

Numerous observations supporting the role of mixtures to suppress or prevent the development of resistance have been published. As long ago as 1976, Pimentel and Bellotti published a study reporting prevention of resistance development to a mixture of toxic chemicals to house flies raised in a culture (see Figure 1 above).

More recently, Zhao et al. published the observation that incorporating more than a single form of *B. thuringiensis* toxin into the genome of a crop plant suppressed resistance development (see Figure 2, right).

Evaluation of a natural product insecticide, azadirachtin, as a single agent versus an extract of its source material with an equal concentration of “active” similarly showed the extract mixture suppressed resistance development (see Figure 3, page 33).

The discovery and development of artemisinin for treatment of chloroquine-resistant malaria was heralded as a breakthrough, and the discoverer was awarded the 2015 Nobel in Medicine. However, broad scale use of artemisinin has led to the emergence of resistance even when the WHO has recommended combination with other antimalarials. Recently the laboratory of Dr. Pamela Weathers has published work demonstrating the efficacy of an intact *Artemisia* leaf preparation to cure patients who had failed two courses of standard artemisinin therapy with the recommended WHO combination drugs (Daddy

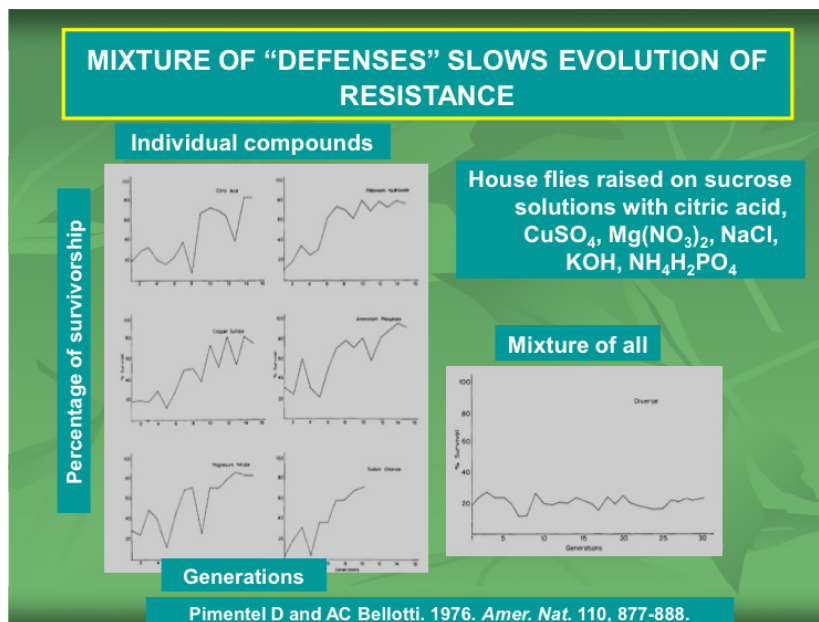


FIGURE 1.
(Pimentel and Bellotti, 1976)

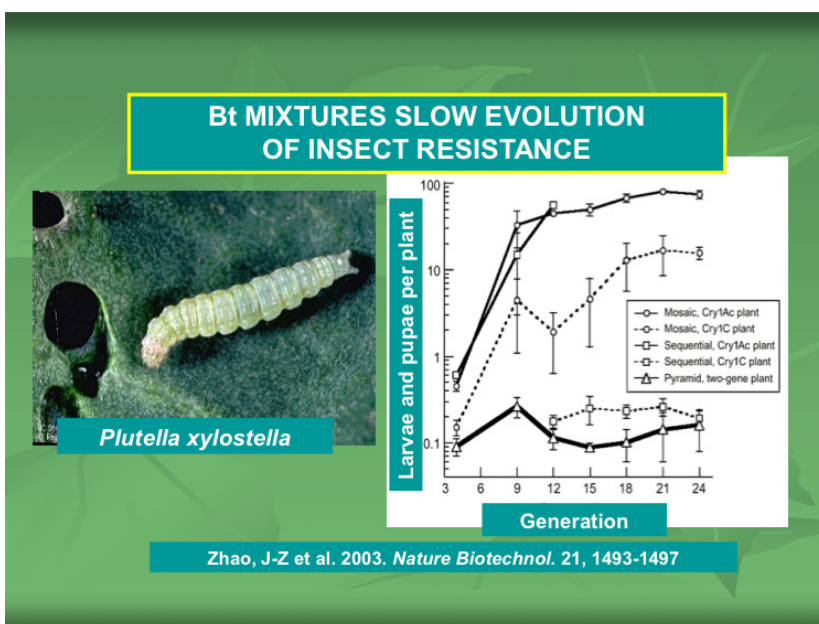


FIGURE 2.
(Zhao et al., 2003)

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The Case for Development of Natural Product Drugs: Back to the Future?

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et al., 2017; Desrosiers and Weathers, 2018; Munyangi et al., 2019).

In a recent series of publications, Chinese researchers have been comparing pharmacokinetic outcomes between single-isolated active-principal preparations; and traditionally utilized whole-plant extracts, containing the active principal in equivalent concentration, are orally administered to laboratory animals, rodents (Zhang et al., 2016). They demonstrated a consistently higher bioavailability, and interestingly when examining the organ tissue distribution of paclitaxel, a potent cancer chemotherapeutic agent, they found that the extract not only significantly increased oral bioavailability, as much as 10-fold, but also increased the distribution of paclitaxel to all organs examined (Zhang et al., 2016). In the case of cytotoxic chemotherapeutic agents, greater systemic distribution, either from greater bioavailability (blood level) or suppression of tissue protective efflux mechanisms (ABC transporters), potentially could lead to greater efficacy but also raise the risk of greater side effect toxicities, a major limiting factor of cancer chemotherapy.

How can/might the mixture of compounds present in the intact leaf material or whole plant extract influence the efficacy of the preparation? There are numerous possibilities: compounds present may add to or synergize the activity of the “active principal”; those compounds may enhance absorption, distribution, or modify the metabolism of the active principal; or those compounds may serve to suppress resistant mechanisms of the infectious agent or those of undesired/unwanted species. There may well be additional mechanisms of enhancing efficacy as yet unidentified. This observed enhancement of efficacy has been dubbed “the entourage” effect.

The public interest in plant-based preparations (botanical drugs, even botanicals popular as dietary supplements (“nutraceuticals”) and the movement to legalize marijuana (medical marijuana) sweeping the country) strongly supports that we revisit the development of plant-based drug preparations.

BOTANICALS: A “NEW” CLASS OF DRUGS

The guidance provided by the FDA defines botanical drugs as a product that contains as ingredients vegetable materials, which may include plant materials, algae, macroscopic fungi, or combinations thereof, that is *used as a drug*. It may be available/formulated as (but not limited to) a solution (tea,

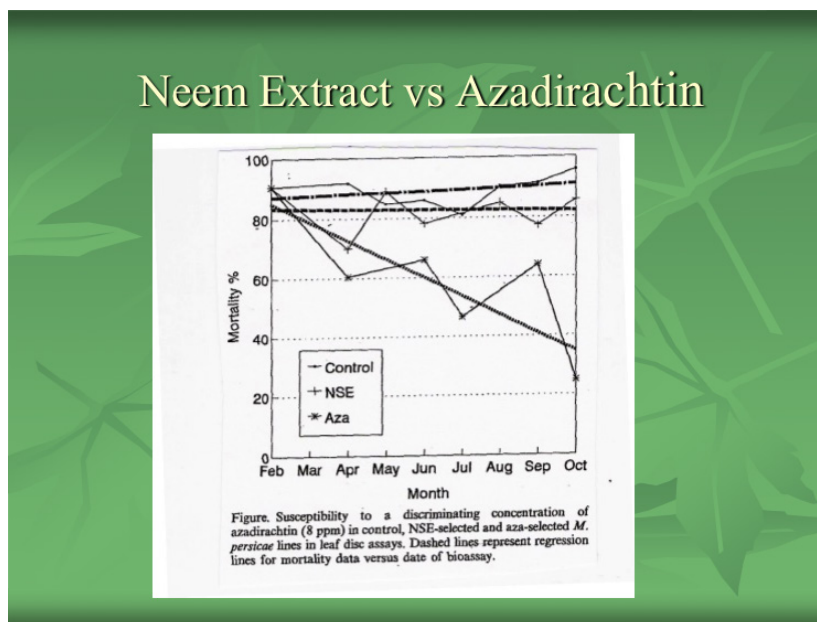


FIGURE 3.
(Feng and Isman, 1995)

e.g.), powder, tablet, capsule, elixir, topical, or injectable. Specifically excluded are fermentation products, highly purified (or chemically modified) botanical substances, genetically modified plants, allergenic extracts, and vaccines which contain botanical ingredients. A detailed discussion of botanical drug development may be found in a recent publication (McChesney et al., 2019)

DISCUSSION AND CONCLUSIONS

Complex botanical derived products, including those used in or marketed as traditional medicines, could still be viable candidates for botanical drug development. FDA's approvals of Veregen and Fulyzaq set up good examples from which to learn. Challenging CMC issues may be adequately addressed by controlling the source and quality of the botanical raw materials, fixed manufacturing processes, extensive chemical analyses, as well as biological assays to ensure batch-to-batch consistency.

Synergism, as the examples demonstrated in the earlier parts of this paper, could be an important indicator for selecting botanical drug candidates. Multiple molecules from one botanical extract or combinations of multiple herbs, should they possess additive or synergistic effects, may be further developed with better potential as new drugs. ■

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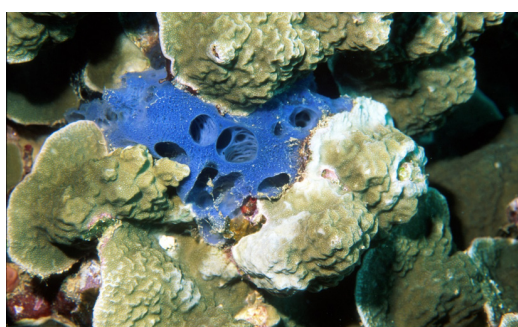
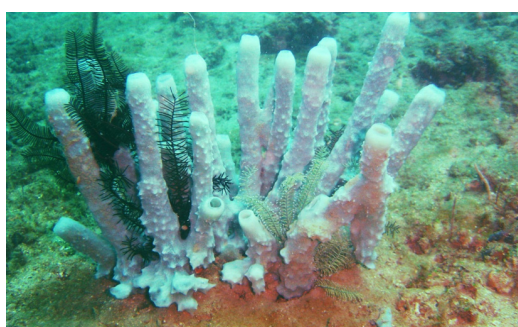
O'Keefe Interviewed for BBC Documentary

By Mario Figueroa, PhD

On September 2020, the BBC released *Extinction: The Facts*, a documentary about the sixth mass extinction. It is narrated by Sir David Attenborough, a natural historian known for his work in BBC's *Life* series. The 58-minute film shows the effects of biodiversity loss and climate change. Attenborough, together with renowned scientists from different fields, provides a series of shocking facts that make this documentary a compulsory watch for all.

ASP Past President Dr. Barry O'Keefe is among the panel of experts that were invited to participate in the BBC project based on his current role as head of the NCI Natural Products Repository, which was originally built by ASP members Drs. Gordon M. Cragg, David J. Newman, and the late Mr. Thomas McCloud. O'Keefe was interviewed for a web-exclusive clip that highlights the importance of natural products research. He elaborates on the current use of natural products as life-saving drugs and explains that losing plants results in the loss of molecules that could be useful in the future of medicine. Reflect-

Above top: O'Keefe being interviewed by the BBC, along with photos of marine organisms and extracts used in building the NCI Natural Product Repository.



ing on his experience with the BBC, Prof. O'Keefe states, "It is important that we pharmacognocists help legitimate documentarians such as the BBC explain the key role of biodiversity to drug discovery as this aids in the public awareness of both the importance of biodiversity and the contributions of natural products research."

Although he does not particularly enjoy being interviewed, O'Keefe feels honored to have had the opportunity to work with the BBC and contribute. He also wants to remind fellow ASP members of the importance of engaging in public outreach efforts. "Both at the local level and in the broader community it is important to highlight the contribution of pharmacognosy, biodiversity and natural products research to the well-being of both human beings and the planet. Breaking down the barriers between the scientific enterprise and the broader public is increasingly vital for everyone... It is really part of every ASP member's job to help us all bridge the divide between the scientific and lay community."

The *Plants and Medicine* clip from *Extinction: The Facts* can be viewed as below: ...■

www.bbc.co.uk/programmes/p08qykq/player

"Both at the local level and in the broader community it is important to highlight the contribution of pharmacognosy, biodiversity and natural products research to the well-being of both human beings and the planet."

2021 ASP Annual Meeting: A Grand Natural Products Adventure

By Arun Rajgopal, PhD and Melany Puglisi-Weening, PhD

Join your ASP colleagues and come make new ones at a Grand Natural Products Adventure, the annual meeting of the ASP, scheduled for **July 24-28, 2021** in Grand Rapids, MI. Participate in one or all of the Saturday workshops, listen to exemplary plenary speakers, and hear cutting edge research on topics including marine pharmacology and fresh water natural products, botanical authenticity and integrity, natural product biosynthesis, natural product options for health and wellness, and traditional medicine applications, just to name a few. Additional details about specific topics and conference events will be shared in future newsletters.

We also invite you to learn more about Grand Rapids, aka Beer City USA! Grand Rapids is home to numerous breweries and distilleries, and many of these crafters sell their products regionally and throughout the US. One such brewer is Founders Brewing Company, who boldly states, "We don't brew beer for the masses." Founders, founded in



1997, is one of the largest craft breweries (Top 10) in the US. Emerging from the brink of bankruptcy, Founders has evolved and delivers unique beers such as KBS Bourbon Barrel-Aged Chocolate Coffee Stout, Red's Rye IPA, All Day IPA, Centennial IPA, Solid Gold, and Breakfast Stout. Check online at <https://foundersbrewing.com/> to find out more about Founders and where their beer is sold at a location near you. Cheers!

Another gem, located very close to Grand Rapids, is the Lake Michigan shoreline. Michigan contains the most freshwater coastline of any other state and, together with its sister lakes of Superior, Huron, Erie and Ontario, makes up the world's largest freshwater system. Water temperatures in Lake Michigan can reach 70°F+ in the late summer months, so it is swimmable and shark free! Lake Michigan has a remarkable fishery, including king salmon and lake trout, is bordered by succession forests teeming with diverse wildlife and has ample beaches for taking in the sun, sand and water!

SPEAKER SPOTLIGHT

Digging dirt's potential!

As professor and head of the Laboratory of Genetically Encoded Small Molecules at Rockefeller University, **Sean F. Brady, PhD** and his team work to discover new natural products from microbial sources, including uncultured soil bacteria. Using diverse methods, the Brady lab isolates DNA directly from the soil to generate environmental DNA libraries. These libraries have the potential to yield new bioactive natural products that could also have therapeutic benefits. Additionally, Professor Brady researches the interactions of commensal and pathogenic bacteria with their human



SEAN F. BRADY

hosts to potentially address issues pertaining to drug resistance. After receiving his PhD in organic chemistry from Cornell University, Dr. Brady was a fellow at Harvard Medical School and scientist at Howard Hughes Medical Institute. At Rockefeller University, Dr. Brady is also an Evnin Professor and Tri-Institutional Professor. His awards include the Beckman Young Investigator Award, the Irma T. Hirschl/Monique Weill-Caulier Trust Research Award, and the Kenneth Rainin Foundation Innovator Award. Dr. Brady will also be an ASP 2021 plenary speaker. ■

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SPEAKER SPOTLIGHT

An exemplary researcher and career!

As an ASP 2021 plenary speaker, **Gunda Georg, PhD** will bring a wealth of scientific knowledge and insight. Serving as the Regents professor and head of the Department of Medicinal Chemistry at the University of Minnesota, Dr. Georg and her team leverage their multiple disciplines to bring forth therapeutic interventions, including those derived from natural products for cancer, epilepsy, contraception and Alzheimer's disease. Dr. Georg's impressive career was launched after earning her PhD in medicinal chemistry from Philipps Universität in Marburg, Germany. Her postdoc experiences brought her to North America, and she has held several positions in universities throughout the United States. Currently, Dr. Georg also serves as the McK-



GUNDA GEORG

PHOTO: SCOTT STREBLE

night Presidential Chair, the Robert Vince Endowed Chair, the director of the Institute for Therapeutics Discovery & Development at UofM, and the co-editor in chief for the *Journal of Medicinal Chemistry*. Her awards and recognitions are vast and include induction into the University of Kansas Women's Hall of Fame, the Nolan and Gloria Sommer Award from the University of Nebraska, the Sato Memorial International Award of the Pharmaceutical Society of Japan, the Academy for Excellence in Health Research at UofM, Research Exemplar from Washington University, and induction into the ACS Medicinal Chemistry Hall of Fame. Dr. Georg also holds several patents, and she and her team have over 250 peer-reviewed publications. ■

SEAN F. BRADY

These libraries have the potential to yield new bioactive natural products that could also have therapeutic benefits. Additionally, Professor Brady researches the interactions of commensal and pathogenic bacteria with their human hosts to potentially address issues pertaining to drug resistance.

GUNDA GEORG

Dr. Georg and her team leverage their multiple disciplines to bring forth therapeutic interventions, including those derived from natural products for cancer, epilepsy, contraception and Alzheimer's disease.

The 2020-2025 Cycle of CARBON Centers

By Barbara C. Sorkin, PhD and D. Craig Hopp, PhD

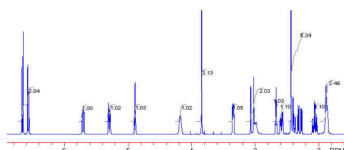
The NIH Office of Dietary Supplements, National Center for Complementary and Integrative Health, and National Institute on Aging were excited to award five new Center awards in July of 2020 to form the core of the [NIH Consortium Advancing Research on Botanicals and Other Natural Products \(CARBON\)](#) Program for the 2020-2025 cycle. The overall goal of the CARBON Program is to advance new approaches to address the longstanding challenges to research on inherently variable, chemically complex natural products.

The new CARBON awards approach these challenges from several different directions and include three different types of center, as well as a pilot project initiative (Fig. 1). The several different center approaches include efforts to fill in critical translational research data to support the design of highly informative future clinical efficacy trials of botanical dietary supplements, to advance non-targeted methods to connect specific chemical components of complex natural products to cellular mechanisms of potential health effects, and to develop a repository for natural product NMR spectral data, along with user-friendly tools for high-yield utilization of that repository.

The Center for High Content Functional Annotation of Natural Products (Hi-FAN), led by Drs. John MacMillan, Nadja Cech and Roger Linington, is developing new methodologies to answer these straightforward but vexing questions: “What’s in this complex mixture?”; “What biological activity does this material possess?”; and “What components of it are responsible for an observed activity?” They tackle these questions with a suite of novel approaches. If successful, these new tools will provide an unbiased assessment of the molecular mechanism(s) of action for a complex material through an improved ability to identify the discrete compounds present in a forest of metabolomic features, and methods to discern which features in that complex metabolomic dataset correlate with specific phenotypic effects.

The three new Botanical Dietary Supplements Research Centers (BDSRC) focus on developing translational data to inform future clinical trials of botanicals. The BDSRC, led by Dr. Ikhlas Khan and Nirmal Pugh, focuses on modulation of resilience to respiratory virus infection by *Arthrospira platensis*-
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NCCIH/ODS CARBON Program



Natural Products NMR Open Data Exchange (U24 Clinical Trial Not Allowed)



Center for Natural Product Technology, Methodology, and Productivity Optimization (U41 Clinical Trial Not Allowed)



Botanical Dietary Supplements Research Centers (U19 Clinical Trial Optional)

Figure 1 Legend:

The components of the interactive Consortium Advancing Research on Botanicals and Other Natural Products (CARBON) include the Center for High Content Functional Annotation of Natural Products (U41), the Natural Products-Magnetic Resonance Database (U24), three Botanical Dietary Supplements Research Centers (U19) titled: *Spirulina* oral supplement for enhancing host resilience to virus infection, Influence of Dietary Botanical Supplements on Biological and Behavioral Resilience (grape-derived), and Botanicals enhancing neurological and functional resilience in aging (*Centella asiatica* and *Withania somnifera*), and pilot projects to be awarded over the next several years.

The new pilot project funding opportunity is expected to broaden the base of researchers and institutions who are official participants in the program, as well as enhancing the inter-center synergies.

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sis products. A center led by Drs. Giulio Pasinetti and James Murrough is focused on the effects of grape-derived products on resilience to stress-induced psychological impairment. The third center, led by Dr. Amala Soumyanath, will focus primarily on *Centella asiatica* (gotu kola) and secondarily on *Withania somnifera* (ashwagandha) for resilience to effects of aging.

The Natural Product Nuclear Magnetic Resonance Database Center (NP-MRD) will address the need for an NMR data repository to complement well-established MS data repositories. PI Dr. John Cort and his team plan to seed the repository with computationally derived NMR spectra for all the world's known natural products. This will be augmented with vigorous efforts to encourage the research community to deposit their experimental data into the repository. A suite of accompanying tools will allow researchers to check their experimental data against the library of spectra to assess likely novelty of a com-

pound as well as its spectral and structural relationships with all other members of the repository.

Pilot projects comprise a fourth planned component of the CARBON. These will be awarded in response to [PAR 20-228](#), which has application receipt dates from June, 2021, through September, 2022. The pilot projects are each required to collaborate with one or more of the BDSRC to leverage resources such as botanical materials or unique models or methods developed in the BDSRC to achieve aims with the potential to nucleate new directions in research on the health and behavioral effects of chemically complex natural products.

The [2015 – 2020 cycle of CARBON Centers](#) was highly productive and collaborative across and within centers, and preliminary data are sparking expectations that the same will be true of the new awards. The new pilot project funding opportunity is expected to broaden the base of researchers and institutions who are official participants in the program, as well as enhancing the inter-center synergies. ■

Grow, provide materials and ensure product integrity

Provide authenticated and well characterized CA and WS derived materials for use in BENFRA as well as for CARBON collaborations



Goal:
Locally grown botanicals
(under controlled conditions)



Development of CA “indoor cultivation”
(Botanical extracts: aerial parts)



Ashwagandha
(leaves, roots)

Natasha Cerruti, Randall Buresh, Oregon's Wild Harvest, Redmond OR

Research Fellowship Opportunity

By Wendy Applequist, PhD

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

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

Please submit the following:

- a brief application letter
- an abstract of 200 words or less
- a two-page research proposal, single-spaced in 12 pt type, giving the project's background and purpose and describing activities to be conducted (proposals will be treated as confidential; proposals longer than two pages will be considered ineligible)
- a one-page budget that explains how funds would be used
- a current curriculum vitae
- for graduate students, a letter from a major advisor certifying enrollment in a PhD program
- copies of permits for fieldwork or studies including animals, research clearances, and permission from governmental agencies for foreign research (if permits are being applied for but have not yet been obtained, please ensure that the proposal explains the situation)

Proposals must be received by January 31.

Mail applications to:

Dr. Wendy Applequist
Missouri Botanical Garden
4344 Shaw Blvd.
Saint Louis, MO 63110

Proposals may also be submitted by e-mail to wendy.applequist@mobot.org.

Please inquire if you do not receive a response to electronic submissions within two business days.



THE GARDEN CLUB of AMERICA



HOT TOPICS IN PHARMACOGNOSY

The Evolution of Dolastatin 10 Derivatives as Sources of ADC Warheads



By David Newman, DPhil

Though natural product chemists who specialize in marine-sourced agents are usually aware of the contribution of structures based upon dolastatin 10 as warheads in antibody drug conjugates (ADCs), targeted against cancers of varying etiologies, the majority of ASP members may not be aware of the significant contributions made as a result of studies by the Pettit group starting in the middle 1960s. (Note, structures are not numbered, simply named.)

ASP member Dr. Bob Pettit and his group at Arizona State University (ASU) were funded by NCI (in the same time frame as Wall at RTI) with the ASU group investigating marine invertebrates, and the RTI group, plants. These led to the bryostatins and dolastatins at ASU, and taxol and camptothecin at RTI.

The dolastatins (which now number about 16 different structures) were initially isolated from the Pacific nudibranch *Dolabella auricularia*¹ and, due to the very small amounts obtainable due to the size of the individual organism, in order to obtain enough material to test in suitable screens, the Pettit group embarked on a “tour-de-force” in the 1980s to synthesize the necessary “building blocks” (modified amino acids) to produce selected dolastatins, including dolastatin 10 (Figure). The isolation and identification of dolastatin 10 was first reported in 1987,² with a patent with ASP member Dr. Sheo Singh (later at Merck in their then Natural Products group) issued in 1990.³ This was followed over the next few years by a series of reports covering the synthetic processes involved with a thorough review up through 1997 by Pettit,¹ and then in 2011, an updated review by Flahive and Srirangam was published as a book chapter with updates by the editors giving data up through that year.⁴

DERIVATIVES OF DOLASTATIN 10

Dolastatin 10 was shown to be a potent tubulin interactive agent, and over the years, the Pettit group synthesized variations on the base structure leading to auristatins E, PHE, PE and PYE, all with IC₅₀ values in the 10-100 pM range (Figure). Though some, including dolastatin 10, auristatin PE (aka soblidotin, TZT-1027 and YH-501) and tasidotin (Figure), entered clinical trials as single agents, none proceeded beyond Phase II due to toxicity and/or lack of efficacy in trials

covering the late 1900s to early 2000s. Dolastatin 10 had some modest efficacy in a Phase I trial but later work showed either no efficacy in a Phase II trial against prostate cancer or minimal activity against advanced breast cancer.⁵ This paper in 2005 was the last one currently known for dolastatin 10 as a single agent. In fact, there is still interest in the basic skeleton even as late as 2018 when Yokosaka et al.⁶ reported on novel “auristatins” with the thrust towards molecules suitable for coupling to monoclonal antibodies. Then in 2019, Yang et al. from Sanofi described a series of methods for linking highly bioactive materials such as dolastatin 10 to antibodies by use of fragment coupling.⁷ Other derivatives will be mentioned later when the current “warheads” are described.

THE “TRUE PRODUCER” OF DOLASTATINS

In 1998, ASP member Dr. Hendrik Luesch, who was then a graduate student in the lab of the late ASP member, Dr. Richard Moore at the University of Hawaii, reported the isolation of symplostatin 1 (Figure) from the cyanophyte *Symploca hydnoidea* collected in Guam and, working with a multidisciplinary group, demonstrated an activity similar to dolastatin 10.⁸ This compound was a close relative to dolastatin 10, and then later, Luesch et al. reported finding dolastatin 10 in *D. auricularia* feeding on the *Symploca* strain VP642 in Palau.⁹ Thus, the dolastatins are cyanophyte metabolites and are “adopted” by the nudibranch as a protective toxin. This is analogous to the sequestration of (probably) insect toxins by tree frogs in Ecuador as described many years ago by NIDDK investigators led by the late ASP member Dr. John Daly.¹⁰

ADCETRIS® THE FIRST DOLASTATIN-RELATED ADC (APPROVED BY THE FDA 2011)

This ADC-used monomethyl auristatin E (Figure) with an average of four molecules linked to the antibody using a valine-citrulline linker. The initial background starting from a mAb linked to auristatin E (Fig 2. 8 in 2019) and/or the monomethyl derivative (MMAE) was first described in 2003 by Seattle Genetics scientists¹¹ with a full description of the developmental history being published by Senter and Sievers of Seattle Genetics in 2012.

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CURRENT STATUS (AS OF 31 OCT 2020) OF DOLASTATIN-DERIVED ADC CANDIDATES.

In the following table, the compounds will be listed in this order: Generic Name; Trade Name; Approved Date; Phase III; Phase II; Phase II/I; Phase I; IND submitted. In each case, the warhead will be given.

MMAE & MMAF Warhead

Belantamab mafodotin	Blenrep	MMAF	Approved FDA 2020
Polatuzumab vedotin	Polivy	MMAE	Approved FDA 2020
Enfortumab vedotin	Padcev	MMAE	Approved FDA 2019
Brentuximab vedotin	Adcetris	MMAE	Approved FDA 2011
Depatuxizumab mafodotin		MMAF	Phase III US Discontinued by ABBV, Phase II/I in Japan
Disitamab vedotin		MMAE	Phase II
Telisotuzumab vedotin		MMAE	Phase II
Tisotumab vedotin		MMAE	Phase II
Ladiratuzumab vedotin		MMAE	Phase II (See note on Merck below)
VLS-101		MMAE	Phase II (See note on Merck below)
Enapotamab vedotin		MMAE	Phase II/I
BA-3021		MMAE	Phase II/I
MRG-002		MMAE	Phase II/I (Shanghai)
OBI-999		MMAE	Phase II/I
ABBV-2029		MMAE	Phase II/I
SGN-86A		MMAE	Phase I
SGN-CD228A		MMAE	Phase I
MRG-003		MMAE	Phase I (Shanghai)
RC-88		MMAE	Phase I
TRS-005		MMAE	IND Filed

Modified auristatin molecules as warheads (most are shown in a review by Newman in 2019¹³)

W-0101	Aur0101	Phase II/I
XMT-1592	Auristatin F	Phase II/I
Lupartumab amadotin	Auristatin W	Phase I
NG-HER2 ADC	Aur0101	Phase I
XMT-1536	Auristatin F-HPA	Phase I
AGS-62P1	Modified MMAF	Phase I
ZW-49	N-acyl sulfonyl MMAE	Phase I

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Merck Rahway's current investments in ADCs

In September 2020, Merck (US) announced that they were making an upfront payment of \$600 million to Seattle Genetics to codevelop the Phase II ADC Ladiratuzumab vedotin and will invest \$1 billion in Seattle Genetics shares (approx. 3% of shares). Then in early November, they paid \$2.75 billion to access VelosBio's ROR1-targeting ADC VLS-101. Both of these ADCs utilize MMAE as their warhead, a compound based on

the auristatin synthesized originally in the Pettit laboratory as a "lineal descendent of dolastatin 10."

The irony in both these acquisitions may not be lost on the old Merck Rahway Natural Products team that was dissolved quite a few years ago, as one of the patent holders on dolastatin 10 was a leader in that group, Sheo Singh. ■

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LITERATURE CITED

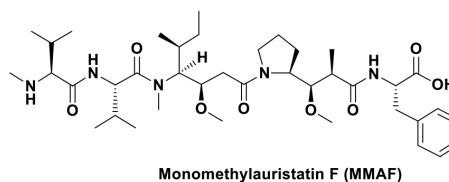
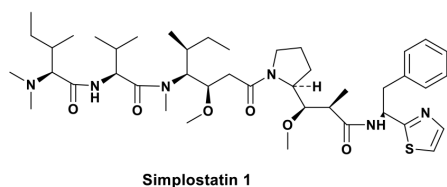
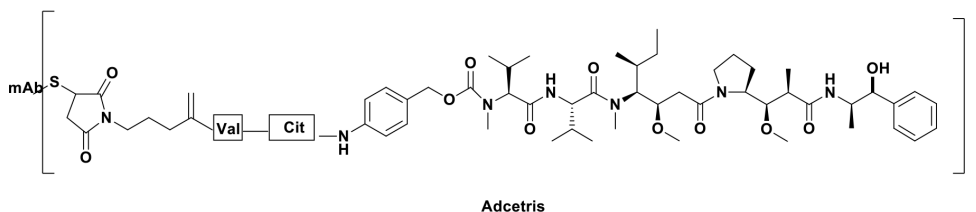
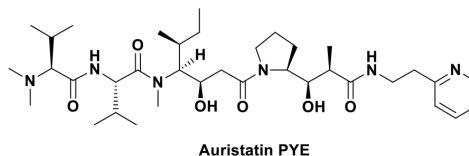
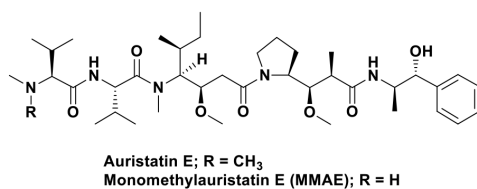
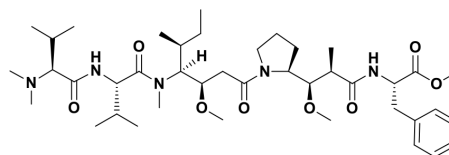
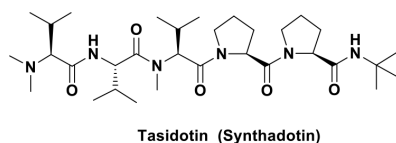
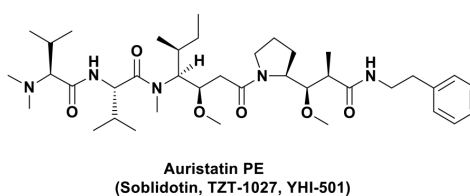
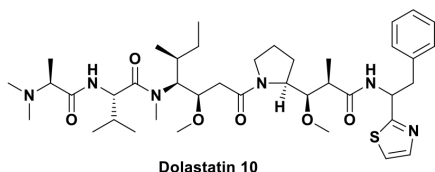
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Structures



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SIDEBAR

Investing in Natural Products

By Cedric Pearce, PhD

After 25 years of working as a scientist in increasingly entrepreneurial environments, including positions at early stage platform and drug discovery/development companies, a late-night chance encounter in 2000 at Raleigh Durham airport with Arthur Pappas, a life science investor, was my introduction into the world of venture capital.

At the time, I had closed the Research Triangle Park natural products discovery site for a New York biotechnology company and, subsequent to airport meeting, started working for Art Pappas as Vice President for Discovery Technologies; this experience resulted in daily encounters with life science entrepreneurs. And although I found this work fascinating, the smell of a working lab was calling, and after my sabbatical year from the bench, I founded Mycosynthetix, Inc with the goal of exploring bioactive compounds from an extensive fungus collection that I acquired.

When I joined the Pappas group, they had already established a strong reputation for their investment strategy, which was (and still is) primarily focused on life science opportunities. Pappas continued to invest in very successful early stage companies, and Art himself has been associated with approximately 22 new drugs being brought forward to the market.

Obviously for the natural products community this latest success for Pappas Ventures (www.pappas-capital.com/pappas-capital-portfolio-company-velosbio-to-be)

is significant on many levels. The initial seminal contribution of Bob Pettit and his colleagues is discussed in Dave Newman's article. The further medicinal chemistry, and antibody attachment, has produced a very promising anticancer treatment. This is also instructive, especially given that the current (US) patenting situation for natural products and generating new active analogues through synthesis or by using biological approaches, and considering novel targeting methods are all methods which can leverage our contributions.

One of the roles of venture capital investment is to take on risky projects and to develop novel technologies for the good of society. Pappas Ventures went an extra step and were involved in founding VelosBio. They invested in a number of financing rounds as VelosBio developed its pipeline, including the crucial VLS-101 (velosbio.com/our-science/pipeline#vls-101). The acquisition by Merck (www.businesswire.com/news/home/20201105005543/en/Merck-to-Acquire-Velos-Bio) demonstrates the significance of the product pipeline and the skill of Pappas and his colleagues.

This example should be kept in mind as promising natural products discoveries, with some potential to be used clinically or in other fields, are made; citing this in grant applications and in your own presentations to investor groups can only help to highlight the importance of what this group has to offer. ■

This example should be kept in mind as promising natural products discoveries, with some potential to be used clinically or in other fields, are made; citing this in grant applications and in your own presentations to investor groups can only help to highlight the importance of what this group has to offer.

Meet a New ASP Member

Dr. Elizabeth (Betsy) Parkinson



Dr. Elizabeth (Betsy) Parkinson, our featured new member in this issue of the Newsletter, began her appointment as an assistant professor in the Department of Chemistry and the Department of Medicinal Chemistry and Molecular Pharmacology at Purdue University in August of 2018. In addition to ASP, Dr. Parkinson is also a member of the American Chemical Society and the Society for Industrial Microbiology and Biotechnology (SIMB). We thank Dr. Parkinson for taking the time to talk with us and are pleased to officially welcome her to ASP.

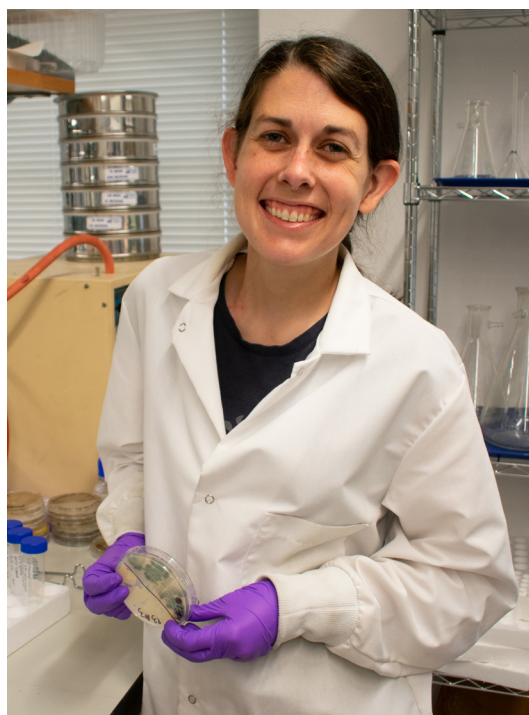
By James Fuchs, PhD

What are your research interests in pharmacognosy?

In the Parkinson laboratory, we are interested in exploring cryptic biosynthetic gene clusters from Actinobacteria. Specifically, as an organic chemistry/chemical biology lab, we are interested in investigating how chemical synthesis can help us to discover new bioactive natural products and derivatives. Currently, we are chemically synthesizing compounds inspired by bioinformatic predictions of the products from biosynthetic gene clusters. Additionally, we are determining their activities against antibiotic resistant bacteria, fungi, and cancer. We are also developing synthetic routes to gamma-butyrolactone signaling molecules that could serve as activators of previously unexplored biosynthetic gene clusters.

What is your scientific and educational background?

I have been interested in the use of natural substances as medicines for as long as I can remember. As a small child I would make “medicines” out of my mother’s flowers (to the great frustration of my gardener mother) for my “sick” dolls. As a junior in high school, I was so excited by the idea of medicines from plants that I applied for a summer program in Costa Rica focused on the medicinal plants that locals use. While I was not selected for the program, that did not quell my interest in science and the discovery of novel medicines. As an undergraduate at Rhodes College (BS in Chemistry, 2010), I was lucky enough to be chosen to participate in the St. Jude Summer Plus program, a program where undergraduates get to perform research in a laboratory at St. Jude Children’s Hospital. I performed my undergraduate research in the laboratory of Dr. Philip Potter, where I focused on identifying molecules that decreased the toxicity of the chemotherapeutic irinotecan. My under-



Parkinson in her laboratory at Purdue University.

PHOTO: CRISSI MARTINEZ-BROKAW

graduate project helped me to realize how noxious many anticancer treatments are, while my experience volunteering with patients opened my eyes to the urgent need for better therapeutics. This motivated me to pursue graduate studies in the development of targeted anticancer agents with Prof. Paul Hergenrother (Chemistry, UIUC). My graduate studies focused on the synthesis of derivatives of the anticancer

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Specifically, as an organic chemistry/chemical biology lab, we are interested in investigating how chemical synthesis can help us to discover new bioactive natural products and derivatives.

**While the regulation of some natural products is understood,
I feel like the regulation of most of them remains a mystery.
This mystery is the inspiration for much of my research!**

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natural product deoxynyboquinone with improved solubility and pharmacokinetic properties as well as its mechanism of action. I graduated with my PhD in chemistry in 2015.

My graduate work on the synthesis of deoxynyboquinone and other bioactive natural products sparked my interest in the discovery and biosynthesis of natural products from actinomycetes. For this reason, I performed my postdoctoral research with Prof. William Metcalf (Microbiology, UIUC). While in the Metcalf laboratory, I isolated novel natural products and determined their biosynthetic pathways. My projects in the Metcalf lab opened my eyes to the large number of biosynthetic gene clusters from actinomycetes that remain uncharacterized. The existence of so many new and likely bioactive natural products greatly excites me. Additionally, the cryptic nature of these biosynthetic gene clusters fascinated me then and continues to fascinate me now. While the regulation of some natural products is understood, I feel like the regulation of most of them remains a mystery. This mystery is the inspiration for much of my research!

How did you hear about the ASP and what led you to join the society?

I first heard about ASP when I was a postdoc in the Metcalf lab. However, I did not really participate with ASP until this past spring. When COVID hit and we were required to quarantine, I found this quite isolating. One day when I was skimming Twitter, I saw that ASP was hosting a virtual webinar series (ASP Natural Product Sciences Webinar Series). I signed up pretty much immediately! I really enjoyed getting to hear about great science going on in ASP and getting to see what a vibrant community it was. It really was one of the highlights of my quarantine! Based on this experience, I wanted to continue to interact with this community.

What would you like to achieve through your membership?

I want to learn more about the great research being performed by ASP members. Additionally, I want to make connections with the people performing this research.

What do you like doing in your spare time?

I enjoy running, cooking, and reading. Recently, I have not gotten to do as many races as I would like. (I particularly like trail races, 10Ks and half marathons.) However, I have gotten to do A LOT more cooking and have even gotten to try my hand at brewing beer.

What are you currently reading?

I tend to read multiple books at once. I am currently reading *The House in the Cerulean Sea* (a very uplifting and sweet fantasy novel), *Let Your Mind Run* (a memoir by the Olympic runner Deena Kastor), and *The Vaccine Race* (a particularly relevant history of the development of the vaccine against rubella).

What has been your biggest adjustment during the COVID-19 era (personally or professionally)?

Learning to teach online. I teach first semester organic chemistry to ~450 students, so we obviously are not in person. I have been trying to figure out the best way to teach organic chemistry online. So far, it has been lots of videos with molecular models, shorter mini-lectures to hopefully keep my students attention, and more frequent/smaller assessments. The one positive is that I now feel like I have the time to have a weekly "bio connection" segment (something I have been wanting to do for the past two years). Many of the students that I teach are pre-health profession or biology majors. It is nice to get to tell them a little more about why organic chemistry matters and how it connects with their interests (e.g., the thalidomide story and how cannabinoids are biosynthesized).

Is there anything else you would like other ASP members to know about yourself?

The Parkinson lab is currently looking for a postdoc in natural product biosynthesis. If you are interested, please email me (eparkins@purdue.edu) with a cover letter, CV, and list of references. ■

New Members of ASP Winter 2020

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 24 full members and 38 associate members. We look forward to meeting you and learning more about you and your work.



American Society of Pharmacognosy

FULL MEMBERS

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United States
Food and Environmental Specialist

**Dr. Andres Mauricio
Caraballo Rodríguez**

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United States
Postdoctoral Scholar

Prof. Jonathan Chekan

University of North Carolina
Greensboro
United States
Assistant Professor

Dr. Marc Chevrette

Wisconsin Institute for Discovery
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St. Catherine University
United States
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Poland
Assistant Professor

Dr. Pedro Leão

CIIMAR – University of Porto
Portugal
Principal Investigator

Prof. Joleen Masschelein

KU Leuven
Belgium
Assistant Professor

Dr. Rodney McKeever

LAC & USC Medical Center
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Dr. Jessie Ochoa

Brightseed
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Dr. John Westerdahl Nutrition
Consultant
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Nutrition and Lifestyle Medicine
Consultant

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University of California at San Diego
United States
Postdoctoral Scholar

Prof. Sayeed Ahmad

Jamia Hamdard, New Delhi
India
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Miss Temitayo Akinkunmi

Federal University of
Technology Akure
Nigeria
Student

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General Manager

Miss Anaïs Biclôt

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Belgium
PhD Student

Ms. Billie Jean Brashears

LSMAMP
United States

Dr. Jane Budel

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Ponta Grossa (UEPG)
Brazil

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American Society of Pharmacognosy

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United States
PhD Student

Mrs. Jessica Cleary

University of Illinois at Chicago
United States
Graduate Student

Ms. Brooke Dunnery

Coastal Carolina University
United States
Student

Miss Mabel Gonzalez

Universidad de los Andes
Colombia
PhD Student

Ms. Madeline Hennessy

University of Illinois at Chicago
United States
Graduate Student

Mr. Max Hohmann

TU Dresden
Germany
PhD Student

Mr. Ivan Kahwa

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and Technology
Uganda
Master's Student

Dr. Bhupendra Kumawat

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India
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Mr. Jason Williams

CSUDH
United States
Student

Mr. Sam Williams

University of Bristol
United Kingdom
PhD Student

Ms. René Xavier

Florida Atlantic University
United States
Graduate Research Assistant

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.

AAAS 2021 Annual Meeting (online)
Understanding Dynamic Ecosystems
February 8–11, 2021
meetings.aaas.org/

C&EN Webinars
Various Days and Times
cen.acs.org/media/webinar.html

ASP Natural Product Sciences Webinar
Bimonthly Zoom Seminars
Thursdays 4 PM ET / 1 PM PT
www.pharmacognosy.us/natural-product-sciences-webinar/

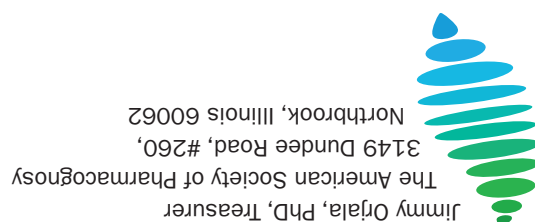
20th International Congress of the
International Society for Ethnopharmacology
April 18-21, 2021
Thessaloniki, Greece
www.ethnopharmacology2021.org

ACS Webinars
Every weekday 2 PM ET / 11 AM PT
www.acs.org/content/acs/en/acs-webinars.html

American Society of Pharmacognosy 2021
Annual Meeting
July 24-28, 2021
Grand Rapids, Michigan
aspmeetings.pharmacognosy.us



American Society
of Pharmacognosy



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

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

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

Jimmy Orjala, PhD, Treasurer, The American Society of Pharmacognosy,
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