The American Society of Pharmacognosy

Discovering Nature's Molecular Potential

The ASP Newsletter: Volume 53, Issue 2

Fogarty Center Threatened with Elimination in Proposed Budget

EDITOR'S NOTE: *Dr. Clardy was part of the first round of International Biodiversity Conservation Groups (ICBGs), worked with other ICBGs, and is currently the PI of one of the latest round of these groups. He has been involved with other ICBGs in the intervening years. He reached out to the ASP Fellows for some of their thoughts about the program, and its significance, and describes how this NIH program with a relatively modest budget, has impacted pharmacognosy research.*

By Dr. Jon Clardy

In April, the White House released a budget outline that proposed an unprecedented $6 billion cut for the National Institutes of Health (NIH). A reduction of this magnitude roughly 20% of the current NIH budget, could only be accomplished by zeroing out many existing programs, and NIH's Fogarty International Center (FIC) was one target.

The FIC oversees the International Biodiversity Conservation Groups (ICBGs) that have played a major role in the development of natural products research, including that of a number of ASP members. Although Congress passed a temporary spending bill that provided a reprieve to FIC, the once and possible future elimination of the ICBG program prompted many of us to reflect on how the ICBG program transformed the field of pharmacognosy in both the US and the world.

The ICBG program has made significant contributions to our field during its existence, and some numbers can give a sense of the magnitude. Over 13,000 species have been collected and analyzed, a number of which are new to science. Over 1,300 bioactive compounds have been identified in areas such as malaria, tuberculosis, human immunodeficiency virus (HIV), antibiotics, cancer, and inflammation. Also, ICBG discoveries resulted in more than 800 publications and dozens of patents. Other impacts include informing the Nagoya

Left: Fiji crinoid, a starfish relative commonly called feather-stars or sea lilies, taken during work on Dr. Mark Hay's ICBG in the Fiji/ Solomon Islands. This program focuses on drug discovery collections on marine microbes and diverse coral reef organisms and their bacterial symbionts.

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Final Preparations Underway for ASP Annual Meeting (page 8)

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EDITOR'S CORNER

As we prepare for the annual meeting in Portland, Oregon in late July, the happenings in the nation's capital continue to have significant and unexpected impacts on science. In March, I was very surprised to read that President Donald Trump's proposed budget for the next fiscal year called for the outright elimination of the National Institutes of Health's Fogarty International Center. The Fogarty has supported the work of a number of ASP members involved in drug discovery with international partners, including the research of ASP Fellow Dr. Jon Clardy. I immediately contacted Dr. Clardy to ask if he would write the cover story for this issue that details the work of researchers involved in International Cooperative Biodiversity Group projects supported by Fogarty, and I am glad that he agreed. On a positive note, a number of ASP members participated in the March for Science, held in cities around the nation. I think now, more than ever, it is important for scientists to communicate their discoveries and contributions to society. We cover the participation of a number of ASP members who marched in cities across the United States.

In our last issue of the *ASP Newsletter* we covered the Executive Order banning travel from several predominately Muslim countries. In this article, we included the response from ASP President Cindy Angerhofer. A few people inquired about the appropriateness of the *Newsletter* covering these political events. I discussed this with the ASP Executive Committee and was reminded that many prominent scientific societies, like AAAS, are involved in lobbying for various issues, including the March for Science. The Executive Committee agreed that covering certain political issues impacting the Society is important, but our viewpoint should never be partisan.

The Society is gearing up for its annual meeting, July 29 to August 2, in Portland, Oregon. The latest information about the meeting can be found at the website **www.asp2017.org**. The scientific program is outstanding, from preconference workshops, to a variety of invited speakers. I hope many members of the Society will be able to join us. Please check out the local favorites article in this *Newsletter,* prepared by the organizing committee, and get fantastic ideas about where and how to spend your free time.

The hot-button issue of fraudulent foods is covered by ASP member Dr. Ara DerMarderosian, along with his daughter Ms. Laura DerMarderosian. Although I used to work for Food and Drug Administration, I was unaware of some the historical examples of fraudulent foods that the DerMarderosians cover in their interesting article. In "From the Archives," we include an excerpt of Dr. Bob Pettit's writings on his travel to Asia as part of the first wave of scientists allowed back in the People's Republic of China in the 1970s. This is a fascinating read, especially considering how much China has developed in the last decades.

This is the first time in the history of the *ASP Newsletter* that we are running ads. I have worked with the ASP Sponsorship Committee, Chaired by Mr. Mark O'Neil-Johnson, to seek out paid advertisements to help cover costs of the *Newsletter*. The advertisements by Waters Corporation and Bruker Corporation are tied to these companies' sponsorship of our annual meeting this year. If you know of other companies that may wish to be a meeting sponsor, or simply run an advertisement in the *Newsletter,* please contact Mr. O'Neil-Johnson.

I hope you have wonderful and productive summer, and I hope to see many of you in Portland.

Dr. Edward J. Kennelly

EMPLOYMENT SERVICE

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

For more information see the services website.
www.pharmacognosy.us/jobs/

NEWSLETTER STAFF

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Fogarty Center Threatened with Elimination in Proposed Budget

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Left: A plant taxonomic identification training activity at Cuc Phuong National Park, Vietnam, at the newly established herbarium institution of Cuc Phuong National Park. ICBG Program led by ASP member Dr. Djaja D. Soejarto in Vietnam and Laos, "Studies on Biodiversity of Vietnam and Laos", 1998-2011, left to right: Mr. Quang, Dr. Soejarto, Mr. Cuong.

MAI VAN XINH (CUC PHUONG NATIONAL PARK)

Center: Dr. Emily Meyers collects ants in the Amazon as part of the ICBG Brazil.

Right: Marine Microbiology at CNRO, Nose Be, Madagascar. Dr. Rado Rasolomampianina (CNRE) and Mr. Matthew Anderson (University of Maryland Center for Environmental Science) isolating bacteria from Malagasy marine invertebrates as part of ASP Fellow David Kingston's ICBG in Madagascar.

RUSSELL HILL

Protocols and other national policies on bioprospecting, building the research capacity of at least 16 countries, and helping to create biodiversity reserves in eight countries. By any measure, the ICBG experiment has been hugely successful.

ASP Fellow Dr. Gordon Cragg and several National Cancer Institute (NCI) staff (Drs. Mike Grever, Saul Schepartz, Ken Snader) were part of an interagency group (NIH, United States Agency for International Development, and National Science Foundation) that organized a workshop in 1991 to discuss how best to coordinate drug discovery and development with biodiversity conservation, sustainable development, and economic growth in source countries, including appropriate forms of compensation.

Representatives of the US government, the private sector (Merck, Smithkline Beecham [now GlaxoSmithKline], and intellectual property lawyers) and several source countries (Brazil, Costa Rica/INBio, Ecuador, Indonesia, Madagascar, and Thailand) participated.[1] The workshop discussions ultimately led to the establishment of the ICBG program in 1992. NCI already had considerable experience in this area with collections ongoing under its Letter of Collection in many countries. In the first round of ICBG funding, five awards were made, and the list of PIs will be familiar to many readers: ASP Fellow David Kingston led a program in Suriname, Dr. Jerrold Meinwald led a program in Costa Rica (I also participated in this program), Past ASP President Barbara Timmermann led one in Argentina, Chile, and Mexico, Dr. Walter Lewis led one in Peru, and Dr. Brian Schuster led one in Cameroon and Nigeria. Each of the programs had a special focus.

For example Dr. Lewis focused on ethnobotanical leads from the Amazonian rain forest, Dr. Schuster focused on traditional cures for parasitic diseases, and Dr. Meinwald worked with the National Biodiversity Institute in Costa Rica on using chemical ecology to identify potential therapeutic agents. Dr. Josh Rosenthal submitted a case study on these early ICBG programs to the Conference of Parties of the Convention of Biological Diversity, and a summary of these early groups is at https://www.cbd.int/doc/case-studies/abs/cs-abs-icbg.pdf.

To understand the ICBG program, it is important to understand some its administrative structure. In common with some other NIH programs that might be familiar to ASP members, most notably the Botanical Centers, the programs are open every few years to a new round of applications. The requirements for an application change in each round as do the funds available. The FIC does not have a sufficient internal budget to support the grants, so the FIC administrators, Drs. Rosenthal and Flora Katz, solicit funds from NIH Institutes and other government agencies. The core funders have been NIH and NSF, and other funders include NSF and several NIH institutes. Other contributors to the last round include the Department of Energy (DOE), United States Department of Agriculture (USDA), and National Oceanic and Atmospheric Administration (NOAA), indicative of the widespread support for ICBG.

The early ICBG grants required having the academic researchers in the US and their collaborators in biodiverse developing countries work closely with an industrial partner. It may seem surprising to many readers that this was an innovation as it is such a common arrangement today. Most academic natural products chem-

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ists conducted their research in their own labs, published the results in technical journals, and sent samples to requestors or friends on an informal basis. Companies, at least in the early days, had their own natural product discovery efforts that were focused largely on soil microbes. The formal connection of academic labs with the pharmaceutical industry was transformational, and in my opinion the most significant outcome for our science.

As ASP Fellow Rachel Mata, who was part of Dr. Timmermann's ICBG put it, "The project gave me the opportunity to appreciate a close university-industry research collaboration that connected basic and applied research." Dr. William Maiese, at the time a senior researcher at Wyeth-Ayerst Research Laboratories, greatly aided my development as a scientist. He made us feel embedded in a real drug discovery adventure with profound implications for the public health, safety and quality of life. Through this interaction, it became clear to me that research institutions need to play a more active role in their relationship with industry in order to maximize the use of the research results."

In many cases, the academic-industry connections outlasted the ICBG project. In my own case, for example, I continued collaborating with Bristol-Myers long after that first ICBG ended. The ICBG program, along with an earlier similar program from the NCI (National Cooperative Drug Discovery Groups or NCDDGs) provided considerable resources to the academic natural products research community and led to a greater focus on molecular function rather than architectural complexity or rarity. As an aside, the NCDDG platform provided early models for industrial collaboration and the ICBG provided structure for working equitably in biodiverse developing countries, especially 'prior informed consent' arrangements tailored to the host country's context.

The current Brazil ICBG team in the Amazon. Dr. Clardy is center, in the floppy hat, Brazilian co-PI, Dr. Monica Pupo, is on Dr. Clardy's left with Dr. Cameron Currie from University of Wisconsin on his right.

"The project gave me the opportunity to appreciate a close university-industry research collaboration that connected basic and applied research."

—ASP Fellow Rachel Mata

As the ICBG program evolved, the benefit to the biodiverse host country became increasingly focused on training and scientific infrastructure. Dr. Mata relates that, "The project also provided my research group at UNAM stable financial support for ten years, which is critical in Latin America countries, allowing the purchase of modern equipment and supplies for natural products chemistry research. It enabled us to pursue additional lines of research that, ultimately, contributed to faculty productivity with additional external funds as well as increased publications." You can find out more about Dr. Mata's experience in *Pharm. Biol.* **1999**, 37, S35-54.

In some cases, ICBGs were very active in creating physical infrastructure. One notable example is an ICBG with ASP Fellow Dr. Chris Ireland as PI that was working in Papua New Guinea (PNG). With ICBG and Fogarty International Research Collaboration Award funding they set up a natural products chemistry/extraction/cell culture/bioassay laboratory at the University of Papua New Guinea (UPNG), Port Moresby, Papua New Guinea, to support student Honors and Masters projects. UPNG had no such capacity up to that time. Since that original setup, the Utah group has developed and sustained the capacity of the UPNG BioDiscovery Laboratory for the isolation and cultivation of microbes, extraction of microbial, marine or plant samples, and their fractionation and bioactivity assessment. Also, this facility supports basic protein electrophoresis to enable venom research and pharmacological and toxicological student training.

All of us that have been fortunate enough to be involved with ICBG projects have our favorite outcomes, but I would be remiss without noting one of the most dramatic. ASP Past President Bill Gerwick had an ICBG in Panama that largely focused on cyanobacteria and anticancer active molecules along with tropical plants and parasitic diseases. Their fieldwork often took place on or near Coiba Island,

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the largest island in Central America. Coiba Island was separated from the mainland 10 to 15 thousand years ago by rising sea levels. This isolation led to the development of an unusual ecology and for most of the 20th century Coiba housed a notorious penal colony, resulting in a bioprospecting paradise.

One notable molecular discovery from Coiba was coibamide, which had exceptional anticancer activity and a novel mechanism of action, and terrestrial explorations led to the identification of some promising antimalarial compounds. The island, which is 12 miles off the coast of Panama, has some 4,200 acres of coral reefs that turned out to be home to seven soft coral species that were previously unknown to science. The island also has over 100,000 acres of primary forests. In 1991, Coiba Island became partially protected as a Panamanian National Park, and when the prison was shut down in 2004, efforts organized by Dr. Gerwick's ICBG led to the Coiba National Park being named a UNESCO World Heritage Site.

Fiji Sea star, taken during work on Dr. Mark Hay's ICBG in the Fiji/Solomon Islands.

DR. MARK HAY

Sea anemone and shrimp taken while Dr. Marcy Balunas was collecting marine cyanobacteria at the Bastimentos National Park in Bocas del Toro, Panama, as part of Past ASP President William Gerwick's ICBG in Panama.

KIM DIVERS

This collective reflection on the ICBG program highlights its importance in a variety of ways, but the clearest indication of how profoundly it affected our science is the popularized and standardized industrial-academic collaboration, focus on biodiversity, international training, infrastructure development, functional assays, and formal arrangements for resource sharing and compensation. ■

Below left: Panama plant collection and taxonomy team, led by Dr. Alicia Ibanez (third from left), as part of Dr. Gerwick's ICBG in Panama.

Right: Seller of traditional botanical medicines at the Samarkand market, Uzbekistan. Dr. Ilya Raskin's Central Asia ICBG focused on discovery of therapeutic agents produced by plants, fungi and prokaryotes from Central Asia.

DR. ILYA RASKIN

LITERATURE CITED

[1] Schweitzer, J., et al. Summary of the workshop on drug development, biological diversity, and economic growth. *J Nat Cancer Inst* **1991**, 83, 1294-1298.

ASP Members Participate in the March for Science

By Dr. Amy Keller

On April 22, 2017, scientists all across the world turned out to show their support for science by participating in the March for Science. ASP members across the country participated from cities such as Ann Arbor, Boston, Denver, New York, and Washington DC. Some ASP members posted photos of their participation in the march on the ASP Facebook page www.facebook.com/pharmacognosy.us/.

ASP Foundation Treasurer (ex officio) Dr. Bob Kreuger at the March for Science in Ann Arbor, Michigan with daughter Allison and granddaughter Linden (named for the tree), a scientist in training. Dr. Kreuger wears an original earth day pin from undergraduate at University of Connecticut School of Pharmacy, University of Connecticut, Storrs, Connecticut.

Above right: ASP President Cindy Angerhofer shows her support for the marches.

MR. TOM O'LEARY

ASP President Dr. Cindy Angerhofer commented, "ASP is a society of scientists that depend upon the environment for subject matter, upon the US Federal government for a large portion of research funding, and on positive public perception and trust in the veracity of scientific research. In our current political climate, all of these foundations appear to be at risk of eroding. I believe it is critical that we are vocal as a society and as individuals to articulate the value of our natural world and the benefits of our research in terms that lawmakers and the public at large understand. The 'citizen science' movement has enticed many non-scientists to learn and participate in scientific projects in their communities and through the internet; I encourage scientists to also fully participate as citizens to assure scientific integrity for our schools, institutions and governmental agencies to utilize and build upon. Our actions now can help to create an informed population and a sustainable future for our planet."

The March for Science drew large crowds throughout the country. Demonstrations were peaceful and consisted of marches, rallies, and events, ranging from speeches to concerts. ASP member Dr. Kurt Reynertson and his son traveled from New Jersey to Washington DC to join fellow marchers. Although the weather was rainy and damp, Dr. Reynertson related, "It is important that my children realize that if something does not make sense to them, they can speak out and not be relegated to the sidelines. Marches like these are ideal ways for them to feel empowered and be part of something large and important."

ASP member Dr. Robert Krueger, who marched in Ann Arbor, Michigan, told the *Newsletter,* "Having my youngest daughter and my youngest granddaughter on the March for Science was awesome. Science is a great career for anyone, but even better for women in my estimation. I hope to instill in all three of my grandkids a love of the natural sciences. My daughters attended many ASP meetings, as we always planned our vacations around them. They are both scientists, so watch out, as the grandkids may join me some day at one of the future meetings!"

ASP member Dr. Marcy Balunas reported to the *Newsletter* that there was a large ASP contingent at the Boston march, and one of her students, Ms. Samantha Gromek was even a presenter. She also saw a member of Dr. Jon Clardy's laboratory. Dr. Balunas noted, "It was a fantastic experience!"

Various scientific organizations around the globe were represented and helped in organizing, and students of all ages, scientists of all disciplines, and supporters of science, turned out to march. The marches had strong editorial support from *Nature*, and organizations such as the American Association for the Advancement of Science, the American Chemical Society, and the Union of Concerned Scientists, officially supported the March for Science. According to the official website, "We unite as a diverse, nonpartisan group to call for science that upholds the common good and for political leaders and policy makers to enact evidence based policies in the public interest."

Positions articulated by scientists for participating in the March for Science were varied, but according to official Facebook pages and news articles, included concern with an anti-science climate in the US, public dismissal of science unsupportive of political positions, deep funding cuts to science proposed by President Trump, and the preservation of science's ultimate service to the world and humanity. As stated in a *Nature* editorial published April 13, 2017, "These worldwide protests give scientists an opportunity to think hard about what they value about science, to recognize the commonalities in the goals they share with others and to reaffirm the scientific process as the best way of informing policy—even if it won't always get the final say." ■

Last Update for Visiting Portlandia!

Left: 6th Ave Hilton Portland Downtown; Right: Oregon Museum of Science and Industry

By Dr. Kerry McPhail

We are excited to see you in a few weeks for the ASP Annual Meeting, July 29 to August 2, 2017. If you are arriving Saturday, July 29, there are plenty of rooms at the 6th Ave Hilton Portland Downtown. If you have not made arrangements yet and are arriving Friday, July 28, please check the nearby Paramount Hotel for availability, a 3-minute walk to the Hilton, as the Hilton is sold out for that night. For transport, the MAX Light Rail system station is just one block from the conference site, and provides access to many Portland attractions.

The diverse pre-conference workshops on Saturday, July 29, include one full day workshop on quantitative NMR applications, and four half-day workshops on scientific writing, anti-cancer mechanisms, grant writing strategies, and extraction to elucidation of natural products. After opening with the welcome reception on Saturday evening, Sunday begins with speakers Drs. Ikuro Abe, Chaitan Khosla, Christina Smolke and Huimin Zhao in the *Natural Products Biosynthesis and Synthetic Biology* symposium. On Monday morning, we welcome Drs. Prakash Nagarkatti, Luc Pieters and Amala Soumyanath as we delve into the *Molecular Pharmacology of Natural Products and Complementary Medicine* symposium.

In the Tuesday morning symposium, Drs. Bill Baker, Julia Kubanek, Pei-Yuan Qian and Ryuichi Sakai lead us to explore *Natural Products from Unique Ecosystems*, while finally the *Awards Symposium* will take up Wednesday morning. The two parallel afternoon sessions daily include invited and contributed oral presentations encompassing natural products biosynthesis, herbal and plant natural products, synthetic biology, synthesis of natural products, epigenetic activity of natural products, microbial natural products, molecular pharmacology of natural products, advanced technologies in natural products research, and plants and neurology. Poster sessions will be on Sunday, July 30, (5-7 pm) and Monday, July 31, (3:30-6:30 pm); note that the maximum poster size is 3 feet tall by 4 feet wide.

Afterwards, we hope you will all join us for the Monday evening outing to the Oregon Museum of Science and Industry (OMSI, (*http://www.omsi.edu/*). Buses leave starting 6:30 pm. The younger members' event on Tuesday evening will include a taste of Oregon microbrews. Note that on Wednesday, an early afternoon pair of contributed oral sessions will provide a further opportunity to explore natural products research, before the annual ASP business meeting and evening banquet. And finally, a reminder that the scientific program ends between 5 – 7pm each day, leaving plenty of daylight (sunset is around 9pm) to take in the local scene.

For detailed information on the meeting's scientific and social programs, hotel and travel, please visit the conference website http://asp2017.org/ and associated social media links! ■

ASP Meeting 2017: Plan Your Portlandia Adventures!

A view to downtown Portland

We are excited to host ASP members for the 2017 Annual Meeting, July 29 to August 2, 2017, and hope you enjoy Portland. To help in your planning, we compiled local perspectives on recreation in Portland, Oregon, City of Roses. **Favorite places to grab lunch** are the food carts (http://www.foodcartsportland.com/), Por Qué No? Taqueria, Lardo Grassa Bunk, Pizzacatto, Verde Cocina in the Pearl District, Bijoux in the Pearl, Pine Street Market, Let's Eat Thai, and Porqueno, are only a few. **Favorite free activities** include the Portland Saturday Market, browsing books at Powell's City of Books, walking the waterfront, visiting Washington Park, the Rose Test Garden, the Japanese Gardens, Lan Su Chinese Garden, hiking in Forest Park, summer outdoor concerts, and visiting waterfalls in the Columbia River Gorge.

Things to splurge on are dinner at the Heathman Hotel, Blue Hour in the Pearl, Le Pigeon, Paley's Place, Toro Bravo, Rey, Higgins, Portland City Grill, Beast or Pok Pok restaurants, tapas and drinks at Ataula, music shows at Dante's Live, a tour of the Shanghai tunnels under the city, or a Timbers game if they are in town. Some of the dinner restaurants mentioned are also good places to **get drinks and socialize**. Others are Clyde Commons (cocktails), Kask (cocktails), Secret Society (good cocktails), Multnomah Whiskey Library, Ground Kontrol (video games and bar), Bailey's Taproom (large beer selection), Edgefield McMenamins, or the waterfront McCormick and Schmick's. For beer drinkers, there are many breweries on the east side of town, as well as in the Pearl District.

It is **recommended to avoid** driving downtown, dining at major restaurant chains, walking Old Town and Burnside near Chinatown at night, or wandering further east then 72nd Street. **Plan on bringing** sunscreen, walking shoes, camera, and an appetite, as well as a rain jacket and various clothing options. Nights can be cool, and Portland weather is unpredictable! **Only in Portland** can you observe the weirdness, walk in the Pearl District, see Multnomah Falls in the Columbia River Gorge, see Mount Hood, and eat Portland Salt and Straw Ice Cream! **Other information to share** is that Portland brew pubs are "kid friendly" with play areas and children's meals (served on Frisbees at 10 Barrel Brewing!). Powell's City of Books has a great children's section where it is perfectly okay to browse on site and not buy. Finally, remember that the 30th Annual Oregon Brewers Festival will be held along the riverfront a few blocks away from the hotel from July 26 to 30, 2017.

For transport, the MAX Light Rail system station is just one block from the conference site, and provides access to the Portland Zoo, the Japanese gardens, Hoyt Arboretum, Forest Park, Portland Saturday Market, the Oregon Museum of Science and Industry (OMSI), and the Portland Art Museum, among other attractions. Whatever type of activity you enjoy, the (Tourist Information Center) Travel Portland website presents a calendar of events and a guide to exploring the 145 square miles of Portland "indoors and outdoors," https://www.travelportland.com/article/top-sights-in-portland/.

With abstracts submitted, we hope you have made your travel and accommodation arrangements for downtown Portland. For detailed information on the meeting's scientific and social programs, hotel and travel, please visit the conference website http://asp2017.org/ and associated social media links! ■

Forest Park, Portland

ASP Fellow Wani Receives Honorary Doctorate

By Dr. Nicholas Oberlies

ASP Fellow, Dr. Mansukh C. Wani, was hooded with an honorary doctorate from the University of North Carolina at Greensboro (UNCG), Greensboro, North Carolina, in May 2017, for his role in the development of two important cancer drugs, camptothecin and Taxol™ (paclitaxel); He worked on these compounds together with Dr. Monroe E. Wall in the early 1960s and 1970s.

Dr. Wani engages with students at the University of North Carolina at Greensboro.

DR. JERRY WALSH

Chancellor Franklin D. Gilliam noted the role that both paclitaxel and camptothecin have had in cancer chemotherapy, with a particular emphasis on paclitaxel's use in breast and ovarian cancers. This was an homage to the fact that UNCG was a Women's College until 1963, and many alumni were likely treated with it. Dr. Wani is a regular visitor and adjunct in the Department of Chemistry & Biochemistry at UNCG, where he has enjoyed interacting with students, inspiring them with his stories of the trials and tribulations of both discovering those compounds and advancing them toward the clinic.

However, what was not known to most people is that Dr. Wani first visited the Department in December of 1971, where he gave an invited lecture on his work on the total synthesis of camptothecin. Camptothecin, as a Na salt of the parent molecule, was first being tested in the clinic, and the original description of paclitaxel was first published. Dr. Wani is very organized and detail oriented, and he even found the original letter of invitation in his files.

For a man of 92, it was a busy, but glorious day. Dr. Wani was hooded during the graduation ceremony in the morning, and was then honored with a lunch for his friends and family. The day concluded with a reception in his honor in the Department of Chemistry & Biochemistry, where Dr. Wani enthralled faculty, staff, and most importantly, students with anecdotes about those discoveries. He emphasized the three "Ps" of research, persistence, passion, and most importantly, perspiration. He also noted that you never know what will happen. When he first visited UNCG in 1971, when the camptothecin and paclitaxel discoveries were just seeds, he had no idea that 46 years later he would be honored in this manner for the great discoveries they would grow up to become.

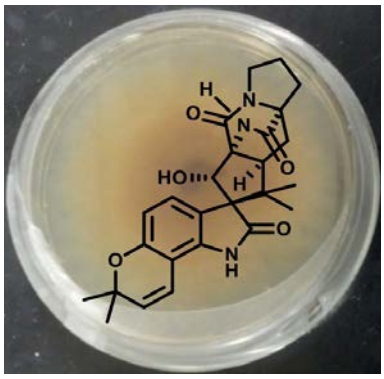
A primer on the historical significance and background of these discoveries can be found here: Oberlies, N.H., Kroll, D.J. Camptothecin and paclitaxel: historic achievements in natural products research. *J. Nat. Prod*. **2004**, 67, 129-134. ■

Chancellor Franklin D. Gilliam noted the role that both paclitaxel and camptothecin have had in cancer chemotherapy, with a particular emphasis on paclitaxel's use in breast and ovarian cancers.

2017 Schwarting and Beal Awards

By Drs. A. Douglas Kinghorn and Amy Keller

The ASP is pleased to announce the winners of the 2017 Arthur E. Schwarting and Jack L. Beal Awards. These awards are given annually by the Foundation of the American Society of Pharmacognosy in conjunction with the editorial board of the *Jounal of Natural Products* for outstanding papers published the prior year in the journal. In this manner, two former distinguished editors of the journal are fondly remembered. The Schwarting Award is open to all papers published in the journal within a given year (either in print or electronically). In turn, the Beal Award is awarded to younger investigators [i.e., persons within 12 years of receiving their Ph.D. degree or within 10 years of gaining their first professional appointment (e.g., Assistant Professor or an equivalent position in industry or government)].



Graphical abstract depicting sclerotiamide, isolated from a fungus.
BIN WANG

The winning publication for the Schwarting Award is by Silas Anselm Rasmussen, Sebastian Meier, Nikolaj Gedsted Andersen, Hannah Eva Blossom, Jens Øllgaard Duus, Kristian Fog Nielsen, Per Juel Hansen,* and Thomas Ostenfeld Larsen* entitled, "Chemodiversity of Ladder-Frame Prymnesin Polyethers in *Prymnesium parvum*," in *J. Nat. Prod*. **2016**, 79, 2250-2256. The Beal Award was given to a paper by Nathan P. Lavey, Jesse A. Coker, Eliza A. Ruben, and Adam S. Duerfeldt* entitled, "Sclerotiamide: The First Non-Peptide-Based Natural Product Activator of Bacterial Caseinolytic Protease P" in *J. Nat. Prod.* **2016,** 79, 1193-1197.

Dr. Hansen represents the Marine Biological Section, Department of Biology, Copenhagen University, Helsingør, Denmark, and Dr. Larsen is in the Department of Biotechnology and Biomedicine, Technical University of Denmark (TUD), Lyngby, Denmark.

Dr. Larsen told the *Newsletter*, "I got really excited when I first heard that we are to receive the 2017 Arthur E. Schwarting Award. After having worked for two decades with fungal natural products, moving into the field of microalgal chemistry turned out to be an exciting challenge. Since fish killing toxins such as prymnesins are only produced in minute amounts, the task of elucidating their complex structures is not trivial at all. To actually reach the goal after three years of hard work, and be able to publish our findings of what we have defined as a novel type of prymnesins in *J. Nat. Prod.,* has been really satisfying. Also, being acknowledged for your work by your fellow peers is simply the best acknowledgement that you can get as a researcher."

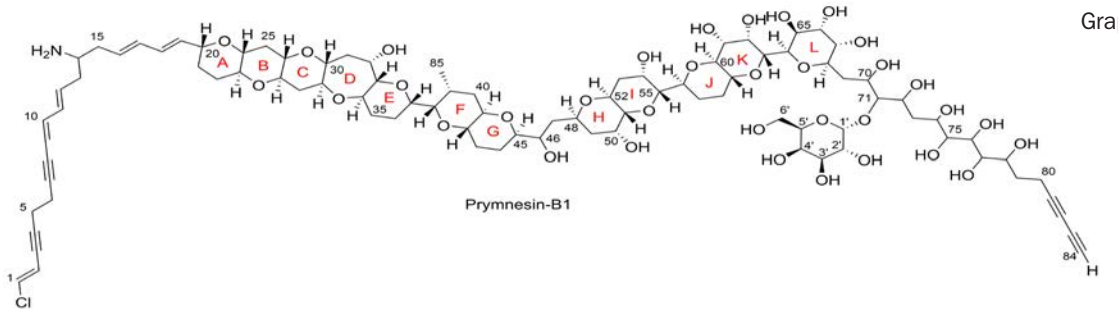
Dr. Duerfeldt represents the Institute for Natural Products Applications and Research Technologies and the Department of Chemistry and Biochemistry, Stephenson Life Sciences Research Center, University of Oklahoma, Norman, Oklahoma.

Upon hearing of the award, Dr. Duerfeldt related, "I feel extremely honored to be awarded the Jack L. Beal Award. As a young lab, it is exciting to know that the work we are doing is catching the attention of prominent scientists and that the scientific community feels as though the contribution was as impactful as we did. Nate and Jesse are two very talented students and I am very grateful for their tenacity in conducting these studies while helping to initiate other projects. We thank the ASP and *J. Nat. Prod.*, and are thrilled to be honored among previous award winners."

A two-tier process was used to determine the winners of the best papers published in *J. Nat. Prod.* in 2016, with editors Drs. Daneel Ferreira, A. Douglas Kinghorn, Cedric J. Pearce, Philip J. Proteau, and Steven M. Swanson having nominated two papers each for the Schwarting Award and one each for the Beal Award. ASP President Cindy J. Angerhofer then appointed an ad hoc committee consisting of Drs. Shmuel Carmeli, Chair (University of Tel Aviv, Israel), Mark Hamann (Medical University of South Carolina), and Amy Wright (Harbor Branch Oceanographic Institute, Florida Atlantic University), to make the final selections.

The corresponding authors of these papers will receive a check and a plaque from the Foundation of the American Society of Pharmacognosy in honor of their achievement. The above-mentioned papers may be accessed from the home page of the *J. Nat. Prod.* (http://pubs.acs.org/journal/JNP). Congratulations to Drs. Hansen, Larsen and Duerfeldt and their co-authors! ■

Prymnesin B1



Graphical abstract depicting sclerotiamide, isolated from a fungus.

Van Skaik: New Director of the Lloyd Library and Museum

We welcome Ms. Van Skaik to her new position and look forward to getting to know her as she directs the library and museum through this next chapter in its history.

By Dr. Amy Keller

Ms. Patricia Van Skaik has assumed the position of Director of the Lloyd Library and Museum. The Lloyd Library is home to the ASP archives and first published the journal *Lloydia*. This journal, now known as the *Journal of Natural Products*, became the flagship journal of the ASP.

ASP President Cindy Angerhofer told the *Newsletter*, "The Lloyd Library has long been a partner of the ASP, with it's marvelous historical collections of documents and artwork related to botanicals and natural medicine, including archives of our Society. I welcome Ms. Van Skaik and the breadth of experience she brings as the new director of this fascinating and vital resource."

Ms. Patricia Van Skaik

COURTESY OF LLOYD LIBRARY AND MUSEUM

Ms. Van Skaik is honored to lead an institution that has been devoted to the sciences and natural products, especially pharmaceuticals, for more than 100 years. "I value the longstanding partnership with the American Society of Pharmacognosy and its significant contributions to scientific research. We look forward to continuing to acquire collections and provide access to resources to build upon our nearly 60 years of collaboration." Ms. Van Skaik hopes to focus on outreach and community engagement, in addition to the library and museum's mission of supporting researchers and scientists.

Ms. Skaik previously served as Manager of the Genealogy and Local History Department of the Public Library of Cincinnati and Hamilton County, Cincinnati, Ohio. Her strengths include history, special collections, and library management, as well as storytelling. Previous curation projects, including work describing Cincinnati's brewing past, make her especially qualified for this position.

The relationship between the Lloyd Library and the American Society of Pharmacognosy can be traced back to when the first ASP President, Dr. Varro Tyler, approached the library about taking over the publication of *Lloydia* in 1959. While the journal is no longer published with the Lloyd as of 1995, it is an integral part of the Society's history. A number of ASP members serve on the Lloyd's Honorary Advisory Board, like Drs. John Beutler, Bob Pettit, Mansukh Wani, and Mr. Mark Blumenthal. In the last decade, the ASP archives have found a home at the Lloyd, and a number of key ASP members, like Drs. Tyler and Norman Farnsworth have entrusted their professional archives to the Lloyd. We welcome Ms. Van Skaik to her new position and look forward to getting to know her as she directs the library and museum through this next chapter in its history. ■

Ms. Van Skaik hopes to focus on outreach and community engagement, in addition to the library and museum's mission of supporting researchers and scientists.

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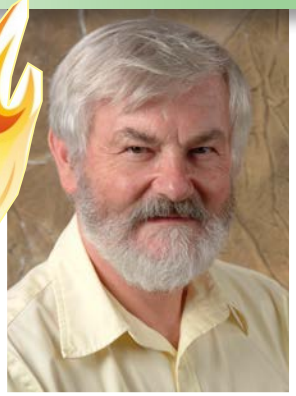
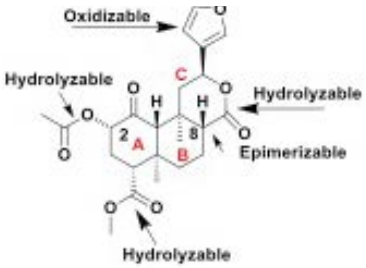
Hot Topics in Pharmacognosy: Miscellaneous Musings from the Current Literature

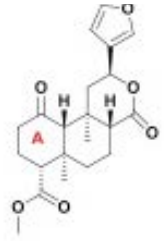


By Dr. David Newman

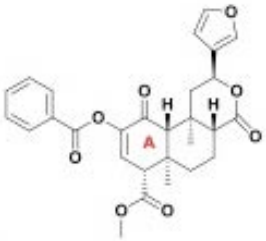
The three recent articles that I will be commenting on "cover the waterfront" from plant, through marine microbes to fungi, though no marine life was disturbed during the discussion!



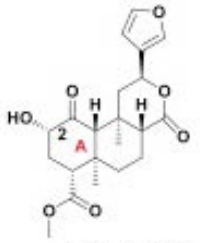
1. Salvinorin A
KOR Selective agent



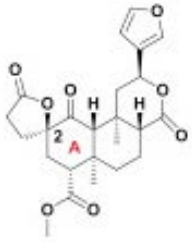
2. Desacetoxy salvinorin A
Inactive at KOR



3. Kurkorin
MOR Selective agonist



4. Salvinorin B



5. Rigid Spirobutyrolactone Derivative
KOR agonist. Inversion at C^2

The first is a paper by an international group from the US and New Zealand, with lead author Sherwood at the School of Pharmacy at the University of Kansas, Lawrence, Kansas.[1] In this paper, they studied the neoclerodane diterpenoid salvinorin A (1), well known as an hallucinogen initially used by the Mazatecs, an indigenous group from Oaxaca, Mexico, who either chewed or smoked the leaves of the host plant *Salvia divinorum*.[2] The potency of this molecule is due to its highly selective *kappa*-opioid receptor agonist (KOR) property, and in addition to salvinorin A, a significant number of variations on the structures are shown in the supplementary information in the Cruz *et al.* paper.[2]

In this report, they took account of the chemical labilities of salvinorin A, including a furan ring that could be oxidized, an epimerizable center at C^8 and hydrolysable moieties including ester, lactone and acetate groups as shown in (1). If one removes the acetoxy group at C^2 (2), then the compound is completely inactive as a KOR agonist, and if the acetate is converted to a benzoate, with one bond in the A ring oxidized, then the resultant compound kurkinorin (3) is now a *mu*-opioid receptor agonist with no *kappa* activity.

The authors postulated that the dysphoric effects of KOR agonists might be due to different KOR-mediated pathways than those causing the analgesic effects, then it might be possible to synthesize new agents (agonists) based upon the salvinorin A skeleton with improved pharmacologic activities and/or resistance to hydrolysis in microsomal preparations *in vitro* which may or may not correlate with *in vivo* efficacies. Starting with salvinorin B (4) obtained by simple hydrolysis from (1), followed by ruthenium catalyzed hydrohydroxy-alkylation at the C2 hydroxyl, the rigid KOR agonist (5), a spirobutyrolactone, was obtained. This compound had epimerized the C-O linkage at C2 and was found to be as active as salvinorin A as a KOR agonist, but was significantly more resistant to microsomal degradation *in vitro;* it did exhibit similar activities/time courses in *in vivo* testing as its parent compound. The correlations between KOR activities *in vivo* and *in vitro* were not linear but this is very frequently found, particularly in studies on opiod and related receptors due to the multiplicity of effects that modulation of these receptors can cause.

Of significant interest is that, in addition to being a rigid molecule that can interact

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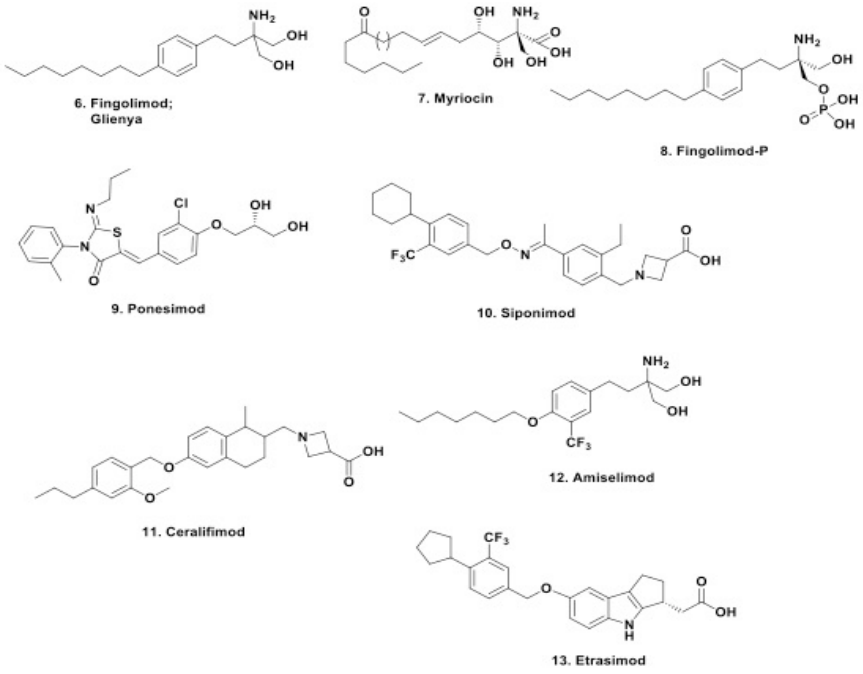
with this receptor at levels comparable to that of salvinorin A (EC_{50} values of 600 pM in each case), is that the C^2 epimer of salvinorin A is completely inactive. Thus, this work has opened up new areas on this molecule that can be further modified to improve pharmacological stability and perhaps target the derivative(s) to other opioid receptors as shown with the benzoate derivative of salvinorin A, kurkinorin (3). If the authors could make the epimer of the spirobutyrolactone, then its biological activities may be of significant interest. This paper demonstrates what can be done with old natural product molecules that may have significant potential in the future.



The second paper is from the Piel group at the ETH Zürich, Zürich, Switzerland,[3] and condenses an immense amount of work into a relatively short paper in the April 2017 issue of *Nature Chemistry,* though the supplemental information covers over 120 pages. If one goes back to the April 5 issue of *Nature* in 2014, the same group published their "tour-de-force" on the interrogation of the uncultivated *Entotheonella* bacterium that was shown to produce at least 30 of the biologically active agents isolated from the sponge *Theonella swinhoei* strain Y.[4] Towards the end of that paper, they pointed out that the whole "reorganization" of the initial ribosomal peptide (the acronym for which is "RiPPS", or ribosomally synthesized and postranslationally modified peptides) to produce the agents found, amounted to just seven enzymes. In this recent paper, they now describe the function of these enzymes, using as their exemplar, the most complex agent so far isolated from that bacterium, the polytheonamides, which they had identified as the product of such a mechanism in a paper in 2012.[5]

In this latest paper,[3] plus an earlier one in 2016 published in *Current Opinion in Chemical Biology*,[6] they demonstrated that it is possible to transfer the necessary biosynthetic complexes to heterologous hosts. In the first series of experiments reported in the COCB paper and references therein,[6] they used an *Escherichia coli* strain to amplify the necessary gene products and demonstrated that the two previously identified *"Entotheonella"* phylotypes initially named as TSY1 and 2 in their 2014 *Nature* paper,[4] have now been renamed with TSY1 being "*Candidatus Entotheonella* factor" and TSY2 being *Candidatus Entotheonella gemina*." Further investigation demonstrated that "E factor" contained the clusters for most of the bioactive polyketides and peptide natural products reported from *T. swinhoei* Y. These included onnamides, cyclotheonamides, keramamides, konbamides, nazumamides, pseudotheonamides and theopederins. Both of the renamed microbes also contain many other putative natural product clusters including nonribosomal peptides (NRPS), polyketides and RiPPS. The identified structures are given in Figure 3 in the *COCB* paper and demonstrate the versatility of this microbe.

Also as reported in this paper,[3] the Piel group were able to express the missing C-methylation enzymes in order to perform the 17 C-methylations required to produce the final polytheonamides. These methylations at non-activated carbons are probably the most remarkable feature of these peptides. It turned out from comparison with other C-methylases, that the required enzymes might be cobalamin (B_{12}) dependent methyltransferases. Attempts to use expression vectors in *Streptomyces* or *Pseudomonas* hosts failed, but two rhizobial strains (*Sinorhizobium meliloti* 1021 and *Rhizobium leguminosarum* bv *viciae* 3841) that contain a cobalamin pathway were used. The latter organism has a potential proteusin locus with homologs to three of the potential enzymes. It turned out that the latter bacterium produced more of the required protein, so all further work was performed using that microbe. Using these methodologies, 13 of the required 17 methylations were seen. So the inspired usage of *Rhizobium* has led to an almost complete expression of the required proteins and production of their product(s).

Since I cannot obtain permission to show "Figure 6" in the 2017 *Nature Chemistry* paper,[3] I recommend that readers attempt to obtain a copy of that paper for themselves as the color-coded figure shows the final resultant of this

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highly complex process. It is also of historical interest that the first RiPP to be used as an antibacterial was nisin and it took roughly 60 years from its discovery in 1928, to demonstrate its genetic origin in 1988.

The third and last paper is a "Perspective" in the *Journal of Medicinal Chemistry*[7] that discusses the current status of molecules that have evolved from the Novartis compound, fingolimod (6; Gilenya®) which was approved as a treatment for patients with the relapsing form of multiple sclerosis (MS) in 2010. This compound was derived from an old fungal metabolite, myriocin (7). The details of the evolution of this drug from the original fungal product was first described by Brinkmann et al from Novartis in 2010[8] and that paper in *Nature Reviews of Drug Discovery* currently has over 500 citations in Scopus. It should also be noted that fingolimod is actually a prodrug; the in vivo phosphorylated version is (S)-fingolimod-phosphate (8).

Currently this derivative of that 1969 fungal secondary metabolite has the following derivatives in Phase III and Phase II clinical trials against a variety of diseases including MS, psoriasis, and ulcerative colitis / Crohn's disease.

- Ponesimod (9) from Actelion/Roche is in Phase III under NCT02907177 for MS patients with active relapsing disease.
- Siponimod (10) from Novartis in Phase III under NCT01665144 for MS patients with secondary progressive MS (the EXPAND trial).
- Ceralifimod (11) from Ono Pharmaceutical/Merck KGaA was in Phase II under NCT01226745 as an extension trial in patients with relapsing-remitting (RR) MS. However, Merck KGaA decided not to continue into Phase III trials with no reason given other than it was not related to any safety and efficacy findings.
- Amiselimod (12) from Mitsubishi Tanabe Pharma is in Phase II clinical trials under the code number MT-1303 and has completed studies at this level for RRMS under NCT01742052. It has also completed trials at the same level against Crohn's disease and chronic plaque psoriasis. Currently there is an extension Phase II trial under NCT02389790 against Crohn's Disease.
- Etrasimod (13) from Arena Pharmaceuticals is in Phase II clinical trials under NCT03139032 for the treatment of ulcerative colitis.

This perspective also covers a very significant number of chemical variations in addition to those above at levels from Phase I to preclinical studies and should be used as a guide to what can be done from the initial discovery of a bioactive natural product. All of the compounds listed can be considered to have started from the original discoveries related to myriocin's mechanism of action, as it was the first agent shown to have activity as a lysophospholipd edg receptor agonist. It is also of interest to note that Mitsubishi Tanabe Pharma were the original developers of fingolimod, not Novartis. ■

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Meet a New ASP Member

Dr. Nandakumara D. Sarma is our featured new member in this summer issue of the Newsletter. *Dr. Sarma is Director of Dietary Supplements and Herbal Medicines at the United States Pharmacopeia (USP) in Rockville, Maryland. His background in pharmacognosy is well suited to his position contributing to the rigor of botanical quality. He also shares his love of running with us. We are grateful for a chance to officially welcome Dr. Sarma.*

By Dr. Dan Kulakowski

How did you hear about the ASP?
As a pharmacognosy researcher, I had the fortune of being in the company of the eminent scholars who belonged to the association. I have also known about ASP widely through professional conferences and the *Journal of Natural Products.*

Why did you join ASP?
The motivation for my joining ASP was the respect for the association and its activities. It is a privilege for me to belong to an association with illustrious history and commitment "to promote and develop the science of pharmacognosy and all aspects of those sciences related to natural products." My joining the ASP was long overdue!

Dr. Nandakumara D. Sarma

POLASANI VANDANA

What would you like to achieve through your membership?
The association provides an opportunity to network with the volunteers and distinguished members. Besides, it is a wonderful forum of the like-minded to serve the scientific community.

Do you belong to any other scientific societies?
I am a member of the Society of Toxicology.

What are your current research interests in pharmacognosy?
My position at USP provides an excellent opportunity to contribute to the quality standards for natural products, which helps me fully utilize my research experience and realize my interests. It involves working with eminent pharmacognocists to deliberate upon cross-functional areas such as the nomenclature, safety, and labeling of natural products, and setting specifications for their quality (including methods and acceptance criteria for the identity, purity, and limits for contaminants). A few areas of current engagement are our work on DNA-based methods for botanical identity, limits for pesticide residues, and quality standards for cannabis. Besides science, my current interests and activities also involve consideration of regulations for natural products as dietary supplements or traditional herbal medicines. Our team is passionate about advocating for quality of natural products in our interactions with industry, healthcare professionals, regulators, and consumers. We contribute to the USP botanical quality standards and guidelines through the *Dietary Supplements Compendium* and *Herbal Medicines Compendium.*

What is your scientific background?
My research background involved isolation, structure elucidation, and pharmacological evaluation of immunomodulatory natural products from Indian medicinal plants. I had isolated and characterized isoquinoline alkaloids and used animal and cell culture models to assess immunomodulatory activities in a septic shock model. This work took me to investigation of the effect of natural products on cell-signaling pathways and the design of a knock-in mouse model through molecular biology methods. Although the latter activity is not directly related to conventional pharmacognosy, the cross-functional pharmacy training helped me to ask questions and explore the answers.

What inspires you in your work?
Our inspiration for working on botanical quality standards is the impact on public health, considering that dietary supplements and herbal medicines are widely used by over 50% of the global population. Appropriate quality standards are necessary to establish identity and purity, discriminate potentially toxic substituents and adulterants, and to control for contaminants. The complex scientific demands and challenges offer an opportunity and an inspiration for us to utilize the cross-functional approaches to provide constructive solutions to a wide stakeholder community.

What do you like doing in your spare time?
I enjoy running long distances in my leisure time. It is a great way to connect with nature! ■

New Members of ASP 2017

ASP would like to welcome new members. The Society's main objectives are to provide the opportunity for association among the workers in pharmacognosy and related sciences, to provide opportunities for presentation of research achievements, and to promote the publication of meritorious research. New members include 14 domestic full members, 4 international full members, and 15 associate members. We look forward to meeting you and learning more about you and your work.

ACTIVE MEMBERS

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Chicago, Illinois

Welcome to ASP!

Fraudulent Foods

By Ms. Laura DerMarderosian, and Dr. Ara DerMarderosian

Both pharmaceuticals and foods alike have been adulterated throughout history. The earliest cases of deception in the food industry go back thousands of years and include the adulteration of olive oil, wine, and spices.[1] Roman winemakers inadvertently sweetened wine with lead acetate, not knowing it was poisonous. It has been said that King Herod experienced dementia, hallucinations, paranoia, extreme thirst, rheumatism and other signs of lead poisoning, due to this consumption of poisoned wine.[1,2] Selling fake tea ("lie tea") was widespread. In 1851, the *British Medical Journal* reported a scandal of colorings and adulterants added to tea, which included sand, dust, and gypsum.[1, 3, 4] Copper salts were also used to add color to green tea, pickles, and French beans.[1, 4] A famous case of adulterated or "swill milk" from cows being fed distillery waste occurred in the 1870's. The milk was watered down and chalk or plaster was added to give the milk a richer, whiter, color, sickening many people.[5]

In the early 1800's, a German chemist named Frederick Accum exposed many of these deceptions in a book entitled, *A Treatise on Adulteration of Food, and Culinary Poisons*.[1,4] In 1855, in Britain, a physician named Arthur Hill Hassall, was of the first to use science-based evidence to identify adulterants in foods, drinks, and drugs, employing botany, chemistry, physics, and microscopy. Many of his observations were published, and were widely read.[1,4]

Eventually, laws were passed to protect consumers from adulteration in England, and later in the United States. In Britain, in 1858, the Bradford sweets poisonings found that lozenges normally made with sugar, gum, and cheap filler such as plaster, had been accidentally altered to contain arsenic, poisoning over 200 people, and killing 20. This prompted the British government to pass regulations in 1868 to avoid poisons being handled by those other than chemists.[1, 6]

In 1906, the United States Congress passed both the Meat Inspection Act, and the original Pure Food and Drugs Act, prohibiting the manufacture and interstate shipment of adulterated and misbranded foods and drugs here in the United States.[7] Under this act, the law directed that any medicines must have their quantities listed on the labels. Still, adulteration problems persisted. In the early 1930s, a famous case involving a fluid extract of ginger, termed "Essence of Jamaica Ginger" (or "Jake") was adulterated with tri-ortho-cresyl-phosphate, or TOCP, by a pair of amateur chemists, trying to add a cheap, undetectable compound to the extract, in order to avoid compliance with the laws. TOCP is a plasticizer, initially thought to be non-toxic, but was later determined to be a poisonous neurotoxin. Those who drank this "Jake," over time developed muscle paralysis in the limbs. This led to an abnormal gait, with the lower limbs dragging abnormally when attempting to walk. This characteristic shuffle was termed "Jake leg." Many cases occurred in the South and became the subject of several "blues" songs recorded during this time entitled, "Jake Leg Blues," and others. Jake Leg Paralysis was estimated to have affected up to 60,000 Americans.[4, 8, 9] The Food, Drug, and Cosmetic Act of 1938 mandated that manufacturers must be required to prove

Original artwork by Ms. Laura DerMarderosian depicting Fraudulent Foods

MS. LAURA DERMARDEROSIAN

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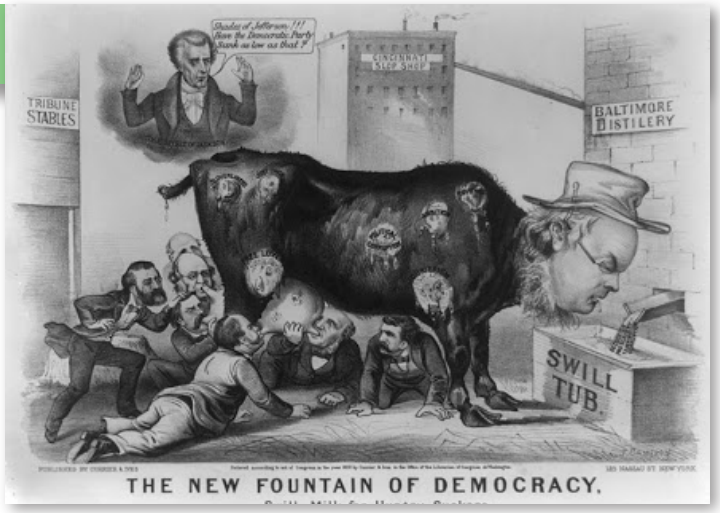
that a drug was safe before it was marketed. A major contributor to further regulation came with the Kefauver-Harris Act in 1962 ('encouraged' by the thalidomide tragedy in 1961 in Europe, which was linked to 10,000 cases of serious birth defects there, but not licensed here in the US due to lack of safety evidence.) This amendment mandated that all new drug applications demonstrated effectiveness for the stated purpose, as tested with randomized, double-blinded, controlled clinical trials.[10, 11]

Food fraud scandals are commonplace in the food industry both in the US and abroad. From the grocery shelves to restaurant menus, deception abounds. Most incidents go undetected. Food fraud can have significant financial consequences and may also result in public health risks.[12] Between 1980 and 2013, 137 unique incidences in 11 food categories were identified, with fish and seafood, honey, spices, and wine being the most common.[13]

Some types of fraud include: Adulteration – defined by section 501(b) of the Food, Drug, and Cosmetic Act to be adulterated if it fails to conform to compendial standards of quality, strength, and purity.[14] A contaminant is an example of this. Examples of contaminants are pesticides, or those from industrial processing such as polychlorinated biphenyls which have both been issues in the food supply for decades.[15] Economically motivated adulteration (EMA) is "the fraudulent, intentional substitution or addition of a substance in a product for the purpose of increasing the apparent value of the product …for economic gain" and can be of six types, including counterfeiting, dilution, concealment, unapproved enhancements, mislabeling, and substitutions.[13, 16] Tampering with a product and packaging fraudulently, diversion to unintended markets, and counterfeit product and packaging are also included in what is defined as fraudulent.[16]



Historical cartoon depicting the dangers of swill milk and corruption leading to the contaminated milk.

In certain applications, analytical detection techniques are being employed to determine food adulteration, including physical (macro/microscopic methods,) chemical techniques (e.g. HPLC,TLC, and GC) and molecular methods (e.g. PCR)[19,20,21]

The shift from an agricultural to an industrial economy, along with an increasing chain of commerce (including processing/transporting/packaging) in the food industry, has dissociated the consumer from the origins of these products. Some good advice is to buy food in its whole/freshest form, and prepare more meals from "scratch." The negative aspects of diminished nutritional value from over-processing will be eliminated. Vitamins and other nutrients will be retained. Excess salt, sugar, flavor enhancers, and other artificial additions can be avoided. Most importantly, the satisfaction from knowing that no fraudulent activity was involved in the making of your meal may improve your health. ■

DATABASES AVAILABLE TO HELP TRACK AND DECREASE FOOD/PHARMACEUTICAL FRAUD, AND RAISE AWARENESS INCLUDE

1. USP (U.S. Pharmacopeial Convention's Database – Food Chemicals Codex,8th ed. – Includes 1305 records composed of both scientific and media reports.[17,18]
2. National Center for Food Protection & Defense (NCFPD) – contains documented Food incidences of food fraud since 1980.
3. Federal Trade Commission (www.FTC.gov) – includes deception in advertising.
4. USFDA (U.S. Food & Drug Administration) – Monitors foods and drugs (www.fda.gov).
5. ABC-AHP-NCNPR (American Botanical Council-American Herbal Pharmacopoeia-National Center for Natural Products Research) website, which is a "coalition of herb quality and identity experts" who examine the adulteration of suspected herbal materials globally.[4]

Fraudulent Foods: Examples of Common Fraudulent Foods

ADULTERATED FOOD	COMMENT	POTENTIAL & PAST HARM (OTHER THAN WASTE OF CONSUMERS MONEY)
Seafood	2% of imported seafood is inspected by FDA Almost all red snapper sold in the US is fake (common substitute for this is tilefish - very high in mercury 74% sushi tested, not what it claimed to be Those ordering white tuna got no tuna at all, 94% of the time Sometimes substituted with cheap escolar fish	High mercury levels contraindicated in pregnancy Adverse GI effects occur from escolar
Olive oil (Truffle oil)	Substituted with lower cost oil, (i.e. from Greece or Turkey, not from Italy) Thinned out with cheaper seed oils or vegetable oils Addition of chlorophyll pigments for richer look Almost no truffle oil is real, flavored artificially	Undeclared nut oil may cause allergy in sensitive individuals 80,000 people were poisoned upon consumption of rapeseed oil containing aniline toxin
Honey Maple Syrup	May have added cheaper corn syrup, various other syrups, beet sugar Honey from "non-authentic" geographic origin is common, to avoid higher customs duties and tariffs from China Maple syrup can be thinned out with sugar or corn syrup, can contain additives, artificial flavors	Allergy
Wine Champagne	Enhancement of colors Only real champagne originates from France and is labeled as such	
Fruit Juice	Cut with cheaper juices especially in expensive juices such as pomegranate Some juice is only water, dye, and sugar, with malic acid	Dye Allergies Clouding agents, which enhance the natural look of the product, and can cause cancer
Spices Saffron, paprika, chili powder, black powder, turmeric, oregano	Saffron is the most expensive spice so is more subject to adulteration. Spices have been found to contain added glycerin, wood dust, tartrazine dye, borax Sudan-red dyes, (carcinogenic), used to color red spices Turmeric containing peanut shells Black pepper and others known to have added starch, seeds, flower, twigs, chopped weeds Different botanical genre contamination	Dye / dust allergy May cause cancer Peanut allergy issues

Fraudulent Foods: Examples of Common Fraudulent Foods

ADULTERATED FOOD	COMMENT	POTENTIAL & PAST HARM (OTHER THAN WASTE OF CONSUMERS MONEY)
Milk products (cheese, butter, etc.)	Cows' milk has been found to contain milk powder and other ingredients Cows' milk substituted for buffalo & goat milk in cheese Wood pulp added to parmesan cheese to increase volume sometimes close to 8%	Allergies Melamine illness from baby formula, sickening 300,000 infants w/6 reported deaths. Diacetyl flavoring in butter linked to Alzheimer's disease
Coffee	Ground coffee cut with leaves, twigs, roasted corn, and other grains	
Tea	Undeclared leaves from other plants, and color additives present	
Kobe Beef and other meat	99% of Kobe beef claims are lies, very scarce Largely un-regulated restaurant/food chain–choice vs USDA Prime–less than 2% beef grades USDA Prime Only small amount of beef is truly grass fed Beef products adulterated w/horse meat in Europe	Class actions lawsuit with chain restaurant serving Kobe Beef during a period when meat was banned, (between 2001-2012) Religions concerns with certain meats, i.e. Halal meat
Wasabi	>90% of fake wasabi reported Most made with dried horse radish, mustard flower, and green dye	
Various other adulterated foods **Rice** **Wasabi** **Tahini** **Pet food**	Undercover video shows fake rice being made in China from plastic resin and sweet potato Paraffin has been detected in rice	The melamine pet food recall of 2007 caused many animal deaths

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Conference Calendar

The *Newsletter* is pleased to announce the following upcoming conferences and meetings. The events portrayed here reflect what listings and notices the *Newsletter* has specifically received. For a more extensive calendar, please visit the ASP website at www.pharmacognosy.us. If you have a conference or event you would like mentioned, please send us relevant information, including any graphics or appropriate fliers, at asp.newsletter@lehman.cuny.edu.

Gordon Research Seminar:
Natural Products & Bioactive Compounds
July 29-30, 2017
Andover, New Hampshire
grc.org/programs.aspx?id=17477

10th European Conference on Marine Natural Products
September 3-7, 2017
Kolymbari, Crete, Greece
ecmnp2017.com/

ASP Annual Meeting
July 29-August 2, 2017
Portland, Oregon
asp2017.org/

International Meeting on Medicinal Plants and Natural Products Research
September 4-5, 2017
Macau, Hong Kong
meetingsint.com/pharma-conferences/naturalproducts

254th American Chemical Society National Meeting
August 20-24, 2017
Washington D.C.
callforpapers.acs.org/dc2017

4th International Conference and Exhibition on Marine Drugs & Natural Products
June 11-13, 2018
Rome, Italy
http://naturalproducts.pharmaceuticalconferences.com/

Brief News from Washington

By Dr. Georgia Perdue

- **The stop gap budget to fund the government until September 2017 includes an additional $2 billion for the National Institutes of Health (NIH), with $300 million for the "Cancer Moonshot" effort.** Sources tell me when the full budget for 2018 is considered, there will be changes, i.e., decreases, in several areas and agencies which received increases for now.
- In late April 2017, National Cancer Institute (NCI) Director Douglas R. Lowy commented on the March 2017 report: **"Annual Report to the Nation: Cancer death rates continue to decline." The report dealt with rates from 1975-2014.** The report is a collaborative effort by the American Cancer Society, Center for Disease Control, and NCI. In a separate statement, Director Lowy noted that for most cancers in men, women, and children, there is a continued decline in mortality. When considering most other causes of death, cancer is the only one in which mortality decreased by 1.7% in 2015. Dr. Lowy also commented on avelumab (BAVENCIO®) **"for a rare and aggressive skin cancer"** for which there had been no effective treatment. "NCI's Center for Cancer Research played an important role in the early trials that led to approval, something we can all be proud," added Dr. Lowy. (see online, *Journal of the National Cancer Institute [JNCI]*)
- **On World Malaria Day, April 25, 2017, with the theme, "End Malaria for Good," National Institute of Allergy and Infectious Diseases (NIAID) Director, Dr. Anthony Fauci, noted World Health Organization data in a statement: between 2000 and 2015 the worldwide rate of new malaria cases and deaths decreased by 41 and 60 percent, respectively. But, in 2015, "an estimated 212 million new malaria cases and 420,000 deaths occurred." NIAID's research program continues its efforts to end malaria through its comprehensive research program, many funded through International Centers of Excellence in Malaria Research, established in 2010. NIAID is also conducting and funding research to find new drugs in the wake of malarial drug resistance.**
- **In early March 2017, President Donald Trump nominated Dr. Scott Gottlieb to be the next Commissioner of the Food and Drug Administration (FDA). From 2003-2004, Dr. Gottlieb had been Deputy Commissioner under the Bush Administration. Afterwards, he was FDA's Director of Medical Policy Development.** He currently serves on several boards as an advisor (GlaxoSmithKline plc, Glytec, Inc., and Tolero Pharmaceutical, Inc.). On April 5, 2017, Senator Lamar Alexander, Chairman of the Senate Health, Education, Labor and Pensions Committee met with Dr. Gottlieb. After the meeting, the Senator noted "…he is well qualified to lead the FDA," adding that he would be discussing the 21st Century Cures Act with Dr. Gottlieb after his confirmation hearing. **On April 27, 2017, the Committee approved Dr. Gottlieb by 14 to 9 (all 14 Republicans voted in favor).** Senator Patty Murray, the ranking Democrat, voted against him because of

Sources tell me when the full budget for 2018 is considered, there will be changes, i.e., decreases, in several areas and agencies which received increases for now.

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"Annual Report to the Nation: Cancer death rates continue to decline." The report dealt with rates from 1975-2014.

Director Lowy noted that for most cancers in men, women, and children, there is a continued decline in mortality.

his "entanglements with industry…." Dr. Gottlieb is a cancer survivor. He will resign from his positions on several boards of pharmaceutical companies and think tanks, such as the American Enterprise Institute.

- **Finally, on May 9, 2017, the Senate confirmed Dr. Scott Gottlieb as FDA Commissioner. The vote was 57 to 42 in favor of confirmation. A few Democrats voted with the Republicans.**
- Renewed interest in **fighting antibiotic resistance** was announced in late March 2017. The initiative, named **CARB-X, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator,** was started in July 2016 and only was recently funded.
- **On April 25, 2017, the FDA sent warning letters to 25 companies accusing them of preying on vulnerable cancer patients with their "bogus cancer cures."** FDA publicized its actions for consumer access. A couple examples of the companies and products advertised include: "Amazing Sour Sop Inc.," for its "Miracle Unleashed" in capsules, tea leaves of *Graviola* "…a potent cancer killer….." One of its chemicals kills colon cancer cells. Another company, Hawk Dok Natural Salve LLC…contains "sheep sorrel and blood root," intended to pull the cancer out of the skin.
- Dr. Janet Woodcock testified on Capitol Hill saying that the **FDA would have to hire specific scientists to implement the 21st Century Cures Act. One example, rare disease specialists.**
- FDA is considering establishing an Office of Patient Affairs "to engage patients in the drug development process."
- Recently the *Washington Post* had a long article on **herbarium specimens**. Those who are familiar with or have used the process would enjoy it (March 2, 2017). [I still have my presses; my many specimens are at the Smithsonian along with some of my husband's choice specimens]. **Many of the specimens at Smithsonian are now being digitized**.
- In a March 2017 statement, **Dr. Anthony Fauci said the "unusually large outbreak of yellow fever, now in rural Brazil, deserves careful attention by world health authorities …."** He also noted **this outbreak "… comes as the Zika virus, spread by the same mosquito as yellow fever virus, [which] continues to affect countries throughout the Americas."** Dr. Fauci noted that in 1793, the Philadelphia yellow fever epidemic claimed thousands of lives in the US. It seems with all the easy worldwide travel, if left unchecked, this could become a grave problem!
- **It has been reported that a Mediterranean diet "may significantly reduce the types of breast cancer."** (see *Journal of Cancer* March 5, 2017).
- **Most everyone is familiar with the HeLa cancer cells, named after Henrietta Lacks, who died in 1951 of cervical cancer. Her cells were preserved for research purposes.** A made-for-TV movie and a book about her life have recently surfaced. Her cells helped in the quest for anticancer drugs. However, back in the 1980s, the premier KB cells used by NCI in their research labs became contaminated with HeLa cells. NCI blamed the KB cells. A big dustup occurred. The problem was not with the KB cells, as one notable NCI scientist loudly claimed. It was contamination with HeLa cells. The person who pointed this out was reassigned from the cancer program. (I know this story first hand, and its terrible details, because that person who dug deeply for the answer to the contamination was my late husband. He later was vindicated). What prompted me to reveal a fraction of the story was a wonderful article in the *Wall Street Journal* by Mr. Richard Harris entitled, *Dismal Science in the Search for Cures* (April 8, 2017). I highly recommend it! It is especially relevant in view of the more recent contaminations at NIH laboratories and who knows where else.
- Everyone who depends on National Science Foundation, NIH, and other similar agencies for grants, which come out the abundance of Federal money in annual budgets, are beside themselves, almost hysterical, because the President's 2018 budget calls for cuts to these sacrosanct agencies. There will likely be cuts, but as with every fiscal year, the cuts are modified before all is said and done. I believe that many of the budgets are not sustainable with all the debt that has been accumulated. So, I suggest everyone take a deep breath and remember that the sky is not falling. Updates will be provided with each future column. ■

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

By Ms. Devhra BennettJones

On February 21, 1972, President and Mrs. Richard M. Nixon arrived in Beijing, China, for an eight day visit filled with official meetings, sightseeing and cultural events. Upon the conclusion of their visit, a Shanghai Communique, issued jointly by the United States and China, pledged that both countries would work for "normalization" of relations. Nixon's diplomacy with the People's Republic of China specifically called for scientific exchanges in the quest to build bridges.[1] In the US, the National Academy of Science was well-prepared with their Committee on Scholarly Communication with the People's Republic of China established in 1966.[2] In November 1972, the US lifted the 22-year ban on travel to China which paved the path for the 1974 National Academy of Sciences Delegation.[3] Esteemed ASP members Drs. Norman R. Farnsworth, S. Morris Kupchan, Thomas H. Maren, George R. Pettit, and Michael A. Schwartz, were among the medicine and pharmacology ambassadors. Dr. Pettit composed a travel log of their 27 day journey in the People's Republic of China.[4] The following is one of three excerpts that will appear in From the Archives.[5]

Dr. George R. Pettit

INSTITUTE OF MATERIA MEDICA SHANGHAI.[6] FRIDAY, JUNE 14.

On Friday morning, June 14, we gathered at 8 a.m. for the approximate 10-minute ride by car to the Institute of Materia Medica. Transportation in Shanghai has been by means of seven cars with two of us assigned to a particular car, host and driver. In my case, I was with Morris Kupchan and our host was Dr. Bai Dong-Lu, deputy head of the Organic Section at the Materia Medica. He is 38 years old and has had 2 years postdoctoral work (1965-1967) at the Bioorganic Institute, Prague, is married to a physician and has one daughter 4 years old. Interestingly, Dr. Bai has studied English for approximately 1 year, primarily through lessons given over the Shanghai radio station. We were able to converse quite well and he proved to be a most helpful, cheerful and thoughtful host. During our period with him we learned that he was trained in the Shanghai Pharmacy School and graduated in 1957. At that time he joined the Institute of Materia Medica and in effect went through a period of graduate training with Professor Kao and another senior organic chemist.

Now, turning to the Institute, we arrived on a very bright and cheerful 70° morning and were greeted by a leading member of the Revolutionary Council and senior staff of the Institute. After a brief introduction the leading member quickly turned proceedings over to Professor Kao, a responsible member of the Institute. Professor Kao, appeared to be a man in his late 60's or early 70's and displayed characteristics of a distinguished scholar and gentleman. Later, I learned in a personal conversation that he was a student with Sir Robert Robinson at Oxford.

The Institute has a staff of approximately 470 of whom 370 are technical people. Before the liberation (1949) the staff numbered four or five. Presently the Institute's mission is uncovering agents for cancer, CNS problems, chronic bronchitis, hepatitis, liver diseases and contraception. They are approaching these problems by isolation and synthetic studies as well as pursuing an antibiotic program.

When the opening statements were concluded, we left on a tour of the Institute. The two principal buildings of approximately three floors a piece appeared quite old and apparently will be replaced by a new building on an adjacent site where construction has just begun. Most of the work reported to us had been carried out some years ago and one had the very definite impression that work in the Institute must have come nearly to a standstill during the cultural revolution (approximately 1966 through 1970). At the time of the cultural revolution the

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Institute was taken out of the Chinese Academy of Science and placed under control of the Shanghai Revolutionary Council. The Institute is still under that jurisdiction and its missions have been changed to concentrate, for example, on the cancer problem and chronic bronchitis. Some aspects of the cancer work proved particularly interesting. The plant vinca (*Catharanthus*) *rosea* (Apocynaceae) grows, for example, in the Shanghai area and in South China The Materia Medica group has developed a simple procedure for isolation of vincristine (VCR) in gram quantities and vinblastine (VLB) in kilogram quantities. They claimed to have greatly improved and simplified the isolation procedure by changing solvents and chromatographic methods. For the isolation they used the whole plant and [I] believe [I] mentioned that vincristine occurs in a concentration of about 1 part per million. Even more interesting was the situation with camptothecin. Tilis Institute was given the task of preparing camptothecin in quantity for clinical use. Now the production of camptothecin is carried out in one of the pharmaceutical factories. They have found that camptothecin occurs in highest quantity in the seeds of the *Camptotheca acuminata* tree which grows abundantly in this area of China. The seeds are used for production which of course leaves the tree intact. The yield of pure camptothecin for the seeds is 0.057oo. The camptothecin prepared in this manner is used clinically for stomach cancer and bladder cancer. Of course, the most interesting aspect was that they have been getting good results in stomach and bladder cancer in the clinic and that camptothecin is now being produced in kilogram quantities.

This writer also asked about the drug form and was shown ampules of camptothecin sodium salt at a concentration of 5 mg/ampules. Also, in some other areas of China the crude extract is being used in combination with other substances for treatment of leukemia. By digging into this problem further, it was learned that they are now preparing enough hydroxy camptothecin and methoxy camptothecin for further screening and possibly clinical trial. Prior to reports from our National Cancer Institute, neither the plant nor camptothecin was employed in China for cancer treatment. On the basis of the preceding information it would seem urgently useful to reevaluate our decision concerning the utility of camptothecin.

In the synthetic area, the institute's chemists have prepared the sodium Bunte salt of GMP which they designate AT1438 for use in leukemia. This is a more soluble form. The m-nitro derivative of an ortho type sarcolysin (AT1258) is being used clinically in squamous cell lung cancer. The substance is called nitrocaphane and is also being used in cancer of the nasopharynx. The diethylamino-ethyl ester of N-(a-2'-naphthyloxyacetamideo)-p-amino-benzoic acid (AT236) is being used clinically for malignant lymphoma. This substance has a very good therapeutic index. Since 1958 they have synthesized about 2,000 other compounds for cancer screening.

In other medical areas, their interest in chronic bronchitis has led to the isolation of rorifone from *Rorippa montana* (Wall) Small. This crystalline compound has the structure $CH_3SO_2CH_3(CH_2)_7CH_2CN$ and is now being prepared in quantity by synthesis from castor oil (base hydrolysis first to give w-decanoic acid). This substance is of interest in connection with chronic bronchitis and apparently increases secretion of phlegm and in general reduces he symptomatology of chronic bronchitis. The toxicity of this substance can be reversed by sodium thiosulfate. The synthetic group has been making analogs and to date the $(CH_2)_9$ analog has proved most active.

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At the time of the cultural revolution the Institute was taken out of the Chinese Academy of Science and placed under control of the Shanghai Revolutionary Council. The Institute is still under that jurisdiction and its missions have been changed to concentrate, for example, on the cancer problem and chronic bronchitis.

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Another success has involved the isolation of tetrahydropalmatine from a *Corydalis* species. The compound has sedative and hypnotic effects with rapid onset and the racemic form is now in general clinical use under the name coryanalgine. The levorotatory form is more active and is being isolated from a *Stephenia* species and widely used as a GI analgesic. Another useful constituent which was isolated from *Andrographis paniculata*, a terpene lactone is now being employed for dysentery. A phenolic chromane from *Potentilla frogrioidis* (Rosaceae) is being utilized in gynecology for excessive bleeding. ■

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

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5 Transcription from the manuscript A View of Medicine, Cancer Treatment and Drug Development in The People's Republic of China by Dr. George R. Pettit, pp. 35-39, June 14, 1974.

6 Now the Shanghai Institute of Materia Medica, Chinese Academy of Sciences (SIMM), has a long history of comprehensive drug discovery in China. SIMM developed from the Peking Institute of Materia Medica, Academia Sinica, founded in 1932 by Professor Chenggu Zhao (T. Q. Chou). The Institute relocated to various addresses in Shanghai and now resides in the Zhang Jiang Hi-Tech Park, Pudong New District in Shanghai. SIMM engages in applied studies, develops new theories, methods and technologies. The SIMM researchers focus on treatments of major diseases, such cancers, cardio-cerebrovascular, neuropsychiatric, metabolic, autoimmune, and infectious diseases. SIMM has cultivated innovative pharmaceuticals, such as Artemether, Dimercaptosuccinic acid, Huperzine A, Depsides salts, a modern Traditional Chinese Medicine (TCM), and Antofloxacin Hydrochloride, a novel fluoroquinolone antibacterial agent.

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