21st Annual OXFORD ICSB

April 24th - 27th 2023

at the Oxford Conference Center | 102 Ed Perry Blvd, Oxford, Mississippi

The Oxford International Conference on the Science of Botanicals is an annual meeting to discuss approaches for post market surveillance, risk and safety assessment, quality control and adverse event reporting (AER) for botanical dietary supplements (BDS) and natural products as well as regulatory aspects with perspectives from government, manufacturers and trade associations

Conference Agenda

- Daily Schedule
- Speaker Abstracts
- Speaker Bios

National Center for Natural Products Research
Oxford ICSB
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NOTES

April 24, 2023

Dear Friends,

On behalf of the Organizing Committee, I would like to invite you to present at the 21st Annual International Conference on the Science of Botanicals (ICSB) to be held April 24th – 27th, 2023 in Oxford, Mississippi. The ICSB is organized by the National Center for Natural Products Research (NCNPR), University of Mississippi, and a FDA Center of Excellence.

In addition, attendance at this event will enable you to hear from an outstanding line-up of world-renowned speakers, gain a perspective on developments in natural products and botanicals. Our meeting allows you to focus on the current trends including regulatory aspects find out about the latest research, interact with researchers during the large poster session, and establish collaborations between universities and research institutes and industry.

Oxford is a town with a rich literary and artistic history and home of the University of Mississippi and the NCNPR. With the help of the Oxford Conference Center, we have put together a program of social and entertainment activities to run alongside our rich and informative scientific agenda. You can find additional information regarding this conference at www.oxfordICSB.org. A cooperative agreement between the NCNPR and the Center for Food Safety and Applied Nutrition (CFSAN) at the U.S. Food and Drug Administration (FDA) supports this conference. Our co-sponsors: the Shanghai Institute of Materia Medica/ CAS, China; the Council of Scientific and Industrial Research (CSIR - India); the Ministry of Indigenous Medicine, Sri Lanka; the American Society of Pharmacognosy (ASP); the Society for Medicinal Plant Research (GA); the Korean Society of Pharmacognosy (KSP) and the Japanese Society of Pharmacognosy (JSP).

We invite you to visit the website of the National Center for Natural Products Research at http://www.pharmacy.olemiss.edu/ncnpr to learn more about our research program. Oxford and the Ole Miss campus are a beautiful setting, and we hope you will get to explore them, especially if this is your first time to visit here. If there is anything, we can do to make your visit more enjoyable, please contact us.

Sincerely,

Ikhlas A. Khan, Ph.D.
Director, National Center for Natural Products Research
Director, FDA Center of Excellence
University of Mississippi

Day 1

8:00-9:00 am Opening Onsite Registration-OCC Lobby

Opening Session-OCC Auditorium

9:00-10:30 am

Ikhlas Khan, *Director, NCNPR, University of Mississippi*-Welcome on Behalf of The International Conference on The Science of Botanicals

Donna West-Strum, *Dean and Executive Director, School of Pharmacy, University of Mississippi*-Welcome on Behalf of The University of Mississippi, School of Pharmacy

Joseph Gladden, *Vice Chancellor, Research & Sponsored Programs, University of Mississippi*-Welcome on Behalf of The University of Mississippi

Gregory Noonan, *Senior Science Advisor for Chemistry, US Food and Drug Administration*-Key Note Address

Ikhlas Khan, *Director, NCNPR, University of Mississippi*-Forensic Pharmacognosy – Plant-based Proteins

10:30-10:50 am Break

Session 1	**NIH Program Updates**	OCC Auditorium
10:50-11:10	Chair: Bill Gurley, *University of Mississippi* **LaVerne Brown, *NIH*-**Resilience as a Complementary Approach to Understanding Health-Remote	
11:10-11:30	**Patrick Still, *NIH*-**Natural Product Research: Overview of Funding Opportunities at NCCIH	
11:30-11:50	**Adam Kuszak, *NIH*-**New Dietary Supplement Reference Material Resources from The NIH ODS Analytical Methods and Reference Materials Program	
11:50-12:00	**Conference Photography-**Meet at OCC Side Patio Across from Cedar Room Dining Hall	
12:00-1:00	Lunch	OCC Cedar Room
Session 2a	**Plants And the Print Media**	OCC Auditorium
1:00-1:30	Chair: Rick Kingston, *Safety Call* **Bill Giebler, *Nutrition Business Journal*-**Growing Interest: The U.S. Herbs & Botanicals Market	
1:30-2:00	**Mark Blumenthal, *American Botanical Council*-**Insights into the US and International Botanical Market & Community: Honoring Fellow Colleagues and Celebrating 40 Years of HerbalGram and 35 Years of ABC Research and Educational Programs	
2:00-2:30	**Stephen Daniells, *William Reed*-**View from The Editor's Chair	

Day 1 Continued

Session 2b	**Biological Screening for Phytochemical Activity**	OCC Magnolia
	Chair: Xing-Cong Li, *University of Mississippi*	
1:00-1:20	**Jiawen Shou, *The Chinese University of Hong Kong***-Berberine Activated PPARδ Following a Gut Microbiota-liver Axis to Suppress Hepatocellular Carcinoma	
1:20-1:40	**Wen Zi-Chen, *Hunan University Of Chinese Medicine***-Uncover The Mechanism Of *Persicaria hydropiper (L.)* Against *Tryapanosoma brucei* Through Network Pharmacology And Molecular Docking	
1:40-2:00	**Matthew Scott, *Pennington Biomedical Research Center***-Extract Of *Artemisia Dracunculus L*. Modulates The Proliferation And Activity Of Osteoblasts	
2:00-2:20	**Serge Alain Fobofou Tanemossu, *Sonoran University Of Health Sciences***-Chemical Novelty And Anti-HIV Compounds From *Hypericum* Species (St. John's wort)	
2:20-3:00	Break	
Session 3a	**Industry Perspective**	OCC Auditorium
	Chair: Loren Israelson, *UNPA*	
3:00-3:30	**Bryce Warning, *Pattern*-**What Executives Need To Know To Work Successfully With Amazon	
3:30-4:00	**Katie Banaszewski, *Now Foods*-**What's In Your Bottle? Bridging The Gap Between Media-influenced Public Perception And The Reality Of Quality, Compliance And Safety Of Dietary Supplements	
4:00-4:30	**Josef Brinckmann, *Traditional Medicinals, Inc*. -**A New Global Estimation Of Medicinal And Aromatic Plant Species In Commercial Cultivation And Their Conservation Status	
Session 3b	**Cannabis In The Clinic**	OCC Magnolia
	Chair: Larry Walker, *University of Mississippi*	
3:00-3:30	**Cassandra Taylor, *FDA*-**Cannabis And Cannabis-Derived Compounds: Quality Considerations For Clinical Research Guidance For Industry	
Session 3c	**FDA Training Program**	OCC Magnolia
	Chair: Amar Chittiboyina, *University of Mississippi*	
3:30-4:00	**Allen Gelfius, *FDA*-**Training Food & Drug Regulators	
Session 4	**2nd Annual JD McChesney Seminar**	OCC Auditorium
	Chair: JD McChesney, *Cloaked Therapeutics, LLC-*	
4:30-5:30	**Pamela Weathers, *Worcester Polytechnic Institute*-**From traditional use To a single molecule And back again: Artemisia or artemisinin?	
6:00-8:00	**Reception/Mixer – Award Presentation: Outstanding Contribution In Natural Product (The Jefferson Oxford-365 MS-6, Oxford, MS 38655)**	

Day 2

Session 5:	**Update And Future Perspectives From The FDA**	OCC Auditorium
8:30-10:00	Session Chair: Gregory Noonan, *FDA* **Betsy Jean Yakes, *FDA* & Shotell Wright, *FDA*-**Identity Verification Of Botanical Constituents **Charles Wu, *FDA*-**Opportunity And Challenge Of Botanical Applications For COVID-19 Management **Sara Handy, *FDA*-**From Barcoding To Baits: Where We Have Been And Where We Are Going With DNA Methodologies In The Quest For Safer Botanicals	
10:00-10:30	Break	
Session 6a	**Impact Of Quality On Supplement Safety**	OCC Auditorium
10:30-11:00	Chair: John Travis, *NSF* **Pieter Cohen, *Harvard Medical School*-**Updates In Supplement Research With Dr. Cohen	
11:00-11:30	**Andrea Lindsey, *The Consortium For Health And Military Performance (CHAMP)*-**Operation Supplement Safety Ingredient Database: A Comprehensive Encyclopedic Collection Of Ingredients	
11:30-12:00	**Shannon Aldrich, *FDA*-** Health Fraud Updates And Emerging Trends	
Session 6b	**Analysis Of Natural Products**	OCC Magnolia
10:30-10:50	Chair: Joe Betz, *Georgetown University School of Medicine* **James Kababick, *Flora Research*-**Rapid Simultaneous Quantitation Of Kavalactones And Flavokavains In Piper Methysticum Root By A-TEEM Spectroscopy	
10:50-11:10	**James Harnly, *USDA*-**Chemometrics: A Valuable Tool For Deriving Information From Complex Data Sets	
11:10-11:30	**Jeffrey Julien, *Horiba*-**Fast Detection Of Adulteration In Lavender Essential Oil Using A-TEEM Multidimensional Spectroscopy	
11:30-11:50	**Ellie Abraham, *Eurofinsus*-**A Chemometric Approach To Berry Dietary Supplement Authentication Based On Targeted Anthocyanin Profiles	
12:00-1:00	**Lunch**	OCC Cedar Room
Session 7a	**Botanical Safety Assessment: Updates From The BSC**	OCC Auditorium
1:00-1:25	Chair: Dan Marsman, *Proctor & Gamble* **Connie Mitchell, *Health And Environmental Sciences Institute (HESI)*-**The Botanical Safety Consortium: An Introduction And Recent Updates.	
1:25-1:50	**Holly Johnson, *AHPA*-**Analytical Tools To Support Botanical Safety	
1:50-2:15	**Amy Roe, *Proctor & Gamble*-**New Approach Methodologies For Screening For Hepatotoxicity For Botanicals As Complex Mixtures	
Session 7b	**Phytochemical Analysis And Reference Material**	OCC Magnolia
1:00-1:20	Chair: Paula Brown, *British Columbia Institute of Technology* **Rachel Harris, *Mobilion Systems*-**More Than Just A Number: Utilizing CCS And Conformational Space Analysis To Characterize Unknowns In Complex Extracts	
1:20-1:40	**Christopher Beekman, *FDA*-**Development Of A Multi-Analyte Method For The Screening Of Dietary Supplement Products	
1:40-2:00	**Cuiying Ma, *USP*-** Monographs For Quality Control Of Different Ginsengs	
2:00-2:20	**Katerina Mastovska, *AOAC*-**AOAC INTERNATIONAL Programs Addressing Analytical Needs In Botanical Ingredients And Dietary Supplements	

Day 2 Continued

2:15-2:30	Break	
Session 8a	**Advancing Kratom Science: New Data On Kratom's Pharmacology, Safety, Pharmacokinetics, Abuse Potential, And Real-World Surveys**	OCC Auditorium
2:30-4:00	Chair: Holly Johnson, *AHPA* **Jack Phenningfield, *Pinney Associates*** **Marilyn Huestis, *Pinney Associates*** **Kirsten Smith, *NIH*** **Rick Kingston, *Safety Call***	
Session 8b	**Evaluating the Safety Of Natural Products: *In Vitro* Methods**	OCC Magnolia
2:30-2:50	Chair: Shabana Khan, *University of Mississippi* **Amy Roe, *Proctor & Gamble***-Prediction Of Clinically Relevant Botanical-Drug Clearance Interactions For *Boswellia serrata* Extract Using Sandwich-Cultured Human Hepatocytes.	
2:50-3:10	**Kelli McDonald, *Auburn University*-**Açaí Fruit Pulp And Supplement Extracts: Potential Induction Of CYP Enzymes And P-gp/OATP-B Transporters	
3:10-3:30	**Igor Koturbash, *University Of Arkansas Medical Sciences***-Organ-on-chip Systems As Reliable Translational Tools For Studies On Herbal And Dietary Supplements	
3:30-3:50	**Islam Husain, *University Of Mississippi***-*Phyllanthus amarus* Modulate CYPs And P-gp Activity And Induce The Risk Of HDIs	
3:50-4:10	**Deval Patel, *Amway***-"History Of Safe Human Use" In Risk Assessment Of Botanicals In Dietary Supplements	
5:30-8:00	*POSTER SESSION* Chair: Amar Chittiboyina, *University Of Mississippi*	OCC Cedar Room
6:00-8:00	Dinner	OCC Cedar Room

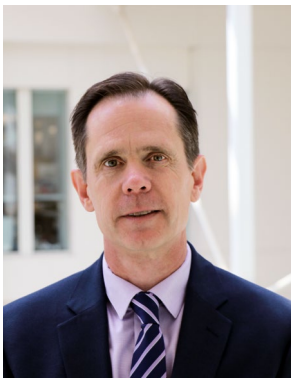
Day 3

Session 9:	**International Perspective**	OCC Auditorium
8:30-10:00	Session Chair: Craig Hopp, *NIH* **Judith Rollinger, *University Of Vienna*-**Let's Take Advantage From Nature's Complexity! **Jo Barnes, *University Of Auckland*-**Advances In Safety Signal Detection For Herbal Medicines **Nikolas Fokialakis, *National And Kopodistrian University Of Athens*-**Global microbial biodiversity: An untapped source for the discovery and development of novel antiaging molecules	
10:00-10:30	Break	
Session 10a	**International Regulations**	OCC Auditorium
10:30-11:00	Chair: Michael Smith, *MJS Consulting* **Sonia Parmar, *Canadian Health Food Association*-**An Update On The Canadian Regulation Of NHPs From An Industry Perspective Providing Updates On Changes For NHPs, Work Around CBD And Other Key Topics	
11:00-11:30	**Jon Wardle, *National Centre For Naturopathic Medicine*-**Findings Of Their Work Around Industry Priorities For Education And Training As Well As An Update From Their National Priority Setting Project	
11:30-12:00	**Thomas Brendler, *Traditional Medicinals Inc*-**The Concept Of Traditional Use In EU Regulations Concerning Food And Medicinal Products	
Session 10b	**Plants vs. Pathogens: When Viruses And Phytochemicals Collide**	OCC Magnolia
10:30-10:50	Chair: Nirmal Pugh, *University of Mississippi* **Gaillen Marshall, *University Of Mississippi Medical Center*-**Clinical Trials for Botanicals and Other Natural Products: Developing Paradigms for Efficient, Sound Evaluations and Indications	
10:50-11:10	**Andrea Bugarcic, *National Center For Naturaopathic Medicine*-**Traditional Evidence And Pre-clinical Research - Alignment, Limitations And Opportunities	
11:10-11:30	**Tahir Mir and Kashif Shamim, *University Of Mississippi*-**Immulina Enhances Host Resilience Against Influenza Virus-induced Illness In A Prodromal Mouse Model	
11:30-11:50	**Stefan Gafner, *American Botanical Council*-**The Impact Of Covid-19 On The Supply Chain And Quality Of Botanical Ingredients	
12:00-1:00	Lunch	OCC Cedar Room
Session 11	**"Synthetic Biology: Exploring The Science And Regulatory Framework"**	OCC Auditorium
1:00-1:25	Chair: Joe Chappell, *University of Kentucky* **Weslee Glenn, *Anya Bio*-**Plant Cell Cultivation In The 21st Century	
1:25-1:50	**Andrew Horwitz, *Inscripta*-**Biomanufacturing: Scalable Access To Rare And Powerful Natural Products- Remote	
1:50-2:15	**Stephanie Hice, *FDA*-**OFAS Pre-Market Review Programs: An Introduction To Food Additives, Color Additives, And GRAS Ingredients	
2:30-4:00	Garden and NCNPR Tours	
3:30-5:00	ICSB Yard Games & Competition	OCC Lawn
5:00-8:00	Bowling And Southern Fish & Chicken (Premier Lanes, 204 Commonwealth Blvd., Oxford, MS)	

Day 4

Session 12:	**AYUSH Update**	OCC Auditorium
8:30-10:00	Session Chair: Josef Brinckmann, *Traditional Medicinals, Inc.* **Ranjit Puranik, *Shree Dhootapapeshwar Ltd*-**Achieving Environmental Targets In Ayurved Manufacturing **Narayanam Srikanth, *Ministry Of AYUSH, Govt. Of India*-**Research and Development Initiatives of Ministry of Ayush for COVID-19 **Sayeed Ahmad, *Jamia Hamdard*-**The Botanical Safety Consortium: An Introduction And Recent Updates	
10:00-10:30	Break	
Session 13	**Botanical Research And Development**	OCC Auditorium
10:30-11:00	Chair: Ryan Yates, *University Of Mississippi* **Nicole Stevens, *doTerra*-**Effects Of A Novel Botanical Supplement On Glycemic Variability And Postprandial Glucose Response	
11:00-11:30	**Mei Wang, *USDA*-**A Novel Approach For Lavender Essential Oil Quality Assessment Using GC/MS, NMR And Chemometrics	
11:30-12:00	**Cecile Bascoul, *doTerra*-**Eucalyptus Essential Oil: A Safety Assessment And Causality Evaluation Of Published Case Reports	
12:00-1:00	Lunch	OCC Cedar Room
Session 14	**Medicinal Cannabis And Protecting Public Health And Safety**	OCC Auditorium
1:00-3:00	Chair: Alena Rodriguez, *The GMP Collective* **David Vaillencourt, *GMP Collective*** **Mahmoud ElSohly, *University Of Mississippi*** **Robert Welch, *University Of Mississippi*** **Nandakumara Sarma, *USP***	
6:30-8:00	Closing Ceremony & Banquet	OCC Cedar Room

"Keynote Address"



Gregory Noonan

Senior Science Advisor for Chemistry in the Office of Regulatory Science, FDA

Dr. Gregory Noonan joined the US Food and Drug Administration in 2002 and is currently the Senior Science Advisor for Chemistry in the Office of Regulatory Science. Since August 2020 Dr. Noonan has occupied various temporary positions in the Office of Dietary Supplement Programs, including acting Office and Deputy Director. In these roles, he worked closely with ODSP staff and CFSAN leadership to provide assistance and continuity to ODSP, while a search for a permanent director was performed. Prior to his temporary positions in ODSP, Dr. Noonan ran the Division of Bioanalytical Chemistry (DBC). DBC includes over 30 scientists performing research and developing analytical methods in numerous subject areas, including, toxic elements analysis, immunodiagnostic and DNA-based allergen detection, radionuclides, pesticide analysis, mycotoxin analysis, and dietary supplements and botanicals. Before becoming Director, Dr. Noonan was a Research Chemist in the Method Development Branch of the Division of Analytical Chemistry. His research focused on developing methods for the determination of food additives, including indirect additives, and process induced contaminants. Dr. Noonan also served as the US Delegate to the Codex Committee on Methods of Analysis and Sampling (CCMAS) from 2012 to 2022, where he chaired the Working Group on the Endorsement of Methods. Dr. Noonan received his PhD in Chemistry from Michigan State University in 1996. After graduation he worked for the Diagnostic Division of Abbott Laboratories, where he developed diagnostic immunoassays for hepatitis A, B and C and HIV. After leaving Abbott Laboratories and prior to joining the FDA, he was a postdoctoral fellow in the Civil and Environmental Engineering department of the Massachusetts Institute of Technology, where he studied the fate and transport of polar, water-soluble environmental contaminants.

NOTES

Ikhlas Khan

Director, Research Professor, NCNPR, University of Mississippi

Dr. Ikhlas Khan is the Director of the National Center for Natural Products Research at the University of Mississippi. He received a D. Litt (Honoris Causa) from University of Hamdard, Delhi, India 2012; a B.S. in Chemistry in 1980 and a M.S. in Organic Chemistry in 1982 from the Aligarh Muslim University in Aligarh, India, as well as a Ph.D. in Pharmacy from the Institute for Pharmaceutical Biology in Munich, West Germany in 1987. He has received numerous awards, the latest being the Wiley Award presented by AOAC International and the University of Mississippi's, Distinguished Professor Award in 2018, the Qihuang International Prize from Chinese Association of Chinese Medicine in 2017 and in 2016, was named University of Mississippi's Distinguished Research and Creative Achievement Award. He authored/co-authored over 800 original research articles, publications, or reviews. He has been invited to speaker at many events and served as a reviewer for several prestigious journals. He is a member of many scientific organizations and served on numerous committees. He was recently awarded fellowships in the Royal Society of Chemist, American Association for the Advancement of Science (AAAS) and American Chemical Society (ASP). He has mentored and advised numerous MS and PhD students and hosted visiting scholars from around the globe.

Forensic Pharmacognosy – Plant-Based Proteins

Khan, I.A.

National Center for Natural Products Research, University of Mississippi, MS 38677, USA

Plants have long been considered an abundant source of natural products for humanity, and, in recent years, many conventional, novel, or exotic plant-based proteins (PBPs) have been introduced to the consumer market, generating a huge demand for alternative proteins. Purported health benefits, environmental sustainability, and the non-animal nature of PBPs also make this food source increasingly attractive to the general public. Nevertheless, PBPs are a challenging task for the food industry due to the overall chemical makeup of an enriched protein extract. The amino acid content may contain insufficient levels of indispensable human dietary amino acids or non-proteogenic amino acids that negatively affect digestion. Indeed, more than 900 non-proteogenic amino acids have been reported from a wide variety of plants. These foreign amino acids can function as antinutrients to humans if consumed in sufficient quantities by functioning primarily as mimics to the 20 common, proteogenic amino acids to which the human body is accustomed. This mimicry mechanism leads to the production of dysfunctional proteins in humans by the mistaken incorporation of a plant non-proteogenic amino acid during RNA translation. In planta, these toxic non-proteogenic amino acids can also serve as defenses against herbivory by mammals and insects alike by obstructing primary metabolism or interfering with neurological processes, a significant concern for the food industry. Moreover, PBPs are usually globular in their native state, necessitating their denaturation before insoluble aggregates can be formed to be shaped into appealing meat-like forms. Finally, since PBPs are usually embedded in poorly digestible polysaccharides, their bioavailability and organoleptic properties can be severely limited. Considering this, food formulators have leveraged the functional properties of PBPs by manipulating the concentrations of intact and hydrolyzed PBPs in extract. Therefore, due to the overall characteristics of PBP extracts, further investigation must be made into plant proteomes to ensure quality and safety.

LaVerne Brown, Ph.D.

Director of Resilience and Health Studies Program, Office of Dietary Supplements (ODS

Education: Virginia Commonwealth University, Ph.D. (Natural Products Chemistry) 1994-1998; Old Dominion University, B.S. (chemistry) 1990-1994

Research Interests: Dr. Brown is interested in research that explores the impact of dietary supplement use on resilience and health in diverse populations. Dr. Brown's work focuses on elucidating mediators of resilience to help gain a better understanding of how recovery from, or adaptations to, environmental and biological stressors may impact nutrient status and overall health status in individuals. In addition, Dr. Brown chairs the Trans-NIH Resilience Working Group and has led the group through the development and harmonization of a resilience definition, Resilience Conceptual model, and Resilience Research Design Tool.

Dr. Brown is a former associate professor of medicinal and organic chemistry; and her previous research interests have included the isolation and chemical characterization of active molecules from natural products, as well as the design and synthesis of novel small molecules to better understand the role of nicotinic acetylcholine receptors in neurological disorders.

Resilience As A Complementary Approach To Understanding Health

LaVerne L. Brown, Ph.D.,

National Institutes of Health, Office of Dietary Supplements

At the National Institutes of Health, the Resilience Research Working Group defined resilience as a system's capacity to recover, grow, adapt, or resist perturbation from a challenge or stressor. The definition was devised upon exploration of various commonalities amongst frameworks, outcome measures and metrics, and interventions and/or protective factors that were representative of the science of resilience across multiple domains. The Trans-NIH Resilience Working Group definition of resilience serves a 1st step towards harmonizing the science of resilience. Following the definition, a conceptual model of resilience and a resilience research design tool were also developed. Here, we demonstrate the applicability of the resilience definition, conceptual model, and design tool using studies that were co-funded by the NIH Office of Dietary Supplements. This work has the potential to advance the science of resilience and may thereby offer new approaches to investigating health benefits of nutritional and botanical interventions.

Patrick C. Still

Associate Professor of Medicine at Harvard Medical School and a general internist at Cambridge Health Alliance in Somerville, Massachusetts

Patrick Still, Ph.D., Program Director, Basic and Mechanistic Research in Complementary and Integrative Health Branch, NCCIH/NIH

Education: University of California, Santa Cruz, Postdoctoral Fellow (Chemistry) 2013-2015; The Ohio State University Ph.D. (Medicinal Chemistry) 2013; Virginia Commonwealth University B.S. (Chemistry) 2003-2007

Natural Product Research: Overview Of Funding Opportunities At NCCIH

Still, P[1]

[1]Program Director, Basic and Mechanistic Research in Complementary and Integrative Health Branch, NCCIH/NIH

The National Center for Complementary and Integrative Health (NCCIH) supports research that analyzes fundamental mechanisms, usefulness, and safety of complementary and integrative health interventions and their roles in improving health and health care. NCCIH welcomes applications that fall within its mission to address both mechanistic and clinical questions. Detailed descriptions about the areas NCCIH supports, including biological activities of natural products, such as prebiotics, probiotics, dietary supplements, botanicals, and vitamins, as well as clinical trials involving natural products, can be found on the NCCIH website.

The Center places emphasis on evidence-based complementary therapies “integrated” with and not used as an “alternative” to conventional medicine and seeks to better define and map a path to whole person health by expanding and building on current activities while advancing new research strategies and ideas. Funding opportunity announcements (FOA) details, NCCIH staff points of contact, and relevant webinars are available on NCCIH relevant webpages.

Adam J. Kuszak

Health Scientist Administrator in the National Institutes of Health (NIH) Office of Dietary Supplements (ODS) and Director of the ODS Analytical Methods and Reference Materials Program (AMRM)

Through the AMRM Program at NIH ODS, Dr. Kuszak works with diverse stakeholders involved in research, industry, and regulatory affairs to support scientific resource development and promote biomedical research on the mechanisms and health effects of dietary supplements and natural products. In addition, Dr. Kuszak provides scientific expertise and analyses to facilitate ODS initiative development, program management, strategic planning, and evaluation. His primary research interests are in the chemical and biological characterization of natural products and therapeutics, including the elucidation of mechanisms of action and effects on cellular signaling networks and physiological systems.

Education and training: Science & Technology Policy Fellow (2014-2015), American Association for the Advancement of Science; Ph.D. in Pharmacology (2009), University of Michigan; B.S. in Pharmacology and Toxicology (2002), University of Wisconsin – Madison

Professional and research organization membership and activities: Association of Official Analytical Collaboration (AOAC) International; (2018 – Present); Journal of AOAC International Editorial Board (2018 – Present); American Association for the Advancement of Science (AAAS) (2014 – Present); American Society of Pharmacology and Experimental Therapeutics (ASPET) (2007 – Present); ASPET Science Policy Committee (2020 – Present); Federation of American Societies for Experimental Biology (FASEB) Science Policy Committee (2022 – Present); United States Pharmacopeia Convention Dietary Supplements Admission, Evaluation, and Labeling Expert Committee, Government Liaison, NIH Representative (2020 – Present); NSF ANSI Dietary Supplements Joint Committee (2015 – Present); Botanical Safety Consortium Chemical Analysis Technical Working Group (2019 – Present)

New Dietary Supplement Reference Material Resources From The NIH ODS Analytical Methods And Reference Materials Program

Adam J. Kuszak[1], Greg Hinkle[2], Chris Hinkle[2], Zoe Ruan[3], Sarah Ajaz[3], Uma Sreenivasan[3], Sanem Hosbas Coskun[1], Hugh Hayes[4], Catherine Rimmer[4], Stephen Wise[1]

[1]Office of Dietary Supplements, National Institutes of Health, Bethesda, MD, USA, [2]NetLink Resource Group, Alexandria, VA, USA, [3]Cerilliant Corp/MilliporeSigma, Round Rock, TX, USA, [4]National Institute of Standards and Technology, Gaithersburg, MD, USA

The NIH Office of Dietary Supplements (ODS) Analytical Methods and Reference Materials (AMRM) Program supports the development of tools that promote quantitative determinations of dietary supplement identity, composition, and purity, as well as assessments of authenticity and contamination of botanical raw materials and finished products. AMRM goals are accomplished through funding and collaboration in three program areas: formal validation of quantitative and qualitative methods, production of certified reference materials (CRMs), and support of dietary supplement focused laboratory quality assurance programs. This presentation will provide updates on recent AMRM activities and highlight newly available resources that should benefit natural product researchers and supplement industry scientists, including availability of an online database and search tool to facilitate identification and comparison of reference materials relevant to dietary supplement chemical analysis, and an expanded portfolio of CRMs that includes calibration solution mixtures of key constituents of popular botanical supplement ingredients.

Bill Giebler

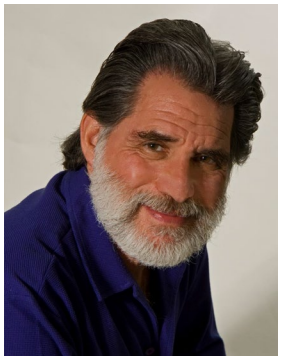
Content & Insights Director, Nutrition Business Journal

An award-winning writer and seasoned natural products industry veteran—with decades of experience in food and supplement retail, lifestyle mail order and textiles product development—Nutrition Business Journal Content & Insights Director Bill Giebler manages the NBJ business with a keen focus on the what, where and why of the dietary supplement market.

Growing Interest: The U.S. Herbs & Botanicals Market

Bill Giebler

Content & Insights Director, Nutrition Business Journal



Mark Blumenthal
Founder and Executive Director American Botanical Council

Mark Blumenthal is the Founder and Executive Director of the American Botanical Council (ABC)—a leading, independent, research and educational nonprofit organization dedicated to disseminating accurate, reliable, and responsible information on herbs and medicinal plants, teas, essential oils, phytomedicines, beneficial plants, and edible and medicinal fungi. Blumenthal is Editor-in-Chief and Publisher of HerbalGram, ABC's international peer-reviewed quarterly journal. For six years, he served as an adjunct associate professor of medicinal chemistry at the University of Texas at Austin, College of Pharmacy, teaching the course "Herbs and Phytomedicines in Today's Pharmacy." He is also the founder and director of the ABC-AHP-NCNPR Botanical Adulterants Prevention Program, a nonprofit international consortium committed to extensively researching and exposing adulteration and fraud in botanical ingredients sold in the global market. He is the senior editor of The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines, a 715-page reference book rated second of all medical books published in 1998. In 2010 he received the American Society of Pharmacognosy's Varro E. Tyler Award and in 2018 he was named Outstanding International Ethnopharmacologist by the Indian Society for Ethnopharmacology. He has appeared on more than 400 radio and television shows and has written more than 500 articles, reviews, and book chapters and forewords for many publications. He was awarded Natural Health magazine's Hall of Fame Award for "…opening America's eye to the healing powers of herbs." Frequently quoted in the media, for more than 48 years, he has been a leader in the global botanical and natural products community, promoting science-based herbal education and respect for scientific and clinical research, ethnobotanical traditions, sustainable and regenerative practices, and authenticity and transparency in the manufacture and marketing of herbs and phytomedicines.

Insights Into The US And International Botanical Market & Community: Honoring Fellow Colleagues And Celebrating 40 Years Of Herbalgram And 35 Years Of ABC Research And Educational Programs

Mark Blumenthal

Founder & Executive Director, American Botanical Council, Editor-in-Chief, HerbalGram
Founder, ABC-AHP-NCNPR Botanical Adulterants Prevention Program

In 2022 after several years hiatus for the ICSB conference due to the pandemic, this presenter was invited to give a memorial tribute to those friends and colleagues who had passed in the previous two years. This year the lives of additional colleagues will be remembered and honored for their contributions to the local or global medicinal plant communities. In addition, there will be discussion of ABC's 35th and HerbalGram's 40th anniversaries and how ABC's Sustainable Herbs Program (SHP) and the ABC-AHP-NCNPR Botanical Adulterants Prevention Program (BAPP) are helping to meet the needs of the growing international herb community by providing timely and much-needed inspiration and educational resources for responsible members of the botanical industry and community at large.

Stephen Daniells

Editor-in-Chief, North and South America, William Reed Business Media

Stephen Daniells is the Editor-in-Chief, North and South America of William Reed Business Media, which includes the market-leading publications NutraIngredients-USA and FoodNavigator-USA. Stephen obtained a PhD in chemistry from the Queen's University of Belfast, Northern Ireland, and held post-doctoral research positions in The Netherlands and France before taking the leap into journalism in 2005. His journalism has been recognized by awards from the American Herbal Products Association (2015 Special Award for Journalistic Excellence), and regionally and nationally by the American Society of Business Publication Editors (ASBPE, 2019, 2020, 2022).

Stephen has presented at numerous industry and association events, including conferences organized by the United Natural Products Alliance (UNPA), the International Probiotics Association (IPA), the Natural Health Products Research Society of Canada (NHPRS), CHFA West, and the Oxford International Conference on the Science of Botanicals (University of Mississippi).

Stephen also acts as the editorial consultant and chair of William Reed's Probiota & Probiota Americas events, and the NutraIngredients-USA Sports & Active Nutrition Summit, and leads the NutraIngredients-USA Awards program. He lives in Chicago.

View From The Editor's Chair

Daniells, S.T.

NutraIngredients-USA, William Reed, Chicago, IL, USA

With the pandemic fading in the minds of most Americans and a return to something we can all recognize as 'normality', there is a slight reset happening in US dietary supplements industry. Consumers who flocked to the industry in record numbers are still there, but spending habits have changed and hot categories like immune support are evolving. We're also seeing technology being leveraged in the search for the next hot ingredient, from artificial intelligence to synthetic biology, and this has implications for the botanicals trade. We also have an industry at odds with itself, with trade associations working against each other on key issues. In this presentation, Stephen Daniells, Editor-in-Chief of NutraIngredients-USA, will look back over the past three years and give his opinion on what this means moving forward. Key points Stephen will cover include:

- The key trends and fads over the past 3 years? Which high growth categories are here to stay? And the losers: What does it mean for those ingredients and product?
- How is the specter of COVID going to shape trends over the next few years?
- Where is the innovation in the ingredient supply chain and what does this mean for botanicals?
- What regulatory challenges is the industry dealing with and how does that impact business?
- And where do we go with DSHEA 2.0?

Jia-Wen Shou

Scientific Officer, Li Dak Sum Yip Yio Chin R&D Centre for Chinese Medicine at The Chinese University of Hong Kong

Education: The Chinese University of Hong Kong Ph.D. (Biochemistry) 2016-2021; Tsinghua University-Peking Union Medical College M.S. (Pharmaceutical Analysis) 2013-2016; China Pharmaceutical University B.S. (Resource and Development of traditional Chinese Pharmacy) 2009-2013.

Research Interests: Major research interests are in the areas of the multiple efficacies and mechanisms of berberine on various diseases, including liver cancer, neurodegenerative diseases and metabolic syndrome; of gut microbiota-host interactions of berberine mediated therapeutic effects; of bioassay-directed phytochemical isolation and biology of potentially active antitussives; and of pharmacokinetic/pharmacodynamic characteristics of phytochemicals.

Honors: Hong Kong Ph.D. Fellowship (Research Grants Council of Hong Kong, 2016-2019); National scholarship (Chinese Ministry of Education, 2011, 2012, 2015).

Professional Duties: Reviewer for Biomedicine & Pharmacotherapy, Scientific Reports, Frontiers in Pharmacology, Journal of Pharmaceutical Analysis, Journal of Pharmacy and Pharmacology, Neurochemical Research, Journal of Ethnopharmacology, European Journal of Pharmacology, and Human Heredity.

Berberine Activated PPARδ Following A Gut Microbiota-Liver Axis To Suppress Hepatocellular Carcinoma

Jia-Wen Shou[1,2], Pang-Chui Shaw[1,2,3]

[1]Li Dak Sum Yip Yio Chin R&D Centre for Chinese Medicine,
[2]School of Life Sciences, [3]State Key Laboratory of Research on Bioactivities and Clinical Applications of Medicinal Plants and Institute of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong, China. Correspondence. P-C. S. (+852 39431361, pcshaw@cuhk.edu.hk)

Rationale: Peroxisome proliferator-activated receptors (PPARs) are a family of ligand- inducible transcription factors governing a variety of essential metabolic activities in the liver and other organs. Recently berberine (BBR) has been characterized as a modulator of PPARs, whereas whether PPARs were involved in the inhibitory effect of BBR on hepatocellular carcinoma (HCC) was not well understood.

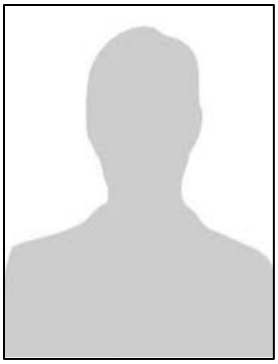
Methods: We studied the role of PPARs in in-vitro and in-vivo models using real-time PCR, immunoblotting, immunostaining, luciferase and chromatin immunoprecipitation coupled PCR assay and adeno-associated virus (AAV)-mediated knockdown.

Results: We identified that, rather than PPARα or PPARγ, PPARδ played an active role in this anti-HCC effect of BBR. Following a PPARδ-dependent manner, BBR suppressed HCC development via triggering an apoptotic pathway. Besides, we noted that the interactions between PPARδ and the downstream apoptotic pathway resulted from the BBR-induced transcriptional function of PPARδ. What is more, gut microbiota also contributed to this suppressive effect on HCC. A functional gut microbial metabolite-butyric acid (BA) acted as a messenger in the gut microbiota-liver axis. Though the direct effects of BA to suppress HCC and activate PPARδ were not potent, BA was able to enhance the efficacy of BBR via reducing PPARδ degradation. Mechanistic studies revealed that BA inhibited the proteasome- ubiquitin system to retard PPARδ degradation, while BBR did not show this effect. Additionally, we found that the anti-HCC effect of BBR or a combination of BBR and BA was much weaker in mice with AAV-mediated PPARδ knockdown than those of the control mice, suggesting the important role of PPARδ.

Conclusion: In summary, it is the first to report that BBR exhibited the suppressive action on HCC through a mechanism of gut microbiota-liver axis mediated PPARδ activation.

Acknowledgments:

J.-W.S. was supported by the Hong Kong Ph.D. Fellowship Scheme (PF15-16899).



Wen Zi-Chen

Hunan University of Chinese Medicine

Uncover The Mechanism Of *Persicaria hydropiper* (L.) Against Tryapanosoma Brucei Through Network Pharmacology And Molecular Docking

Wen Z-C[1,2], Wang W[1,2], Li B[1 2], Peng C-Y[1,2]

[1] School of pharmacy, Hunan University of Chinese Medicine, Changsha, 410208, Hunan, China,[2] TCM and Ethnomedicine Innovation & Development International Laboratory, Changsha, 410208, Hunan, China

Persicaria hydropiper (L.) is a traditional ethnic medicine, which has the functions of detoxifying, detumescent, killing insects and relieving itching, and is widely used in southeast Asia. Previous experiments showed that 5 compounds (vanicoside F, Isorhamnetin, 2',4'-dihydroxy-6'-methoxychalcone, Pinosylvin, and (+)-ketopinoresinol) extracted from *Persicaria hydropiper* (L.) had anti-Trypanosoma effects *in vitro*, but the mechanism was unclear. In this paper, the targets of *Persicaria hydropiper* (L.) and trypanosomiasis were obtained through literature search (Pub med) and database mining (STITCH, SWISS, DisGeNET, OMIM, TTD, and Drug Bank), and the targets were analyzed by network pharmacology, enrichment analysis (Gene ontology and Kyoto encyclopedia of genes and genomes pathway enrichment analyses) and molecular docking. Finally, 59 active compounds from *Persicaria hydropiper* (L.) with 161 potential targets were collected, 282 targets of trypanosomiasis were collected, and there have 39 common targets of *Persicaria hydropiper* (L.) and trypanosomiasis. The results showed that *Persicaria hydropiper* (L.) could inhibit Trypanosoma by regulating inflammatory targets (IL-6, TNF, IL-10, MMP-9, etc.) *in vivo*, and it had the characteristics of multi-target and multi-pathway. In vitro molecular docking results show that vanicoside F binds to Trypanosoma cysteine protease and ornithine decarboxylase with lower binding energies than the positive control. These in vivo and in vitro results provide directions for subsequent pharmacological experiments.

Acknowledgments:

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Matthew Scott

Post-Doctoral Researcher

BS Kinesiology, Louisiana State University, 2012, MS Kinesiology, Louisiana State University, 2014, PhD Kinesiology, Louisiana State University, 2021

Dr. Scott is a postdoctoral fellow in the Ubiquitin Biology Lab and is funded by a NIH Botanical T32 Fellowship. He is currently working on bone marrow cell differentiation, with a focus on describing a potential role of Siah2 in the balance between osteogenesis and adipogenesis and exploring how botanical compounds may impact osteogenesis or osteoclastogenesis. Broadly, Dr. Scott is interested in bone metabolism in the context of lifestyle modifications such as diet and exercise. Dr. Scott also finds purpose in spending time with his wife, raising his two children, exercising, and doing household chores.

Extract Of *Artemisia Dracunculus* L. Modulates The Proliferation And Activity Of Osteoblasts

Matthew C. Scott[1], Brenda J. Smith[2] and Z. Elizabeth Floyd[1]

[1]Pennington Biomedical Research Center, Baton Rouge, Louisiana 70808, [2]Indiana School of Medicine, Indianapolis, Indiana 46202

Thiazolidinedione (TZD) treatment significantly improves insulin sensitivity and lowers blood glucose via action on adipocytes. Unfortunately, the pro-adipogenic property of TZDs is also associated with bone degradation by inhibiting the action of bone forming cells, or osteoblasts. An ethanol extract of *Artemisia Dracunculus* L., termed PMI 5011, improves blood glucose and insulin sensitivity via action on muscle cells, rather than fat, and may therefore spare bone while lowering blood glucose levels. Here we examine in vitro the effects of PMI 5011 on a pre-osteoblast cell line, MC3T3-E1 cells, during osteogenic differentiation. We hypothesized that PMI 5011 will not inhibit osteogenesis, based on histology, gene expression, and protein expression. To test our hypothesis, MC3T3-E1 cells were induced towards a more mature osteoblast lineage with and without PMI 5011 treatment at concentrations of 0, 3, 10, and 30 µg PMI 5011/mL of culture media. Cell lysates were probed for osteogenic gene and protein expression. Further, cultures were stained for osteogenic endpoints, including alkaline phosphatase, collagen, and mineralization. Contrary to our hypothesis, PMI 5011 at 30 µg/mL significantly increases osteogenic gene expression (e.g., Osteocalcin, Osterix, and Bone Sialoprotein) and initiates earlier mineralization. While cultures treated with 30 µg/mL PMI 5011 display earlier mineralization, mineralization at later timepoints is inhibited in comparison to non-treated cells. PMI 5011 treatment at 30 µg/mL significantly reduced cell proliferation by about twelve percent and may partially explain the disparity in early versus late mineralization. While the current studies do not address the impact of PMI 5011 on bone homeostasis in vivo, our in vitro analysis suggests PMI 5011 has the potential to spare bone health via improved osteoblast maturation and bone formation while enhancing insulin action in skeletal muscle.

Acknowledgments:
NIH T32AT004094

Serge Alain Fobofou Tanemossu

Assistant Professor / Principal Scientist, Sonoran University of Health Sciences

Dr. Serge Fobofou is currently a Principal Scientist at Ric Scalzo Institute for Botanical Research and an Assistant Professor at Sonoran University of Health Sciences (formerly Southwest College of Naturopathic Medicine (SCNM)). He leads research in the phytochemistry and analytical chemistry labs at Sonoran University. Dr. Fobofou received his doctoral degree in chemistry at the Leibniz Institute of Plant Biochemistry and the Martin-Luther University Halle-Wittenberg in Germany, where he worked on the chemical analysis, isolation and structure elucidation, and metabolomic studies of medicinal plants. His postdoctoral positions were at Harvard Medical School (Boston) and Baylor College of Medicine (Houston), where he studied natural products from the human microbiome.

Over the last years, he has taught postgraduate courses on drug discovery from medicinal plants, structure elucidation of natural products, and drug targets identification. He served in leadership roles as Junior Group Leader at the Technical University Braunschweig (Germany) and Principal Scientist / Assistant Professor at Sonoran University of Health Sciences (USA). His research areas include phytochemistry and microbial natural product chemistry.

Chemical Novelty And Anti-HIV Compounds From *Hypericum* Species (St. John's Wort)

Serge Alain Fobofou Tanemossu

Ric Scalzo Institute for Botanical Research, Sonoran University of Health Sciences, Tempe, Arizona, USA

Hypericum L. is a genus of plants belonging to the family Hypericaceae. The genus comprises more than 450 plant species growing in temperate regions and tropical highlands. *H. perforatum* L, also known as common St. John's wort, is the most common species found within the genus *Hypericum*. *H. perforatum* is used against mild to moderately severe depression in Europe and North America, where preparations of the plant are readily available over the counter (OTC). Especially, in Germany *H. perforatum* is among the most popular medicinal plants. Hyperforin and hypericin are the main active principles found in commercial *H. perforatum* preparations. Despite the growing attention to *H. perforatum*, more than 60% of plants in this genus remain underexplored both chemically and pharmacologically. In our search for new bioactive compounds from the genus *Hypericum*, we developed a metabolomic approach based on LC-MS and NMR coupled with multivariate data analysis for the semi-high throughput analysis of *Hypericum* species for bioactive compounds discovery. We have submitted 17 different *Hypericum* species to this analysis to discriminate extracts with high potential for chemical novelty and identify compounds (LC-MS) or classes of compounds (NMR) from extracts prior to any isolation. As a proof of concept, more than 20 new compounds were discovered from 3 extracts belonging to the discriminated *Hypericum* species. Bichromonol, a novel dimeric coumarin isolated from *H. roeperianum* exhibits significant anti-HIV activity. Especially, against the resistant variants A17 and EFVR, bichromonol is more effective than the commercial drug nevirapine and might thus have potential to serve as a new anti-HIV lead.

Bryce Warning

Vice President of Global Business Development at Pattern

Education: Master of Business Administration - Kellogg School of Management, Northwestern University, 2011 - 2013; Bachelor of Science, Business Strategy - Brigham Young University, 2002 – 2008

Professional Experience: Bryce Warning oversees Pattern's global business development and brings more than a decade of e-commerce, marketplace and cross border experience. Prior to joining Pattern, Bryce served as VP of Revenue for Zonos, a Series A funded cross-border SaaS company. Previously, Bryce held senior positions over a seven-year period with Amazon, both in the US and Australia. He was a member of the Amazon Australia country launch team where he served as Category Leader for Consumer
Electronics.

What Executives Need To Know To Work Successfully With Amazon

Bryce Warning

Global Business Development at Pattern

Katie Banaszewski

Sr. Director of Quality, NOW Foods

Katie Banaszewski is a Sr. Director of Quality at NOW Foods, who strongly believes great things are never done by one person, but a team. Driven by curiosity and her passion for science, she joined NOW in 2013 with a plan to transform the analytical capabilities of their labs. During her tenure at NOW, she has led the development and implementation of a routine pesticide residue monitoring program and plays an integral role in growing the company's analytical capabilities. Katie focuses on exploring new scientific approaches to analytical challenges and her areas of expertise are mass spectrometry and elemental analysis. In her current role, Katie focuses on recent issues within the dietary supplement industry and ensures NOW remains the industry leader in holding high quality standards. Prior to joining NOW, Katie spent 5 years at the Institute for Food Safety and Health, working in collaboration with the academia, industry and the FDA. Katie authored and co-authored multiple journal articles and is actively involved with the scientific community, learning and sharing her knowledge with others. Katie holds degrees in Biotechnology and Chemistry form William Paterson University of New Jersey.

What's In Your Bottle? Bridging The Gap Between Media Influenced Public Perception And The Reality Of Quality, Compliance And Safety Of Dietary

Katie Banaszewski

NOW Foods

Josef A. Brinckmann

Research Fellow Traditional Medicinals, Inc.

Working in the medicinal plants sector since 1979, Josef presently serves as 'Research Fellow for Medicinal Plants and Botanical Supply Chain' for Traditional Medicinals, Inc. (Sebastopol, CA), a manufacturer of herbal medicinal products. He also serves as President of the American Botanical Council (ABC) Board of Trustees, and as an advisory group member of the ABC Sustainable Herbs Program. In 2008, Josef was a founding Board of Trustees member of the FairWild Foundation, a non-profit, standard-setting organization for the sustainable wild collection of medicinal and aromatic plants, and now serves on its advisory panel. Presently serving in his fourth 5-year term (since 2005) with the United States Pharmacopoeia (USP), Josef is an elected member of the USP Botanical Dietary Supplements and Herbal Medicines Expert Committee (BDSHM-EC), and of the USP DSHM Nomenclature Joint Sub-Committee. Since 2006, he has also served the American Herbal Pharmacopoeia (AHP) as an advisor on commercial sources & handling and international regulatory status for AHP monographs. Since 2002, he has functioned as a consultant on market intelligence for medicinal plants and natural products for different agencies and programs of the United Nations.

A New Global Estimation Of Medicinal And Aromatic Plant Species In Commercial Cultivation And Their Conservation Status

Brinckmann, J.A., Traditional Medicinals, Inc. (Sebastopol, CA)

Historically, the majority of medicinal and aromatic plant (MAP) species has been harvested in the wild. In recent decades, there has been concern that certain species appear to face threats due to overexploitation related to increasing global demand coupled with loss of habitat due to development and land use change. Earlier studies estimated that about 900 species were produced, to some extent, by cultivation. This study, carried out for the German Federal Agency for Nature Conservation (BfN) between June 2017 and October 2020, aimed to update previous estimates by applying a systematic approach for obtaining data from a large number of different sources of information and knowledge. A broad categorization scheme for forms of cultivation is introduced. Using multiple methods of data collection, we found evidence of commercial cultivation of 3,227 taxa, belonging to 235 different plant families. The most frequently identified forms of cultivation were agroforestry, intensive farming, and controlled cultivation, followed by, to a much lesser extent, extensive farming, and natural fostering. Of the identified species, 954 have a global International Union for Conservation of Nature (IUCN) Red List assessment, of which 82 species (2.5%) are threatened to some degree according to IUCN Red List categories and criteria. Of the 3,227 cultivated taxa, 1,732 (54%) have also been assessed by national red lists, of which 688 taxa are assessed as threatened in at least one country. Additionally, 109 of the 3,227 cultivated species are included in the Convention on International Trade in Endangered Species (CITES) Appendices. The results of this research show that the number of cultivated plants is significantly higher than previously estimated. Potential consequences of threat status on the domestication of MAP species are discussed.

Acknowledgments:
Brinckmann, J.A., Kathe, W., Berkhoudt, K., Harter, D.E.V., Schippmann, U. A New Global Estimation of Medicinal and Aromatic Plant Species in Commercial Cultivation and Their Conservation Status. Economic Botany 76, 319–333 (2022). https://doi.org/10.1007/s12231-022-09554-7

Cassandra Taylor

Chemist at U.S. Food and Drug Administration

A Chemist at U.S. Food and Drug Administration within the Center for Drug Evaluation and Research (CDER) and is a member of the Botanical Review Team (BRT) residing within the Office of Pharmaceutical Quality (OPQ) and serves as an expert resource on all botanical issues. Dr. Taylor serves as a cannabis subject matter expert (SME) for CDER and across FDA, concentrating on the botanical and quality aspects of cannabis. Dr. Taylor received her B.S. in Chemistry from St. Francis University (2005), and her Ph.D. in Analytical Chemistry from the University of Maryland (2014). Dr. Taylor has evaluated over 100 botanical drug submissions across CDER's clinical divisions, with a focus on reviewing cannabis submissions and was the technical lead on the draft and finalized FDA guidance for industry titled "Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research." She leads and coordinates the internal CDER Cannabis working group and leads many cannabis initiatives within CDER and FDA. Dr. Taylor is an active SME in the FDA cross-agency cannabis working group, Cannabis Products Committee (CPC). She collaborates with colleagues across FDA to help close substantial knowledge gaps about the science, safety, and quality of cannabis and cannabis-derived products.

Cannabis And Cannabis-Derived Compounds: Quality Considerations For Clinical Research Guidance For Industry

Taylor, Cassandra[1]

[1]Food and Drug Administration

This guidance outlines FDA's current thinking on several topics relevant to clinical research related to the development of human drugs containing cannabis or cannabis-derived compounds. As defined in section 201(g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), drug includes any product that is intended to diagnose, cure, mitigate, prevent, or treat a disease, or any product (other than food) intended to affect the structure or any function of the body. In general, this means any product (including one that contains cannabis or cannabis-derived compounds) marketed with a claim of therapeutic benefit, or with any other disease-related claim, is considered a drug. To be legally marketed in interstate commerce, drugs that are not biological products generally must either (1) receive premarket approval by FDA through the new drug application (NDA) or abbreviated new drug application (ANDA) process, or (2) for certain over-the-counter nonprescription drugs, meet the requirements in the FD&C Act for marketing without an approved NDA or ANDA. The recommendations in this guidance are intended for products that meet the legal definition of a drug under the FD&C Act.

Allen Gelfius

Consumer Safety/Training Officer, U.S. Food & Drug Administration

Since October 2001, Allen Gelfius has been a training officer for the FDA Office of Training, Education & Development (OTED.) He develops training courses and educational materials for FDA, state, local and tribal regulators covering topics ranging from HACCP principles to the Food Code, Foodborne Illness & Traceback Investigations, Dietary Supplement Good Manufacturing Practice, and other regulatory and industry initiatives. He also coordinates the delivery of these training courses in various states across the country and participates in the instruction and presentation of the course materials. In July 2011, Allen helped launch FDA's Coordinated Outbreak Response & Evaluation Network (CORE) and served as lead for one of the outbreak response teams for seven months. His team coordinated the investigation of Listeria monocytogenes in whole cantaloupe from Colorado, one of the largest outbreaks in the U.S. in nearly 70 years.

Prior to joining FDA, Allen completed his B.S. in Public Health at Indiana University and worked for 12 years in the Hawaii State Department of Health's Food and Drug Branch as a field inspector (for the first 4 years) and then as the Data & Training Manager. His work included management of inspection data; the promulgation of laws and regulations to regulate foods, drugs, cosmetics, and medical devices sold in Hawaii; and the development and implementation of training programs and educational materials on various public health issues. He led the Hawaii Food Safety Advisory Council in the development of a training video and education program targeted at newly hired food handlers in retail food and food service operations which is still in use.

Allen was awarded the 1995 National Achievement Award from the Association of Food & Drug Officials (AFDO) for his professional training efforts and has been recognized with numerous FDA awards for his training, development & facilitation skills.

Training Food & Drug Regulators

Allen Gelfius

Consumer Safety/Training Officer, U.S. Food & Drug Administration

Pamela J. Weathers

Professor of Biology & Biotechnology; joint with Biomedical Engineering at Worcester Polytechnic Institute

Michigan State University Plant Research, Ph.D. (Botany and Plant Pathology); Marquette University, B.S. (Biology).

Research: Major interests focus on explaining the science behind the broad therapeutic efficacy of per os consumption of Artemisia annua and A. afra especially for treating TB and covid-19. She is also studies engineering plant tissues as scaffolds for mammalian cells for biomedical and food (meat) applications.

Organizations: AAAS; Sigma Xi WPI chapter Pres 2011-12; Society for In Vitro Biology White Award, 1993-99, Chair 1993; Student Awards Committee member 2000, Student Affairs Chair 2003, 2004-; Public Policy Chair 2004-12. Member of SIVB Board of Directors 2004-12.

Honors: 2022-19, 1014, 2012, 2004 Distinguished Service Awards, Society for In Vitro Biology; 2019 & 2015 Kalenian Award in Entrepreneurship at WPI; 2017 MA House of Representative Official Recognition for "developing a plant-based therapy for drug-resistant malaria"; 2016 Natl Academy of Inventors, WPI chap; 2014 Fellow, AAAS ; 2011 WPI Sigma Xi, Outstanding Senior Faculty Researcher Award; 2009 WPI President's Circle; 2009 Fellow, Society for In Vitro Biology; 2008 Who's Who among Executives and Professionals, Honors Edition; 2007 Democracy in Action Award, Middlesex & Worcester Democratic Coalition; 2006- , Who's Who in America; 2005- Who's Who in American Education; 2005- Who's Who of American Women; 2004 Who's Who: Great Women of the 21st Century; 2000 WPI Trustees' Award for Outstanding Research and Creative Scholarship; 1999- International Who's Who of Professional & Business Women; 1995 YWCA Katherine F. Erskine Award for Outstanding Woman in Science and Medicine in Central Massachusetts; 1994- The World Who's Who of Women; 1991- Who's Who in Science & Engineering; 1987 Special Distinction Award, MOET HENNESSEY international competition for technologies in "Innovation of Plant Production", for nutrient mist technology

From Traditional Use To A Single Molecule And Back Again: Artemisia Or Artemisinin?

Weathers P

Department of Biology and Biotechnology, Worcester Polytechnic Institute, Worcester, MA 01609 USA

Artemisia annua L. has >2,000 yrs. of documented traditional use as a therapeutic medicinal plant for treating "fever", that is usually the result of an infection. Still widely used globally, modern therapeutic emphasis, however, is on the sesquiterpene lactone, artemisinin, and its semi-synthetic derivatives mainly used to treat malaria in an artemisinin combination therapy. A related species, *Artemisia afra*, lacks artemisinin but also has traditional therapeutic activity against many of the same diseases. We have focused on explaining the science behind the *per os* efficacy of these 2 species used either in the traditional mode as a tea infusion (TEA) or in a form that is somewhat hybrid between traditional and modern as powdered encapsulated dried leaves (DLA; Dried Leaf Artemisia). Specifically, we have studied how the plant increases the bioavailability of artemisinin when delivered as DLA instead of as a pure molecule. Both *Artemisia* species are potent against tuberculosis (TB) and covid 19 (SARS-CoV-2) *in vitro,* and we are beginning to understand how the complex plant material is efficacious against these diseases. Results from those studies will be shared. Although artemisinin is not necessarily the active component against these diseases, it does play a role in these and many other therapeutic activities of *A. annua* so results related to artemisinin bioavailability and safety from orally consumed *A. annua* also will be shared. Our overall research goal is to explain the science behind these traditional delivery methods and provide the information needed in order to obtain approval of *Artemisia* as a Botanical Drug thereby providing a more cost effective and sustainable approach for treating a number of infectious diseases.

Acknowledgments:
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Betsy Jean Yakes

Chief, Identity and Status Branch in the Office of Dietary Supplement Programs

Education: Iowa State University, Ph.D. (Analytical Chemistry) 2002-2007; Luther College, B.A. (Chemistry/Math) 1998-2002; Madison Area Technical College, Emergency Medical Technician (1999)

Biography: the Chief of the Identity & Status Branch in the Division of Research & Evaluation, ODSP at FDA's Center for Food Safety and Applied Nutrition. She's responsible for leading & providing oversight to subject matter experts in ISB who evaluate dietary ingredients/supplements, including in new dietary ingredient notification reviews. She coordinates the technical evaluation of regulatory & scientific issues regarding dietary ingredients & other ingredients in dietary supplements. She & her team respond to inquiries from other FDA components & provide expert support for ingredient analysis, policy, & action as appropriate.

Betsy spent over 15 years in the Division of Analytical Chemistry in the Office of Regulatory Science. As a Research Chemist & principal investigator for research on portable devices & biosensors, she developed accurate biosensor detection for toxins & pathogens as well as spectroscopy methods for improved authentication & adulteration evaluation for foods, dietary supplements, food contact materials, & cosmetics. She has over 45 publications & obtained 2 patents in both novel advancements that furthered the mission of the Agency & garnered international impact. She served as the FDA Chair of the Portable Devices Technical Advisory Group for foods, the CFSAN/ORS coordinator for an FY18 Congressional special appropriation to study seafood decomposition, the FDA Liaison to the international USP the CFSAN/ORS coordinator for an FY18 Congressional special appropriation to study seafood decomposition, the FDA Liaison to the international USP Skim Milk Powder Advisory Group, & the Chair of the Forensics & Security Section at SciX.

Identity Verification Of Botanical Constituents

Wright S[1] & Yates BJ[1]

[1]U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Dietary Supplement Programs, 5001 Campus Drive, College Park, MD 20740, USA

FDA's authority for dietary supplement regulation originates in the Federal Food, Drug and Cosmetic Act (FD&C Act) with modifications laid out in the Dietary Supplement Health and Education Act of 1994 (DSHEA). DSHEA provides a framework for dietary supplement regulation, establishes the definitions of a dietary supplement and dietary ingredient, and defines new dietary ingredient (NDI) notification requirements. Herbs, botanicals, and their concentrates, metabolites, constituents, and extracts are specifically defined as dietary ingredients by Congress under DSHEA. In the case where the substance is purported to be a constituent of a botanical, there can be challenges to supporting the conclusion that the compound is indeed isolated from a botanical. This presentation will briefly discuss how FDA regulates botanical constituents under DSHEA, highlight some of the challenges encountered when investigating substances purported to be botanical constituents, and provide examples of best practices used to confirm (or verify) a compound is a constituent of a botanical (e.g., sampling practices, plant authentication, chemical identity methods).

Shontell Wright

Chemist, ISB in the ODSP, CFSAN, U.S. Food and Drug Administration

A chemist in the Office of Dietary Supplement Programs (ODSP) within the Center for Food Safety and Applied Nutrition (CFSAN) at the U.S. Food and Drug Administration (FDA). She is a member of the Identity and Status Branch (ISB) in the Division of Research and Evaluation (DRE) where she reviews the identity, manufacturing, and specification information provided in new dietary ingredient (NDI) notifications; determines the regulatory status of dietary ingredients and supplements; responds to consumer and industry inquiries; assists with the development of guidance documents; and provides scientific rationales for the development and assessment of FDA's actions related to the safety of dietary supplement products.

Identity Verification Of Botanical Constituents

Wright S[1] & Yates BJ[1]

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Charles Wu

FDA Botanical Review Team Lead

Dr. Charles Wu, Ph.D., Master Pharmacology/Pharmacognosy Reviewer and the Botanical Review Team Lead in the Office of Pharmaceutical Quality (OPQ) of the Center for Drug Evaluation and Research (CDER), the United States Food and Drug Administration (FDA).

Education Dr. Wu trained in Clinical Medicine including Traditional Chinese Medicine (TCM) for his MD and earned his Ph.D. in Medical Science from the Medical Center, University of Amsterdam, the Netherlands.

Dr. Wu began his career at FDA in 2001 as a product reviewer in the Center for Biologics, Evaluation and Research (CBER) and then as a senior Pharmacology/Toxicology reviewer in CDER. In 2013 Dr. Wu joined the Botanical Review Team (BRT) and have been promoted to the BRT lead since 2017. He also served as the FDA's Focal Information Contact (FIC) to the WHO-IRCH (International Regulatory Corporation for Herbal Medicine) since 2019 and becomes the Steering Group (SG) Member and Vice-Chair (2021-2023), as well as serving as an Expert for Regional Consultation of Traditional Medicine to COVID-19 Response in the African Region. During his tenure at FDA, Dr. Wu has gained extensive regulatory experience and scientific knowledge as a result of work with a variety of therapeutic products, including chemical, biological and botanical drugs.

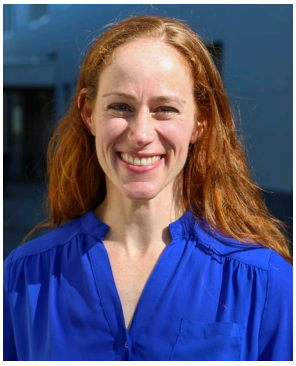
Dr. Wu has published over 30 peer-reviewed journal articles including SCIENCE and scientific book chapters.

Opportunity And Challenge Of Botanical Applications For COVID-19 Management

Charles. Wu

Botanical Review Team, Office of Pharmaceutical Quality, CDER, FDA

Since the onset of COVID-19 at the end of 2019, FDA has played a critical role in the authorization of vaccines, treatments, and diagnostic tests for the disease. Traditional herbal medicine (THM) has been used for thousand years for a variety of medical conditions, such as licorice for bronchitis and the common cold. In addition to exploring specific conventional medicine to effectively manage symptoms of COVID-19, herbal/botanical products, as important complementary and alternative medicine therapy to conventional therapies were studied to reduce infection risk, mitigate symptom, and strengthen immunity. During the outbreak of covid-19 pandemic, FDA has received 48 PIND/INDs and 3 Emergency Use Authorization (EUA)s with botanical components for prophylaxis, modulation of immunity, symptom relief, antiviral potential of COVID-19. Most IND trials are still ongoing and 3 EUAs recommended for more robust clinical studies and safety data. Initial Botanical Applications in COVID-19 Management appear encouraging even though some regulatory and scientific challenges remain.



Sara Handy

Research Biologist in the Office of Regulatory Science within the Center for Food Safety and Applied Nutrition (CFSAN)

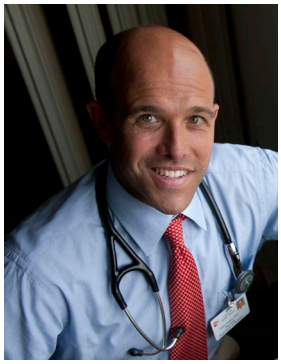
a Research Biologist in the Office of Regulatory Science within the Center for Food Safety and Applied Nutrition (CFSAN) at the United States Food and Drug Administration (FDA). Her work focuses on developing, evaluating, and validating genomic methods to identify plant and animal species in foods and dietary supplements. She is an expert in PCR/ real-time PCR methods, DNA sequencing, sequence libraries and phylogenetic analyses. She has used these tools on a wide range of species. Her current primary project has been building and developing methods from, a DNA reference library targeting botanical species of FDA interest called GenomeTrackrCP (Bioproject in NCBI's GenBank: PRJNA325670). She has authored or coauthored over 55 manuscripts primarily focused on DNA based identification methods. She was a key contributor for "Out of the Box" Health and Human Services Innovates award recognizing innovations representing a new methodology, approach or technology for addressing a difficult problem relevant to HHS. Previously, she obtained a B.Sc. in Ecology and Evolutionary Biology at the University of TN, Knoxville and her Ph.D. in Oceanography at the University of Delaware in 2007 with a dissertation focused on DNA based identification of harmful algal species. From there she took a postdoctoral position the University of Maryland in the department of Cell Biology and Molecular Genetics on the evolution of dinoflagellates. In 2009, she began her work at FDA-CFSAN.

From Barcoding To Baits: Where We Have Been And Where We Are Going With DNA Methodologies In The Quest For Safer Botanicals

Sara M. Handy[1], Elizabeth Sage Hunter[1], Robert Literman [1], Matthew Johnson[2] and Jun Wen[3]

[1] Center for Food Safety and Applied Nutrition, Office of Regulatory Science, U.S. Food and Drug Administration, College Park, Maryland, United States, [2]Department of Biological Sciences, Texas Tech University, 2901 Main Street, Lubbock, Texas 79409, USA, [3] Department of Botany, National Museum of Natural History, Smithsonian Institution, Washington D. C., United States

In 2011, FDA-CFSAN published a method for streamlined universal DNA barcoding of fish for the identification of food products. Based on the success of this method we had hoped to produce similar barcoding methods for plants but as many of us are acutely aware, plants are not as simple to identify. First there is the issue of vouchers. In general, DNA based identification methods for most species suffer from a lack of available high quality sequence data from authenticated vouchers, as it is costly and time consuming to collect, store, and sequence these specimens. To circumvent this FDA-CFSAN collaborates with many groups, including the Smithsonian, to collect and identify plant voucher specimens. Additionally, there are common challenges associated with designing universal plant barcodes that either render the barcodes too broad (i.e., will not get to species level) or too specific (i.e., good at the species level but will not work well outside of a specific group). Next, our focus turned to whole chloroplast genomes and next generation sequencing technologies. We then discovered that DNA based identification using chloroplast genomes suffers from several *potential* limitations including functionally constrained evolutionary rates and lack of resolution with respect to hybrids or and hybrid/allopolyploid taxa depending on what the question is. Moving forward, our group is focused on building customizable species/population identification pipelines that better leverage genome-scale data via reference-free analysis of nuclear data, as well as attempting to harness a simplified bait method and bioinformatic analysis pipeline that will allow for a global screen for plant species. This talk will be a higher-level look back on the past 10 years of this work regarding using DNA sequencing to identify botanicals in foods and dietary supplements, as well as a look forward to where we, as FDA-CFSAN, are going by leveraging the methods that already exists in addition to those we are currently developing.



Pieter Cohen

Associate Professor of Medicine at Harvard Medical School and a general internist at Cambridge Health Alliance in Somerville, Massachusetts

Dr. Pieter Cohen, a graduate of Yale School of Medicine, is an Associate Professor of Medicine at Harvard Medical School and a general internist at Cambridge Health Alliance in Somerville, Massachusetts. Dr. Cohen is a national expert on the safety of dietary supplements and his work has been published in the top medical and public health journals.

Updates In Supplement Research With Dr. Cohen

Pieter Cohen

Medicine at Harvard Medical School and Cambridge Health Alliance in Somerville, Massachusetts

Andrea Bugarcic

Senior Lecturer, The Consortium For Health And Military Performance (CHAMP)

Education: University of Auckland PhD (Virology), MSc (Virology)

Research Interests: Understanding synergistic cellular actions of herbal medicines in bacterial infections (biofilms) and Parkinson's Disease using the backdrop of traditional evidence, contemporary herbal medicine practice and complex co-culture cellular models. Developed a tradition/research/practice nexus framework for a more focused and relevant pre-clinical research that is transferable to any disease/condition/infection context.

Editorial and peer reviewer duties: Special issue Editor for Cells (Focus on Cellular Parkinson's Disease — From Gut to Brain) and peer reviewer for several journals including, Advances in Integrative Medicine, Nutrients, Molecules and Cells.

Traditional Evidence And Pre-Clinical Research - Alignment, Limitations And Opportunities

Bugarcic A[1], Steel A[2], Foley H[2], Geldard C[1], Imtiaz I[1], Oliviera E[1], Wardle J[1]

[1]National Centre for Naturopathic Medicine, Southern Cross University, Lismore, Australia, [2]Australian Research Centre in Complementary and Integrative Medicine, University of Technology, Sydney, Australia

The World Health Organisation (WHO) defines traditional medicine as the "sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness" (World Health Organization, 2018). Traditional herbal treatments, substantial part of traditional medicine across all traditional medicine systems, were prepared through the use of whole herb(s) and/or parts of plants and in different forms, including decoctions, teas, tinctures, powders, and poultices which remained the main preparation methods until the 18th century (Fridlender et al., 2015; Ogbonna et al., 2012). While traditional evidence offers an avenue for exploring approaches to disease, it is also often misinterpreted and used in a non-traditional, reductionist way to develop new pharmaceuticals and products. Researchers across the world create compound libraries using fractionation approaches - compounds that are then screened simple pre-clinical biological assays. While this bio-fractionation approach can lead to development of new drugs, it ignores the complexity and chemical synergy of medicinal plants and their traditional medicinal use resulting in expensive, lengthy and often ineffective drug development processes and criticism of medicinal plants effectiveness in the applicable disease state.

To address alignment between traditional knowledge and pre-clinical research with the ultimate view of drug development process that still aligns with the current staged approach, we have developed a tradition-research nexus framework that considers not just medicinal plant complexity and their use but also extends pre-clinical research into using more complex *in vitro* models. Tradition-research nexus seeks to first understand traditional knowledge and design appropriate co-culture/primary in vitro models to ultimately test medicinal plants in the way that they were used using multiple biological assays. Current presentation will describe the framework and its implementation into drug development projects currently underway in our laboratory. Presentation will also discuss limitations and opportunities of using this approach - is framework flexible to capture all available traditional knowledge, how do we account for plant complexity and possible synergy, what are intellectual property issues to consider, are in vitro models robust and reproducible, is the overall approach aligned to the current staged approach for drug development, what are the implication of natural products industry and how does this benefit custodians of the traditional knowledge?

CDR Shannon Aldrich

Consumer Safety Officer, Food and Drug Administration

CDR Aldrich is a Consumer Safety Officer (CSO) at the Food and Drug Administration, Office of Regulatory Affairs (ORA), Office of Policy, Compliance and Enforcement, Division of Compliance and Enforcement, Health Fraud Branch (HFB). In ORA/HFB, she conducts complex investigations into firms selling fraudulent products. Prior to ORA, she was a CSO at the Center of Biologics Evaluation and Research, Office of Compliance and Biologics Quality, Division of Case Management investigating firms marketing unapproved stem cell products direct to consumers. She has a Masters of Public Health from the George Washington University, a Graduate Certificate in Cyber Threat Research & Analytics from Carlow University and a Regulatory Affairs Certification (RAC). She has been a Public Health Service Commissioned Corps Officer since 2013.

Health Fraud Updates And Emerging Trends

CDR Shannon Aldrich

Food and Drug Administration

James Kababick

Founder and Director of Flora Research Laboratories, LLC (FRL)

James Kababick is the founder and Director of Flora Research Laboratories, LLC (FRL) which specializes in the research and analysis of botanicals, dietary supplements and related compounds. He is also the interim President of the North American Chapter of the HPTLC Association. For many years he served as an adjunct faculty at Bastyr University where he taught botanical drug identification by microscopy and thin layer chromatography. He serves on multiple expert committees for AOAC, USP, NIH, AHPA, and others. James is the pioneer of the field called "Phytoforensic Science." Phytoforensic Science involves utilizing numerous technologies from microscopy to mass spectrometry to detect adulteration and contamination in the global food supply chain with a special focus on dietary supplements. In 2010 James was named "Fellow of AOAC." He currently serves on the 2020-2025 USP Botanical Dietary Supplements & Herbal Medicines Expert Committee, the USP Joint Standard Settings Subcommittee, the Subcommittee on Modern Analytical Methods, the USP Dietary Protein working group, and the Saw Palmetto Modernization working group.

Rapid Simultaneous Quantitation Of Kavalactones And Flavokavains In Piper Methysticum Root By A-TEEM Spectroscopy

Kababick J, Wise S, Flora Research Laboratories, Grants Pass, OR, 97526

Individual botanical marker compounds are mostly analyzed by HPLC utilizing UV detection. Even with the advent of fused core and UHPLC column technologies, the technique involves the use of mobile phase solvents, calibration standards, system suitability and other time consuming and resource intensive steps. We present a novel approach to the simultaneous quantitative analysis of kavalactones and flavokavains in Piper methysticum root materials utilizing A-TEEM Spectroscopy (simultaneous Absorbance-Transmission fluorescence Excitation and Emission Matrix acquisition). The sample extract is diluted and ran directly in a cuvette with no chromatographic separation. Quantitation is carried out using chemometric modeling. Data correlates well with data obtained from a SLV validated HPLC method for each kavalactone and flavokavain. The method offers a faster, easier and greener option to HPLC for routine testing of kava root.

James Harnly

Research Leader, USDA

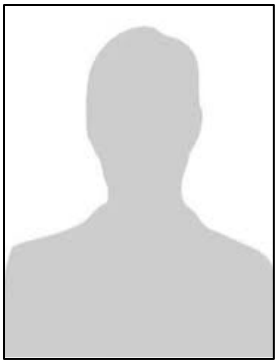
James Harnly, PhD, is an analytical chemist with expertise in atomic and molecular spectroscopy and authentication of food and botanical materials using chemometric methods. He has more than 40 years of experience in industry and government. He serves as the Research Leader for the newly organized Methods and Applications Food Composition Lab, where he is responsible for FoodData Central, the new USDA food composition database system, and the analytical support group. Dr. Harnly has authored more than 150 peer-reviewed papers, 18 technical reports and book chapters, and holds two patents. He served as the US editor of the Journal of Analytical Atomic Spectrometry and as Editor-in-Chief of the Journal of Food composition and Analysis. He is a member of the Society for Applied Spectroscopy, American Society for Nutrition, American Society for Mass Spectrometry, and AOAC International. He served on the Board of Directors and a President of the Board for AOAC International and is on the Advisory Board for the American Botanical Council. He received his Bachelor of Arts from the University of Colorado and his Ph.D. in Analytical Chemistry from the University of Maryland.

Chemometrics: A Valuable Tool For Deriving Information From Complex Data Sets

Harnly J

Methods and Applications Food Composition Lab, Beltsville Human Nutrition Research Center, Agricultural Research Service, US Department of Agriculture, Beltsville, MD, USA

Chemometrics is a subset of machine learning which has been defined a set of advanced mathematical and statistical methods for the analysis of data. This defines many methods such as chemometrics, artificial neuro networks, support vector machines, and rule building expert systems. Chemometrics allows us to draw information from multivariate raw data, i.e., to discover patterns, causes of the patterns, and, with appropriate algorithms, the variance associated with the patterns. The most commonly used forms of chemometrics are principal components analysis (PCA for modeling) and partial least squares-discriminant analysis (PLS-DA for classification), unsupervised and supervised methods, respectively. In its simplest form, PCA makes no assumptions about the data and allows examination for patterns based on any known experimental factors (metadata) such as genotype, growing location, processing, age, etc. In its supervised form, soft independent modeling of class analogy (SIMCA), a separate PCA model is built for each class of samples and the models are compared for similarity. Unknown samples may fall into one, or more classes or no class. PLS-DA is more restrictive, always requiring identification of the classes of the samples and forcing an unknown sample into one of the specified classes. One-class PCA modeling, SIMCA with only one class of samples, is an ideal tool for authentication. A model is constructed for a set of authentic samples and the unknown sample is judged to be authentic (fitting inside the specified model limits) or adulterated (outside model limits). If PCA provides separate of samples into distinct clusters, the loadings can identify the variables (e.g., chromatographic peaks or mass spectral ions) that permit discrimination. Finally, PCA has been coupled to analysis of variance (ANOVA-PCA) to allow determination of the variance associated with each experimental factor. For example, the total variance of a set of botanical samples might be attributed to variance between runs, between genotypes, between growing locations, and the residuals from analytical variability. In conclusion, the many forms of chemometric analyses provide the analyst with powerful, well documented tools for deriving information from raw data sets.



Jeffrey Julien

Horiba

Fast Detection Of Adulteration In Lavender Essential Oil Using A-TEEM Multidimensional Spectroscopy

Julien, J

Horiba Instruments, Inc., Piscataway, NJ 08854

Absorbance-Transmission Excitation Emission Matrix, or "A-TEEM" is a multimodal spectroscopic approach that incorporates UV/Vis and 3D fluorescence for a 2-in-1 measurement. This attractive methodology promotes a rapid and cost-effective alternative for analyses in areas as diverse as water treatment, food & beverage, natural products, and pharmaceuticals. One of the key attributes responsible for its appeal is the very low limit of detection, often in the parts-per-billion to parts-per-trillion range, which is several orders of magnitude better than competing technologies such as NIR, FT-IR, and Raman. In addition to having high sensitivity and specificity, A-TEEM has proven to be a robust tool for samples with complex matrices and analytes of interest that are present at low concentrations, which is often the case for natural products. Separation techniques such as liquid (HPLC) or gas (GC) chromatography tend to dominate in this field, where the components of interest must be separated from the matrix for detection. However, the pitfall associated with utilizing these methods is that they are expensive on a per-measurement basis, as the cost of solvents, columns, standards, waste disposal fees, and annual maintenance fees must be considered. In light of these limitations, A-TEEM has demonstrated the capability to characterize these complex samples prior to separations, which if feasible, provides a significant time and cost savings. Here, we will demonstrate how A-TEEM can be used to rapidly screen samples of lavender essential oil to detect signs of adulteration.

Acknowledgments:
Thank you to Amar G. Chittiboyina, Ph.D., FRSC, Assistant Director, National Center for Natural Products Research, School of Pharmacy, The University of Mississippi, for supplying the lavender samples.

Ellie Abraham

Botanical Marketing Intern and Technical Writer at Eurofins Botanicals Testing

Ellie Abraham is a Plant Biology Ph.D. student at Penn State University, where she investigates the potential applications of untargeted metabolomics and multivariate statistical modeling in the herbal product industry. Her bachelors in biology and chemistry (Winthrop University, 2018) and background in plant molecular biology provides a unique perspective in natural product research. Ellie's current marketing role with Eurofins Botanical Testing includes educational content creation, sharing current research, and contributing to innovative research projects. In addition to consumer content, including blogs, white papers, and infographics, Ellie has published peer-reviewed research articles and review papers. She has won multiple public speaking awards and aims to make analytical chemistry and botanical safety an approachable subject for non-scientists and natural product consumers.

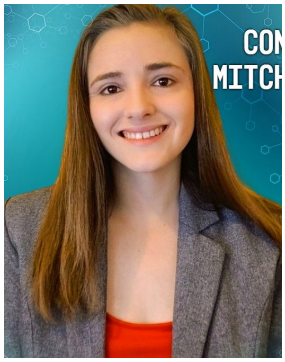
A Chemometric Approach To Berry Dietary Supplement Authentication Based On Targeted Anthocyanin Profiles

Abraham, E.[1,2], Chastain J.[1], Zhou Y.[1]

[1]Eurofins Botanical Testing, Brea, CA. [2] Interdepartmental Graduate Degree Program in Plant Biology, The Pennsylvania State University, State College, PA.

Botanical supplement regulatory testing becomes costly when following ideal batch testing guidelines, however, there are limited efforts to reduce testing requirements and time. This proof-of-concept study evaluated the potential introduction of a chemometric model–based screen to quickly determine if supplements match the claimed ingredient identity based on targeted anthocyanin profiles. First, anthocyanin levels of three berry species were quantified in botanical reference standards (BRMs) for Principal Component Analysis (PCA). These profiles allowed full separation of the three species based solely on the differences in anthocyanin concentration. Next, an evaluation of PCA's ability to distinguish common botanical adulterants from the three target species demonstrated that all but one adulterant (96%) was successfully separated. Finally, the model was used to evaluate species identity claims of commercially available botanical supplements. 72.73% of unverified samples clustered with the claimed species BRMs, while the other 27.27% of samples grouped either with another species or the non-target BRMs. Based on these findings, we would suggest the incorrectly classified samples move forward with HPLC, HP-TLC, or other analytical analysis for identity investigation, but the correctly classified samples can skip additional pricey analysis.

Acknowledgments:
This study was funded by Feihe Dairy Co. Ltd. We would like to thank Dr. Hong You and Chris Lund for this guidance on this project.



Connie Mitchell

Scientific Program Manager at the Health and Environmental Sciences Institute (HESI)

Connie Mitchell is a Scientific Program Manager at the Health and Environmental Sciences Institute (HESI), a science non-profit based in Washington, DC, USA. Prior to joining HESI in early 2020, she was a Fellow at the US Environmental Protection Agency working on chemical prioritization under the Toxic Substances Control Act. She completed her graduate studies in Environmental Toxicology at the University of California Riverside. At HESI, Connie co-manages the Botanical Safety Consortium, which is a multi-partite, multi-stakeholder international effort that brings together key scientific experts to develop and gain confidence in new approach methods applied to botanicals as complex mixtures. As a Scientific Program Manager, she provides scientific, strategic, and administrative support to collaborative scientific committees involving academic, government, nonprofit, and private sector scientists. She also co-manages other projects related to toxicology and risk assessment, including the Emerging Systems Toxicology for the Assessment of Risk (eSTAR) and the Next Generation Ecological Risk Assessment Committees.

Updates On The Development Of A Botanical Safety Toolkit

Mitchell C A[1], Embry M[1], Johnson H[2], Oketch H[3], Sudberg E[4], Rider C[5], Welch C[6], Kelber O[7], Roe A[8]

[1]Health and Environmental Sciences Institute (HESI), [2]AHPA, [3]USP, [4]Alkemist Labs, [5]NIEHS, [6]US FDA, [7]Bayer, [8]P&G

Botanicals have inherent complexity with respect to their chemical composition, which makes them difficult to assess for toxicity and efficacy. In cases where botanicals lack history of use data (which already does not consider factors like delayed effects [e.g., cancer] or susceptible subpopulations [e.g., people with diabetes]), additional toxicity data may be needed. However, testing in mammalian models is resource intensive and typically limited to evaluation of a single sample, which may or may not represent the compositional range of the botanical ingredient available in the market. Additionally, regulatory agencies have called for action to move away from animal testing to more predictive approaches. New Approach Methods (NAMs) including *in vitro* and *in silico* technologies have been developed and applied to single chemicals but have yet to be fully vetted for application to complex mixtures. All these factors lead to the need for NAMs to evaluate potential toxicity in botanicals.

A cross-sector initiative, the Botanical Safety Consortium (BSC), is working to bring together key scientific experts to enhance the botanical safety toolkit and bring clarity to botanical dietary ingredient assessments. The focus of this effort is to assess the suitability of toxicity assays for botanicals as complex mixtures; however, the authentication of botanicals, and the constituent identification and quantification are also essential. In this session, we will discuss updates from the BSC, including the ongoing assay evaluation of NAMs for botanicals as complex mixtures and updates on constituent identification and quantification.

Speaker 1: Brief introduction and updates on the 2022 activities of the BSC

Speaker 2: Analytical methods to identify and quantify botanical constituents

Speaker 3: NAM method evaluated for botanicals as complex mixtures

Holly Johnson

Herbal Products Association (AHPA)

Holly E. Johnson, Ph.D. is Chief Science Officer for the American Herbal Products Association (AHPA), an alliance of over 400 member
companies doing business in the natural products industry. Dr. Johnson took a Ph.D. in Pharmacognosy and conducted medical ethnobotany fieldwork in a variety of indigenous communities. Holly is an active expert volunteer in standards setting for AOAC in foods, dietary supplements, and botanicals; she is a member of the United States Pharmacopeia (USP) Expert Committee for Botanical Dietary Supplements & Herbal Medicines and the USP Cannabis Expert Panel. She also serves on the Advisory Boards of the American Botanical Council and the American Herbal Pharmacopeia, and on the Steering Committee & Pharmacognosy working group for the Botanical Safety Consortium. Holly has over two decades experience in botanicals research and spent many happy years giving courses at the University of Hawaii.

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Speaker 1: Brief introduction and updates on the 2022 activities of the BSC

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Amy L. Roe

The Procter & Gamble Company

Dr. Roe has 23+ years of experience as a practicing toxicologist in government, pharmaceutical and consumer product industries, through positions at both the FDA and The Procter & Gamble Company. Her professional experience is in general, descriptive, and regulatory toxicology as well as specialized expertise in drug/xenobiotic metabolism and pharmacokinetics. Her industry experience is quite broad and includes toxicology support of drugs, medical devices, herbal/dietary supplements, foods, and water filtration devices. As a project leader, she has led multi-disciplinary drug development teams. Dr. Roe is a board-certified toxicologist (DABT) and a Fellow of the Academy of Toxicological Sciences (ATS). She is well-recognized externally in her field as evidenced by her service on a number of professional boards and committees including the USP Dietary Supplement Admission Evaluation & Labeling Expert Committees and Probiotic Expert Panel, SOT Regulatory & Safety Evaluation Specialty Section (Past-President), Food Safety Specialty Section (Vice-President Elect) and an NIH/NCCIH Expert Advisory Panel related to natural product-drug interactions. Dr. Roe is on the Steering Committee of the Botanical Safety Consortium (BSC), a public-private consortium led by FDA and NIEHS and serves as co-chair of the hepatotoxicity/ADME sub-committee of the BSC. She serves on the Editorial Board of Applied In Vitro Toxicology and Toxicological Sciences.

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[1]Health and Environmental Sciences Institute (HESI), [2]AHPA, [3]USP, [4]Alkemist Labs, [5]NIEHS, [6]US FDA, [7]Bayer, [8]P&G

Botanicals have inherent complexity with respect to their chemical composition, which makes them difficult to assess for toxicity and efficacy. In cases where botanicals lack history of use data (which already does not consider factors like delayed effects [e.g., cancer] or susceptible subpopulations [e.g., people with diabetes]), additional toxicity data may be needed. However, testing in mammalian models is resource intensive and typically limited to evaluation of a single sample, which may or may not represent the compositional range of the botanical ingredient available in the market. Additionally, regulatory agencies have called for action to move away from animal testing to more predictive approaches. New Approach Methods (NAMs) including *in vitro* and *in silico* technologies have been developed and applied to single chemicals but have yet to be fully vetted for application to complex mixtures. All these factors lead to the need for NAMs to evaluate potential toxicity in botanicals.

A cross-sector initiative, the Botanical Safety Consortium (BSC), is working to bring together key scientific experts to enhance the botanical safety toolkit and bring clarity to botanical dietary ingredient assessments. The focus of this effort is to assess the suitability of toxicity assays for botanicals as complex mixtures; however, the authentication of botanicals, and the constituent identification and quantification are also essential. In this session, we will discuss updates from the BSC, including the ongoing assay evaluation of NAMs for botanicals as complex mixtures and updates on constituent identification and quantification.

Speaker 1: Brief introduction and updates on the 2022 activities of the BSC

Speaker 2: Analytical methods to identify and quantify botanical constituents

Speaker 3: NAM method evaluated for botanicals as complex mixtures

Rachel Harris

Application Scientist, MOBILion Systems, Inc.

Education: Ph.D. in Chemistry, Vanderbilt University (2015-2021); Bachelor of Science in Chemistry, University of North Carolina (2011-2015)

Honors: Vanderbilt Chemistry Warren Fellowship (2020), NSF-GRFP Honorable Mention (2016), Vanderbilt Institute of Chemical Biology Fellowship (2015), Harold Stirling Vanderbilt Graduate Scholarship (2015), Eastern Analytical Symposium Student Research Award (2014), National Merit Finalist (2011)

Professional Organizations: The American Society of Mass Spectrometry, Alpha Chi Sigma Chemistry Fraternity, Phi Beta Kappa – Alpha of North Carolina

Biosketch: Rachel Harris is an applications scientist at MOBILion Systems. She first began her research in the field of ion mobility-mass spectrometry as an undergraduate at UNC Chapel Hill, in the lab of Dr. Gary Glish, where she worked on a prototype FAIMS device. She later received her PhD in Analytical Chemistry from the lab of Dr. John McLean at Vanderbilt University. Her dissertation research focused on the combination of multiple analytical techniques for lipid structural characterization, including ion mobility, ozonolysis, and surface induced dissociation. At MOBILion Systems, she generates applications-specific content to show off the MOBIE platform's capabilities and serves as the in-house small molecules expert, providing actionable feedback for product improvements. More recently, she has been utilizing high-resolution ion mobility to construct a "conformational space" map of cannabinoid species to enable the rapid classification of unknowns in hemp extracts.

More Than Just A Number: Utilizing CCS And Conformational Space Analysis To Characterize Unknowns In Complex Extracts

Rachel A. Harris[1], Frederick G. Strathmann[RH1] [1]

[1]MOBILion Systems, Inc., Chadds Ford, PA 19317

Natural products from plants, either as pure compounds or as prepared extracts, are widely recognized for their near unlimited potential due to their unmatched and rich chemical diversity. Challenging aspects in the use of natural products include the recognition that unknown compounds are not included in spectral databases, have no chemical standards, and discrimination of structurally similar isomers requires knowledge of isomer presence and potentially difficult and time-consuming chromatographic separations.[FS1] Ion mobility (IM) is a gas phase analytical technique that separates ions based on differences in their size, shape, and charge in the gas phase. Increasingly, IM is being utilized in combination with mass spectrometry (MS) and liquid chromatography-mass spectrometry (LC-MS) for various purposes such as reducing interferences and decreasing LC runtimes for improved throughput, separating challenging isomeric compounds unresolvable via LC, and increasing identification confidence using collision cross section, a unique molecular identifier that can be derived from IM arrival time measurements. A unique feature of combined IM-MS analyses is that different classes of analyte molecules partition into different regions of what can be termed “conformational space” due to class-specific structural folding in the gas phase. Mapping out these CCS vs. m/z trendlines can be a powerful tool that can be applied to extracts to rapidly classify potential unknowns. Herein we report our use of the MOBIE® high-resolution ion mobility system (HRIM) from MOBILion with an Agilent QTOF to determine the CCS values for a series of cannabinoid standards, including isomeric cannabinoids such as delta-8 and delta-9 THC, to map out the conformational space for this class of analytes. The ~250 resolving power of the HRIM MOBILion system allows for the separation of very structurally similar species with CCS differences of ≥ 0.5% in the absence of any chromatographic separation, which enables the construction of a more finely detailed and analytically useful conformational space plot. The application of the developed HRIM-MS methodology and conformational space mapping to various extracts, including hemp, is ongoing.

Christopher R. Beekman

Chemist at the U.S. Food and Drug Administration (FDA), (CFSAN), ORS

Education: University of Florida (Gainesville, FL) Ph.D. Chemistry 2011-2015; King's College (Wilkes-Barre, PA) B.S. Chemistry, B.S. Biology 2007-2011

Research Interests: Current research focuses on the development of methods for the screening and quantitative detection of adulterants in dietary supplements. Before joining CFSAN, Chris was a Chemist in the Center for Drug Evaluation and Research (CDER) at the FDA where his role centered on providing bioanalytical support for research projects focused on the examination of the bio-distribution and bioequivalence of reference and generic drugs. His major research interests include working with novel technologies and instrumentation, such as ion mobility mass spectrometry, to improve separation and quantitation of small isomeric molecules.

Professional Organizations: American Society for Mass Spectrometry (ASMS) Member 2011-Present

Honors: University of Florida Department of Chemistry Teaching Award (2013): U.S. FDA, Office of Clinical Pharmacology, Excellence in Science Group Award, iron colloid laboratory group for resolving a complex regulatory issue regarding the bioequivalence standards for ferric gluconate (2016); U.S. FDA, CDER, Group Recognition, for collaborative lab research to support equivalence demonstration of generic iron complex drug products (2017); U.S. FDA, Office of Pharmaceutical Quality, Office of Testing and Research, Group Award, Compounded Intravitreal Tri-Moxi Incident Investigational Team (2017); Hood College ORISE Mentor Appreciation Award (2018); U.S. FDA, Regulatory Science Excellence, for impactful method development and testing to meet the requirements of the CDER Taskforce related to the Valsartan/ARB incident (2019); U.S. FDA, Commissioner's Award of Excellence, for the development and pilot of laboratory safety assessments (2019)

Editorial Duties: American Society for Mass Spectrometry (ASMS) Program Committee (2021, 2022)

Development OF A Multi Analyte Method FOR THE Screening OF Dietary Supplement Products

Beekman C[1], Pawar R[1]

[1]Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration

The dietary supplement market can be perceived by consumers as a safer and natural alternative to some conventional medicines to support bodily needs and functions. The market is diverse including a variety of dietary ingredients (e.g., vitamins, minerals, herbs, amino acids, and enzymes) which can be manufactured in many forms (e.g., tablets, capsules, softgels, powders, and liquids). Additionally, products marketed as dietary supplements may have unallowed ingredients, substitutions of an intended botanical ingredient, or the addition of adulterants such as active pharmaceutical ingredients. To assist in monitoring and to enforce regulations on the composition of products marketed as dietary supplements, this research will include the development and validation of a high-resolution mass spectrometry (HRMS) method for compound screening, identification, and quantification.

Phase one of the project includes the development of a liquid chromatography (LC)- HRMS screening method for the identification of known ingredients and potential adulterants in dietary supplement products. Sample data are generated by non-targeted data dependent acquisition and post-processed using a custom library of 300+ compounds. In phase two, positive compound identifications are targeted for confirmation and quantification by LC-HRMS. In this presentation, the method workflow will be piloted using an initial target list of 29 compounds. For each target, compound dependent parameters (retention time, normalized collision energy, ion transitions) were optimized on a Thermo Orbitrap IDX mass spectrometer. Using generic extraction conditions, recovery was assessed in priority sample matrices including tablets, capsules, softgels, liquids, and gummies. Combined, the platform will provide a validated method for laboratories to test products marketed as dietary supplements and deliver an approach for extending the method to new analytes of interest based on future changes in the dietary supplement marketplace.

Cuiying (Macy) Ma

Principal Scientist US Pharmacopeial Convention

Cuiying (Macy) Ma, Ph.D., is a principal scientist at U.S. Pharmacopeial Convention (USP) responsible for monograph development of botanical dietary supplements and traditional herbal medicines. Dr. Ma joined USP in 2006 as a scientist doing reference standards development and evaluation until 2013. Before joining USP, Dr. Ma conducted her postdoctoral research in College of Pharmacy, the University of Illinois at Chicago, performed research on bioassay guided isolation, structure elucidation of bioactive compounds from plants. She worked for eight years in the National Institute for the Control of Pharmaceutical and Biological Products (NICPBP, current name is NIFDC), Beijing, China, focused on quality control methods development for Traditional Chinese Medicines (TCM). Dr. Ma holds a Ph.D. degree in natural products chemistry from the Hong Kong University of Science and Technology; a M.S. degree in analytical chemistry; and a B.S. degree in pharmacy (TCM) from the Beijing University of Chinese Medicine and Pharmacology.

USP Monographs For Quality Control Of Different Ginsengs

Ma C

Science, Dietary Supplements and Herbal Medicines, U.S. Pharmacopeial Convention, 12601 Twinbrook Parkway, Rockville, MD, US

Ginseng species are members of the genus *Panax* and are characterized by the presence of ginsenosides. American ginseng, Asian ginseng, Tienchi ginseng, and red (steamed) Asian ginseng roots and their extracts are very popular ingredients of dietary supplements. Quality control of ginseng products and differentiation of different ginseng articles are important for guaranty of quality and correct labeling. USP monographs for different ginsengs provide quality control procedures with suitable reference standards (RS) to help ensure correct and qualified ginseng ingredients are used.

USP ginseng monographs include both UHPLC and HPTLC identification tests of ginsenosides, which can efficiently identify different ginseng roots species, ginseng powders and ginseng extracts, and distinguish each ginseng ingredient from others. The major differences among them includes the following: Asian ginseng root contains ginsenoside Rf, which can differentiate it from American ginseng and Tienchi ginseng roots, while Tienchi ginseng root contains notoginsenoside R1, which can differentiate it from Asian ginseng and American ginseng roots; Asian ginseng root also contains malonyl ginsenosides Rb1, Rb2 and Rc but red Asian ginseng root does not contain malonyl ginsenosides because it is obtained by steaming the Asian ginseng, which degrades the malonyl ginsenosides. USP Powdered American Ginseng Extract RS, USP Powdered Asian Ginseng Extract RS and USP Panax Notoginseng Root and Rhizome Dry Extract RS are used in related monographs to help identify the UHPLC/HPTLC peaks/bands.

Determination of the total content of ginsenosides provides a surrogate measurement for strength of the ginseng ingredients. Each USP ginseng monograph includes a UHPLC assay using USP Ginsenoside Rg1 RS and USP Ginsenoside Rb1 RS to quantitate total ginsenosides with the calculation to use relative response factors. The content ratios of ginsenosides also contribute to the identity of different ginseng species and whether the ingredient was steamed.

Acknowledgments:

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- Analytical Development Laboratory, USP, MD, USA.
- Dr. Gabriel I. Giancaspro from Science, Documentary Standard and Compendial Policy, USP, Rockville, MD, USA
- Dr. Virginia S. Goldman from Science, Dietary Supplements and Herbal Medicines, USP, Rockville, MD, USA

Katerina (Kate) Mastovska

Deputy Executive Director and Chief Science Officer at AOAC INTERNATIONAL

Dr. Katerina (Kate) Mastovska is Deputy Executive Director and Chief Science Officer at AOAC INTERNATIONAL, where she is responsible for leadership of all science programs and projects. She joined the AOAC staff in January 2023 but has been a very active member of AOAC INTERNATIONAL since 2004. Kate is a Fellow of AOAC INTERNATIONAL and received the Association's highest scientific honor, the Harvey W. Wiley Award, in 2021. She has worked for the University of Chemistry and Technology in Prague, the US Department of Agriculture, and founded her own independent consulting business, Excellcon International. In 2009, she began her work at Covance Laboratories where her responsibilities grew rapidly. After the acquisition of Covance Food Solutions by Eurofins Scientific, she has most recently served as Chief Scientific Officer, Eurofins US Food Division. Kate holds a Ph.D. in Food Chemistry and Analysis from the University of Chemistry and Technology in Prague.

AOAC INTERNATIONAL Programs Addressing Analytical Needs In Botanical Ingredients And Dietary Supplements

Katerina Mastovska

AOAC INTERNATIONAL, Rockville, MD, USA; kmastovska@aoac.org

AOAC INTERNATIONAL has a long experience in providing analytical solutions for the botanical ingredient and dietary supplement sector. In recent years, this effort has been concentrated into dedicated programs. In collaboration with the National Institutes of Health Office of Dietary Supplements, AOAC carried out a stakeholder program in 2013-2018 to develop voluntary consensus standards and methods for 25 high-priority ingredients/issues. In 2018, AOAC Cannabis Analytical Science Program (CASP) was established to serve as a forum discussing the science related to the analysis of hemp- and cannabis-based matrices, develop standards and methods, and provide training and education to this relatively new and fast-growing analytical community. And, most recently, AOAC has initiated a new Botanical Ingredients and Dietary Supplement Integrity (BIDSI) program to address emerging and ongoing challenges, method gaps and other needs related to the analysis of botanical ingredients and dietary supplements. The first BIDSI initiative involves development of a voluntary consensus standard for the determination of pyrrolizidine alkaloids in teas, herbs, herbal infusions, seed spices and botanical dietary supplement ingredients to meet the European Commission Regulation (EU) 2020/2040. Another potential initiative on ethylene oxide is in an initial stage of formulating the main issues that should be addressed when it comes to the residues of ethylene oxide and its marker compound, 2-chloroethanol, in various botanicals and dietary supplement products, including empty capsules. This presentation will focus on the current AOAC initiatives and programs, discuss how AOAC can build on the past accomplishments, and solicit feedback from the audience on the main challenges, gaps and needs that they would like to see addressed.

Jack E. Henningfield

Johns Hopkins University & Pinney Associates

Jack E. Henningfield, PhD, Professor, Adjunct, Dept. Psychiatry & Behavioral Sciences, Johns Hopkins University, and Vice President, Research, Health Policy & Abuse Liability, PinneyAssociates. Former Chief, Clinical Pharmacology Branch, and Biology of Dependence & Abuse Potential Assessment Section, National Institute on Drug Abuse (NIDA). His abuse potential research began with preclinical studies in 1971 and clinical studies in 1978. He has contributed to FDA guidance for abuse potential assessment since 1991, and remains an active contributor to the evolution of abuse potential assessment methods to meet the challenges of diverse nicotine, opioid, and more recently, psychedelic products and novel mixed acting new substances and products including dietary substances such as kratom. Most of his approximately 500 publications and reports for NIDA & the World Health Organization involved abuse/dependence potential across a broad range of CNS active substances and new drugs

Advancing Kratom Science: New Data On Kratom's Pharmacology, Safety, Pharmacokinetics, Abuse Potential, And Real-World Surveys

Johnson H[1], Henningfield J[23], Huestis M[2], Smith K[4], Kingston R[5]

[1]American Herbal Products Association (AHPA), [2]Psychiatry & Behavioral Sciences, Johns Hopkins University, [3]Health Policy & Abuse Liability, PinneyAssociates, [4]National Institute on Drug Abuse Intramural Research Program, [5]SafetyCall International L.L.C

Kratom, a botanical with CNS-active alkaloid constituents, has been used as a food and traditional medicine for centuries in Southeast Asia and is currently consumed by millions of Americans with increasing prevalence. Kratom research has accelerated dramatically over the past 5 years with over $30 million in new funding from the National Institute on Drug Abuse (NIDA), National Institutes of Health. There were more than 100 new research studies addressing the safety and abuse potential of kratom including experimental and real-world study designs. The expert panel will present new developments in kratom pharmacology from in vitro, preclinical, and human research. For the first-time, comprehensive safety data from Johnson Foods recently completed single and multiple ascending dose kratom clinical study will be presented.

Acknowledgments:
Through Pinney Associates, Drs. Henningfield and Huestis consult to the American Kratom Association and Johnson Foods. Johnson Foods has submitted an NDIN to FDA for a kratom leaf ingredient.

Marilyn A Huestis

Senior Scientist at Pinney Associates

Professor Huestis conducted controlled drug administration studies at NIDA for 23 years. She is Senior Scientist at PinneyAssociates, Professor at multiple universities & President Huestis & Smith Toxicology. Research includes cannabinoids, mitragynine & psilocybin neurobiology, in utero drug exposure & DUID. She published 554 manuscripts. She has degrees in biochemistry, clinical chemistry, toxicology & a honorary doctorate & received the 2023 Mechoulam ICRS, 2021 AACC Outstanding Lifetime Achievement, 2021 NSC Distinguished Service to Safety Awards & others. She serves on WADA Prohibited List Committee, was SOFT & TIAFT past president & past Toxicology Chair, AAFS.

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Kirsten Smith **Kirsten Smith**

Research fellow at the National Institute on Drug Abuse Intramural Research Program (NIDA IRP)

Dr. Kirsten Smith is a postdoctoral research fellow at the National Institute on Drug Abuse Intramural Research Program (NIDA IRP) in the Translational Addiction Medicine Branch. Dr. Smith has investigated real-world kratom use since 2016 when she encountered it during her clinical training. At NIDA IRP she recently completed a K99-supported nation-wide study that involved ecological momentary assessment coupled with kratom product assay, and an observational laboratory substudy investigating acute effects of commercial kratom products among regular users. She will continue her clinical research at the Johns Hopkins University Behavioral Pharmacology Research Unit as Assistant Professor beginning in August 2023.

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Rick Kingston

SafetyCall International L.L.C

Rick Kingston PharmD is Co-Founder, President, Regulatory and Scientific Affairs, and Sr. Clinical Toxicologist at SafetyCall International L.L.C., a multidisciplinary healthcare firm academically affiliated with the University of Minnesota and focused on providing consumer product manufacturers' services in the area of post-market medical surveillance, regulatory reporting support for adverse events, and product safety. His professional and academic career spans over 40 years including previously serving as co-founder and Director of the Minnesota Regional Poison Center and serving as a full Professor in the Department of Experimental and Clinical Pharmacology at the University of Minnesota, College of Pharmacy where he continues to serve as a Clinical Professor. He also holds an Adjunct appointment at the Rank of Professor at the University of Mississippi College of Pharmacy and its National Center for Natural Product Research which is co-funded by the US FDA. He has published and presented extensively in the field of clinical toxicology and regulatory policy, and serves on numerous scientific panels, advisory boards and non-profit professional organization scientific committees advising on issues of product stewardship, science and safety. His professional expertise spans the areas of consumer product post-market surveillance, poisoning epidemiology, natural product toxicology, clinical toxicology and pharmacology, injury prevention, poison control and product safety regulatory policy.

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Amy L. Roe

The Procter & Gamble Company

Dr. Roe has 23+ years of experience as a practicing toxicologist in government, pharmaceutical and consumer product industries, through positions at both the FDA and The Procter & Gamble Company. Her professional experience is in general, descriptive, and regulatory toxicology as well as specialized expertise in drug/xenobiotic metabolism and pharmacokinetics. Her industry experience is quite broad and includes toxicology support of drugs, medical devices, herbal/dietary supplements, foods, and water filtration devices. As a project leader, she has led multi-disciplinary drug development teams. Dr. Roe is a board-certified toxicologist (DABT) and a Fellow of the Academy of Toxicological Sciences (ATS). She is well-recognized externally in her field as evidenced by her service on a number of professional boards and committees including the USP Dietary Supplement Admission Evaluation & Labeling Expert Committees and Probiotic Expert Panel, SOT Regulatory & Safety Evaluation Specialty Section (Past-President), Food Safety Specialty Section (Vice-President Elect) and an NIH/NCCIH Expert Advisory Panel related to natural product-drug interactions. Dr. Roe is on the Steering Committee of the Botanical Safety Consortium (BSC), a public-private consortium led by FDA and NIEHS and serves as co-chair of the hepatotoxicity/ADME sub-committee of the BSC. She serves on the Editorial Board of Applied In Vitro Toxicology and Toxicological Sciences.

Prediction Of Clinically Relevant Botanical-Drug Clearance Interactions For Boswellia Serrata Extract Using Sandwich-Cultured Human Hepatocytes

Roe AL[1], Vyas D[2], Sharp A[2], Moseley C[2], Kralj T[2], Majeed M[3], Mundkur L[3], Nagabhushanam K[4] & Brouwer K[2]

[1]The Procter & Gamble Company, Cincinnati, OH 45040, USA. [2]BioIVT, Durham, NC 27713, USA. [3]Sami-Sabinsa Group, Bengaluru, India. [4]Sabinsa Corporation, East Windsor, NJ 08520

Boswellia serrata extract (BSE) is used in dietary supplements for its anti-inflammatory properties. There are reports in the scientific literature that BSE has the potential to inhibit CYP450 enzymes. We have shown that sandwich-cultured human hepatocytes (SCHH) are an excellent model for predicting clinically relevant botanical-drug interactions (BDI) since they integrate metabolism and transport. When using SCHH the BDI potential with BSE appears low; however, our previous work did not include an assessment of CYP450 induction potential. We present an intrinsic clearance approach using SCHH to evaluate an overall net effect (inhibition and induction) of BDI potential with BSE. SCHH (BioIVT) were incubated for 72 hr. with BSE (Boswellin®Super, Sabinsa Corp) concentrations ranging from 0.04 to 30 µg/mL, 0.1% DMSO, 25 µM Flumazenil, 50 µM Omeprazole, 1000 µM Phenobarbital, 20 µM Rifampicin and 20 µg/mL St. John's wort. Enzyme induction was assessed by activity and mRNA for CYP1A2, CYP2B6, and CYP3A4. No induction in either enzyme activity or mRNA was observed for CYP1A2 or CYP2B6 at any tested concentration of BSE. CYP3A induction was observed with BSE at 30 µg/mL based on CYP3A activity and CYP3A4 induction was observed with BSE at 10 µg/mL based on CYP3A4 mRNA. The calculated EC50 (µg/mL) was 13.16 ±1.86 and Emax (fold over control) was 25.98 ±1.98. Metabolic intrinsic clearance of CYP2C9 and CYP3A4/5 was assessed in SCHH following 72 h treatment with 10 µg/mL BSE, 0.1% DMSO, 10 µM Rifampicin, or 20 µg/mL St. John's wort. After 72 hr. treatment, cells were then treated with clinically relevant probe drugs; 25 µM Diclofenac (CYP2C9) and 10 µM Midazolam (CYP3A4/5) and disappearance determined at 1, 2, and 4 hr. post-treatment. Diclofenac clearance was decreased 1.27-fold by treatment with BSE indicating a slight inhibition potential of CYP2C9. Midazolam clearance was increased by 0.62-fold by treatment with BSE indicating a slight induction potential of CYP3A4/5. These findings would indicate that this BSE would have minimal BDI potential for CYP2C9 and CYP3A4/5 substrates. We believe that this clinically relevant *in vitro* approach is an appropriate strategy to screen botanical-based mixtures for drug interaction potential as it takes in to account the additive or synergistic effects between phytochemical constituents.

Kelli L. McDonald

PhD student Auburn University

Kelli L. McDonald, M.S., PhD student - Department of Drug Discovery and Development, Harrison College of Pharmacy (HCOP). Auburn University

Research Interests: My research is focused on botanical-drug interactions. As the use of botanical supplements is exponentially growing, we are analyzing their effects on Cytochrome P450 (CYP) enzymes, as well as drug transporters (P-gp, OATP-1B1, and OATP-1B3). Inhibitory or inductive effects could alter the efficacy of co-administered medications, potentially causing fatal adverse reactions.

Education: Florida Atlantic University M.S. (Biomedical Sciences) 2005; University of Central Florida B.S. (Forensic Science) 2000;

Professional Organizations: American Society of Pharmacognosy (ASP) (2021 - present); American Association of Pharmaceutical Scientists (AAPS) (2021 - present); American Association of Pharmaceutical Scientists - Auburn Student Chapter (AAPS-AU) (2021 - present); American Chemical Society (ACS) (2021 - present)

Toastmasters International (2016 - present)

Honors: ASP (Lynn Brady Travel Award and Oral Presenter, 2022); AAPS-AU (Vice President-Elect, 2021; President-Elect, 2022); Presidential Graduate Research Fellow (PGRF) (2020 - present); HCOP Research Symposium (2nd place - Graduate Oral Presentation, 2022); Auburn University Student Symposium (Oral Presenter, 2022, HCOP Best Oral Presentation, 2021); Technological Advances in Science, Medicine, and Engineering (TASME) Oral presenter, 2021)

Açaí Fruit Pulp And Supplement Extracts: Potential Induction Of CYP Enzymes And P-gp/OATP-B Transporters

McDonald KL[1], Heck K[1], Salamat J[2], Dennis C[1], Keeton C[1], Almy M[1], Pondugula S[2], & Calderón AI[1]

[1]Department of Drug Discovery and Development, Harrison College of Pharmacy, Auburn University, AL 36849, [2]Department of Anatomy, Physiology, and Pharmacology, College of Veterinary Medicine, Auburn University, AL 36849

Euterpe oleracea Mart., commonly known as açaí, is among the top 40 botanicals currently used in the United States. Its presence in food products and botanical supplements is growing exponentially. To better ascertain potential açaí-drug interactions, we are analyzing the effects of açaí extracts on CYP induction and P-gp/OATP-B drug transporters. Certified organic açaí fruit powder from Mountain Rose (MR) Herbs (Eugene, OR, USA) and dietary supplement capsules containing aqueous extracts of *Euterpe oleracea* Mart. (açaí) fruit from Nature's Way (Green Bay, WI, USA) and Natrol (Chatsworth, CA, USA) were obtained. The Mountain Rose powder is representative of what is present in açaí food products and was extracted in acidic methanol (AC), 95% ethanol (ET), methanol (ME), and water (AQ) individually. The Natrol and Nature's Way capsule brands were chosen based on the 2019 Amazon Market Report and their commercial availability. These 2 açaí botanical supplements were extracted in methanol (ME) and acidic methanol (AC) individually. The lyophilized extract powders were optimized for solubility, found to be a 15% acetonitrile: 85% H_2O solvent mixture. Sandwich cultured primary human hepatocytes (SCHH) were treated with a human-relevant dose concentration (2.321 ng/mL of cyanidin 3-glucoside) of the individual, standardized açaí extracts. CYP induction (CYP3A4, CYP2B6, and CYP1A2) was analyzed via RT-PCR. None of the açai extracts displayed CYP3A4, CYP2B6, or CYP1A2 induction at the human-relevant dose concentration. Additionally, the evaluation of açaí extracts on drug transporters (P-gp and OATP-B) is underway. These effects will be analyzed via RT-PCR for transcriptional induction, as well as substrate probe assays and confirmation of activity levels via LC-MS analysis. This study highlights the importance of a rigorous experimental design to assess the potential for botanical-drug interactions with açaí supplements through CYP and transporter induction.

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Igor Koturbash

University of Arkansas for Medical Sciences

Igor Koturbash is an Associate Professor and Chair at the Department of Environmental Health Sciences and the Founder and Co-Director for the Center of Dietary Supplements Research, at the College of Public Health, University of Arkansas for Medical Sciences (Little Rock, AR). He received his M.D. from the State Medical University in Ivano-Frankivsk, Ukraine (2001), and his Ph.D. in Biomolecular Sciences from the University of Lethbridge, Canada (2008). The major focus of Igor's research is safety, efficacy and mechanisms of action of dietary supplements and understanding how diet and dietary supplements can modulate tissue response to cancer therapy. Dr. Koturbash is heavily involved in a number of safety and efficacy studies on various dietary supplements and herbs, including methionine supplementation, green tea extract and cannabidiol. He has published over 100 peer-reviewed articles and book chapters, serves as an Associate Editor for peer-reviewed professional journals Radiation Research and Journal of Dietary Supplements and is a recipient of the Michael Fry Award from the Radiation Research Society.

Organ-On-Chip Systems As Reliable Translational Tools For Studies On Herbal And Dietary Supplements

Clement K[1,2], Skinner CM[1,2], Ewing L[1,2], McGill MR[1,2], Kennon-McGill S[1,2], Walker LA[3,4], ElSohly MA[3,4], Gurley BJ[2,3], Koturbash I[1,2]

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Animal systems do not always recapitulate human biology, and *in vitro* systems cannot mimic the complexity of living organisms. As a result, these experimental approaches often fail to adequately predict human responses to medicines, food, and chemicals. The recent development of human cell-based "organ-on-chip" technologies capable of emulating many of the functional complexities of human organ systems may help bridge these gaps. Here, we investigated the potential of a novel human organ-on-chip system to emulate cannabidiol-rich cannabis extract (CRCE)-induced liver injury previously described in mice. Mice of two strains, C57BL6/J and B6C3F_1, were subjected to 0, 61.5, 184.5, or 615 mg/kg of CRCE in sesame oil for 10 days. Liver-on-Chip platforms, comprising human primary hepatocytes, sinusoidal endothelial cells, as well as Kupffer and stellate cells were subjected to 0, 300, 1,200, or 4,400 ng/mL of CRCE (8 h exposure followed by 16 h washout) for 5 days. Administration of CRCE in both mouse strains and liver-on-chips resulted in a robust and dose-dependent induction of several key cytochrome P450 enzymes: *Cyp1a2 (CYP1A2), Cyp2b6 (CYP2B10), Cyp2e1, Cyp2c9 (CYP2C19),* and *Cyp3a4*. Furthermore, there was significant congruency in the magnitude of cytochrome P450 induction between mouse livers and human liver-on-chips. CRCE also produced a modest but dose-dependent elevation of alanine-aminotransferase (ALT) in both model systems, indicative of mild liver injury. Evidence of mild hepatotoxicity was confirmed by elevated plasma and decreased liver levels of miR-122 in both experimental models. The results of this study confirm the utility of organ-on-chip systems in translating animal data into clinical practice.

Islam Husain

Post-Doctoral Research Associate, NCNPR, University of Mississippi

Dr. Islam Husain is currently working as a Post-Doctoral Research Associate at the National Center for Natural Products Research, School of Pharmacy, University of Mississippi, United States, since December 2018. He earned his Ph. D. in Microbiology from Rani Durgavati University, Jabalpur, India, in 2016. He has published several research articles in peer-reviewed journals such as Plos One, Biochimie, International Journal of Biological Macromolecules, Chemical Communication, Phytomedicine, Planta Medica, and Journal of Ethnopharmacology etc., and delivered several oral/poster presentations in various scientific meetings. Dr. Husain is also a reviewer of many peer-reviewed Journals. His expertise includes herb-drug interaction (HDIs), especially medicinal herbs and finished products like herbal medicine and botanical dietary supplements (BDS). Dr. Husain is working on the ADMEs of medicinal herbs and their active metabolites.

Phyllanthus amarus Modulate CYPs And P-gp Activity And Induce The Risk Of HDIs

Islam Husain,[1] Balkisu Abdulrahman,[1,2] Olivia R. Dale,[1] Zulfiqar Ali[1], Bill J. Gurley,[1] Amar G. Chittiboyina[1], Ikhlas A. Khan[1,3], & Shabana I. Khan[1,3]

[1]National Center for Natural Products Research, School of Pharmacy, The University of Mississippi, MS 38677, United States, [2]Department of Biochemistry and Molecular Biology, Faculty of Life Sciences, Federal University Dutsin-ma, Katsina State, Nigeria, [3]Department of Bio-Molecular Sciences, School of Pharmacy, The University of Mississippi, University, MS 38677, United States

Phyllanthus amarus Schumach. & Thonn. (Phyllanthaceae) is a widely used herb in various traditional medicinal philosophies worldwide. This plant possesses various medicinally important phytochemicals including alkaloids, flavonoids, lignans, polyphenols, and terpenoids. In the present study, we evaluated the interaction of an ethyl acetate of *P. amarus* (PA) and its major lignans with pregnane X receptor (PXR), cytochromes P450 isoenzyme (CYP3A4), and ABC-transporter (P-gp). The results showed that PA and tested lignans activated PXR in intestinal (LS174T) and hepatic (HepG2) cells (2-5-fold). The RT-PCR analysis revealed that PA and lignans increased the mRNA expression of CYP3A4 and P-gp to various extents. Study is in progress to determine if PA or any of the tested lignans modulate the functional activity of CYP3A4 and P-gp in various cell lines. In summary, the data indicate that the over-consumption of *P. amarus* could affect the normal homeostasis of CYPs and ABC-transporters which may pose the risk for herb-drug interactions (HDIs) with conventional medications if consumed concomitantly. Furthermore, in-depth studies are required to validate current findings

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Deval Patel

Senior Toxicologist

Deval Patel is a Senior Toxicologist at Amway / Nutrilite where she is currently responsible for the safety of Amway's dietary supplement, food and beverage products. In her role, Ms. Patel leads and advise on issues related to safety of botanicals, micro nutrients and dietary ingredients. Her work also includes conducting risk assessment and risk management in support of new products and technologies. Her experience at Amway also involves serving as technical safety expert in botanical ingredient development for use in cosmetics, personal care and oral care. MS Patel is a trained Pharmacist and a Board-Certified Toxicologist. She has represented Amway at various scientific societies and international platform as an invited speaker.

"History Of Safe Human Use" In Risk Assessment Of Botanicals In Dietary Supplements

Deval Patel

Senior Toxicologist, Amway

Herbal supplement sales have significantly increased in recent years as consumers are gravitating towards plant-based products to help maintain health and wellness. The perception that these products are safe, natural, and effective is accompanied by scrutiny for safety evaluation and regulatory compliance. The existing toxicity testing scheme is designed to evaluate single chemicals while botanicals are complex mixtures and their constituents vary based on original material (plant part), degree of processing, final dosage form and exposure / storage pattern. The inherently complex nature of botanicals makes it challenging to identify a reliable safety toxicity testing system. There is a general consensus for the need to incorporate history of safe use in the risk assessment of botanicals to support human consumption. This safety evaluation method has been used in various regulatory frameworks for the approval of new dietary ingredients and botanicals. However, a harmonized criteria on what would constitute a history of safe human use is generally lacking. This presentation explores the existing approaches and methodologies from literature along with critical factors to consider when leveraging "history of safe use" in the risk assessment of botanicals in dietary supplements using various case studies and examples.

Judith M. Rollinger

Full Professor of Pharmacognosy / Pharmaceutical Biology and Head of Phytochemistry & Biodiscovery at the Department of Pharmaceutical Sciences / Division of Pharmacognosy, Faculty of Life Science, University of Vienna, Austria

Judith M. Rollinger is Full Professor of Pharmacognosy / Pharmaceutical Biology and Head of Phytochemistry & Biodiscovery at the Department of Pharmaceutical Sciences / Division of Pharmacognosy, Faculty of Life Science, University of Vienna, Austria. Since 2019 she has been a senator of this University.

She received her Ph.D. in Pharmacognosy of the University of Innsbruck/Austria. For her venia docendi she was among the first to combine cheminformatics, phytochemistry, and ethnopharmacology (habilitation in 2007).

In 2014 she was appointed full Professor at her present institution. Since 2020 she is the president of the Society for Medicinal Plant and Natural Product Research (GA) - the largest European learned society, focusing on research on natural products, nature-based drug discovery, medicinal plant and quality control of herbal medicines.

Rollinger is project leader in various national and international projects and has received several awards in her field, e.g., the PHOENIX Science Award 2005, the Science Award 2010 of the Capital Innsbruck, and the Science Award 2020 of the federal state Vorarlberg/Austria.

Her research focuses on the interdisciplinary field of integrating big data analysis (cheminformatics, chemometry) in natural product research as strategy for the discovery of natural lead structures against viral infections, metabolic syndrome and inflammation. Publications resulting from her research have appeared in highly ranked journals (>120), and as book contributions and patents.

Let's Take Advantage From Nature's Complexity!

Rollinger, Judith M. [1]

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Nature has historically proven to be the best chemist on earth protecting the host with a complex and potent chemical arsenal. Accordingly, extracts derived from natural resources usually contain hundreds of metabolites. Bioactivities are scattered among these chemicals and hard to decipher at a first glance. The exploration of chemical and biological data available in the public domain combined with computational power and the advances in natural product technologies offer new possibilities to handle and utilize Nature's complexity to disclose hidden treasures. In this lecture I will present some latest application examples, where we used big data analysis to unravel bioactive constituents and to identify multipotent anti-infective and neuroprotective compounds from natural sources (Kirchweger et al. 2022; Langeder et al. 2022; Wasilewicz et al, 2023).

Acknowledgments:

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Jo Barnes

Professor in Herbal Medicines, and Deputy Head of School

Jo Barnes BPharm(Hons) PhD MPS RegPharmNZ FISoP FLS is Professor in Herbal Medicines, School of Pharmacy, University of Auckland, New Zealand. Previously, she has held academic positions at the Centre for Pharmacognosy and Phytotherapy, School of Pharmacy, University of London, UK, and Department of Complementary Medicine, University of Exeter, UK. Jo's research explores the use, safety, efficacy and particularly pharmacovigilance (safety monitoring) for these products. Jo has a professional certificate in pharmacovigilance and pharmacoepidemiology (London School of Hygiene and Tropical Medicine). Jo is an herbal-medicine safety signal reviewer/clinical expert committee member, Uppsala Monitoring Centre, Sweden, which runs the WHO's Programme for International Drug Monitoring. In the International Society of Pharmacovigilance (ISoP), Jo was founding chair, Herbal and Traditional Medicines Special Interest Group (2017-2022), Co-Ordinator of the Western Pacific chapter (2020-current), and member of the ISoP Executive Committee (2006-09). In 2006, Jo led a 3-day conference on Pharmacovigilance for Herbal Medicines with the Royal Pharmaceutical Society of Great Britain, ISoP, WHO-UMC, ESCOP, GA, and other partners. Jo is a member of the Advisory Board, American Botanical Council, Associate Editor of Phytochemistry Letters, and long-standing member of the editorial boards of Drug Safety, International Journal of Pharmacy Practice, and Phytotherapy Research. Jo is editor of a new book Pharmacovigilance for Herbal Medicines: Advances, Challenges and International Perspectives (Springer, 2022), co-author of a contemporary pharmacognosy textbook (Heinrich M, Barnes J, Gibbons S, Prieto J, Williamson EM. Fundamentals of Pharmacognosy and Phytotherapy, Elsevier, (4th edition in press)], and was principal author for Herbal Medicines [Barnes J, Anderson LA, Phillipson JD. Herbal Medicines (2nd and 3rd eds). London: Pharmaceutical Press, 2002 and 2007].

Jo is a registered pharmacist in New Zealand, and was elected Fellow of the Linnean Society of London (2003) and of the International Society of Pharmacovigilance (2020).

Advances In Safety Signal Detection For Herbal Medicines

A/Prof Jo Barnes

School of Pharmacy, University of Auckland, New Zealand

Herbal medicines (HMs; botanicals) are a popular healthcare choice among patients/consumers worldwide; a substantial proportion of the population in low-middle-income countries relies on herbal and other 'traditional' medicines as their main form of healthcare. People use HMs for general well-being and health maintenance, as well as for prevention/treatment of symptoms and chronic medical conditions. HMs, and other 'natural health' products ('dietary supplements'), are typically regulated as 'low-risk' products, and are perceived by users as being natural and 'safe'. However, as with conventional medicines, harms, including serious harms, associated with HMs do occur. Comprehensive information on the safety profile of most HMs is lacking and, as with conventional medicines, it is important to monitor the safety of HMs in real-world use.

Identification of harms associated with HMs currently relies on voluntary spontaneous reporting of suspected adverse drug reactions (ADRs) to national pharmacovigilance schemes, but under-reporting is substantial, and there are other challenges for HMs. There is international recognition of the need to improve pharmacovigilance for HMs, including through developing methods building on existing systems, such as intensive monitoring methods. This presentation will summarize current approaches to safety signal detection for HMs, consider advances and new methods for identifying herbal safety concerns, and discuss future directions for pharmacovigilance for these products.

Nikolas Fokialakis

Asst. Professor of Pharmacognosy, at the University of Athens, Greece

Education: University of Athens Ph.D. (Pharmacognosy) 2000-2004; University of Athens M.S. (Pharmacognosy) 1998-2000; University of Athens B.S. (Pharmacy) 1993-1998.

Research Interests: Nikolas Fokialakis is a pharmacist with expertise in Pharmacognosy & Natural Products Chemistry. He obtained his PhD in 2004, working on medicinal plants and the synthesis of bioactive derivatives. As a post doc he has worked on the discovery of novel biopesticides in USDA in US and since 2006 he has joined the Faculty of Pharmacy of National and Kapodistrian University of Athens in Greece. Initially he had been working on medicinal plants but his true passion were fungi. So, after his sabbatical in CNRS (France) and Fondation Medina (Spain), in 2012 he established his own research group and has focused on the discovery of bioactive molecules from terrestrial and marine microorganisms. He has implemented numerous EU and national projects focusing on the discovery of small molecules with different biological activities. Since 2011 he has been serving GA as a board member and since 2022 as a vice president.

Professional Organizations: GA-Society for Medicinal Plants (Member since 1999, Vice president 2022-2023) - American Society of Pharmacognosy (Member, 2004-present)

Global Microbial Biodiversity: An Untapped Source For The Discovery And Development Of Novel Antiaging Molecules

N.Fokialakis

Department of Pharmacy, National and Kapodistrian University of Athens, Greece

In collaboration with industrial and academic partners our research team has established a pipeline for discovery small molecules with antiaging activities. More specifically an innovative scientific and technological platform has been built aiming to the discovery of novel bioactive molecules originating from global terrestrial and marine biodiversity using emerging and state of the art technologies in the field of natural products chemistry, biotechnology, and applied microbiology.

In most cases already existing culture collections have been screened incorporating modern high throughput platforms (*in silico* & *in vitro*) for the rational and targeted selection of the most promising strains. Advanced approaches based on LC-HRMS, and molecular networks were used for the rapid dereplication of active extracts. Further analytical techniques for the accelerated fractionation, isolation and identification of natural compounds, were applied. For the evaluation of the antiaging properties of extracts, fractions, and pure molecules, a broad spectrum of bioassays and novel analytical approaches were incorporated. More specifically, it has been evaluated the antioxidant capacity (based on chemical and cell-based assays), the skin-protecting activity (proteasome homeostasis, anti-elastase and anti-collagenase inhibitory potential), and skin-whitening activity (anti-tyrosinase activity). In order to ensure sustainability, attention was given to the selection and optimization of fermentation technologies for the production of final products at pilot scale. Overall, in the frame of several national and international research grants, small molecules that exhibit activities comparable to well-established molecules have been discovered.

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Sonia Parmar

Vice President, Regulatory Affairs and Government Relations, Canadian Health Food Association (CHFA)

As Vice President of Regulatory Affairs and Government Relations for the Canadian Health Food Association (CHFA), Sonia Parmar works to represent the largest trade association dedicated to natural, organic and wellness products in Canada. The CHFA is a national not-for-profit association, members include manufacturers, retailers, wholesalers, distributors, and importers committed to getting more healthy living products into the hands of more Canadians. Prior to the CHFA, Sonia held the position of Director of Policy and Strategic Planning in the Regulatory Affairs Sector (RAS) of the Treasury Board Secretariat, where she was responsible for leadership in providing central oversight and modernization of Canada's regulatory system by reporting to Parliament and to Canadians, on the government's ability to deliver regulatory reforms and policy frameworks. She also brings with her, over 15 years of Health Canada experience, including a deep knowledge of the Good Manufacturing Practices, the Food and Drugs Act and Regulations, Natural Health Product Regulations, and the Cannabis Act and Regulations.

Canadian Natural Health Products And Regulations From An Industry Perspective

Parmar, Sonia[1]

[1]Affaires réglementaires et relations gouvernementales, 235 Yorkland Blvd., Suite 201, Toronto ON M2J 4Y8

Natural health product (or NHP) is a term used in Canada to refer to a range of health products including: vitamin and mineral supplements, herbal and plant-based remedies, traditional medicines (such as Traditional Chinese Medicines), homeopathic medicines, omega and essential fatty acids and probiotics. All Natural Health Products sold in Canada are subject to the Natural Health Products Regulations, which came into force on January 1, 2004. The purpose of the Regulations is to help assure that NHPs that are safe, effective and of high quality. Health Canada assesses all natural health products before letting them be sold in Canada. All NHPs must have a product license, and the Canadian sites that manufacture, package, label and import these products must have site licenses. To get product and site licenses, specific labelling and packaging requirements must be met, good manufacturing practices must be followed, and proper safety and efficacy evidence must be provided.

With almost 20 years of having been regulated under the Natural Health Product Regulations, the natural health product industry is now facing new and upcoming regulation which is threatening innovation, jobs, and competitiveness in the sector. This presentation will provide the industry's perspective on regulatory hot topics in Canada, including the self-care framework, labelling, CBD, research, and innovation.

Jon Wardle

Professor, Public Health, Maurice Blackmore Chair of Naturopathic Medicine and Director of the National Centre for Naturopathic Medicine at Southern Cross University

Jon is Professor of Public Health, Maurice Blackmore Chair of Naturopathic Medicine and Director of the National Centre for Naturopathic Medicine at Southern Cross University. In addition to clinical qualifications in nursing and naturopathic medicine, Jon has postgraduate qualifications in public health, law and health economics and holds visiting positions at Boston University, Chinese University of Hong Kong and Oxford University. Jon has published over 200 research publications, has leadership positions in the Public Health Association of Australia and American Public Health Association in relation to traditional and complementary medicine policy, and leads several World Federation of Public Health Associations and World Health Organization initiatives in traditional, complementary and integrative medicine, health policy, primary health care and developing health research capacity in developing countries. Jon and currently serves as Deputy-Chair of the Australian government's National Health and Medical Research Council's Natural Therapies Advisory Committee. Jon works on traditional, complementary and integrative medicine, Indigenous health perspectives, public health and primary health care policy with numerous governments, non-government organizations and international bodies.

Findings Of Their Work Around Industry Priorities For Education And Training As Well As An Update From Their National Priority Setting Project

Jon Wardle

the National Centre for Naturopathic Medicine at Southern Cross University

Thomas Brendle

Principal Scientist at Traditional Medicinals Inc., Sebastopol CA, CEO at Plantaphile, Collingswood NJ, Research Associate at the University of Johannesburg, Department of Botany and Plant Biotechnology

Education: University of Johannesburg, Department of Botany and Plant Biotechnology, PhD (Botanical Sciences) 2015-2022

Professional Organizations: Society for Medicinal Plant and Natural Product Research (GA), International Society of Ethnopharmacology (ISE), American Society of Pharmacognosy (ASP), American Chemical Society (ACS), American Botanical Council (ABC), American Herbal Products Association (AHPA), Society of Ethnobotany (SEB), United Natural Products Alliance (UNPA), American Herbal Pharmacopoeia (AHP).

Honors: Director of Association for African Medicinal Plant Standards (2005-2018), member of the advisory board of the American Botanical Council (since 2011), fellow of the Linnean Society (since 2012), member of the USP Expert Committee Botanical Dietary Supplements and Herbal Medicines (since 2015); ABC Champion Award (2019); member of the board of the International Society of Ethnopharmacology (since 2023).

Editorial Duties: Author and editor of the PDR for Herbal Medicines (1998ff); member of the editorial board of Phytotherapy Research (since 2006); consulting editor for American Botanical Council's HerbClips (since 2010); editor-in-chief of the African Herbal Pharmacopoeia (2010); member of the editorial board of Journal of Ethnopharmacology (since 2018); associate editor of Frontiers in Pharmacology – Ethnopharmacology (since 2020).

The Concept Of Traditional Use In EU Regulations Concerning Food And Medicinal Products

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In 2004, Directive 2004/24/EC introduced a simplified registration procedure for traditional herbal medicinal products (THMPs). THMPs must have been used for at least 30 years, including at least 15 years within the EU. A full quality dossier is required for Traditional Herbal Registrations (THRs). Harmonized sets of information for an herbal substance or preparation for evaluating THRs in form of EU monographs and list entries have been created for reference.

Regulation EU 2015/2283 on novel foods and novel food ingredients brought with it a simplified notification procedure for traditional foods from a third country. Such foods need to have been consumed as a significant part of the customary diet in a third country for at least 25 years. The administrative and scientific requirements for this procedure were recently updated in Commission Implementing Regulation EU 2020/1824.

This presentation updates on the progress in the implementation of these key regulations for traditional use products and, as guidance to industry, focusses on what defines – category-specific – traditional use, what constitutes eligible evidence and how to present it.

Gailen D. Marshall

Professor of Medicine, University of Mississippi Medical Center

Gailen D. Marshall, MD PhD is the R Faser Triplett Sr MD Chair of Allergy and Immunology, Professor of Medicine, Pediatrics , Pathology and Population Health Science, Executive Director of the Mississippi Clinical Research and Trials Center, Medical Director of the UMMC Clinical Research Support Program, Vice Chair for Research in the Department of Medicine, Director of the Division of Allergy, Asthma and Clinical Immunology and Chief, Laboratory of Behavioral Immunology Research at the University of Mississippi Medical Center in Jackson. He received both his PhD in Immunology and MD from the University of Texas Medical Branch in Galveston, did internal medicine training at the University of Iowa and completed his internal medicine residency, chief residency and Allergy-Immunology fellowship at the University of Tennessee at Memphis. He is an active clinician, educator and research investigator. His major research interests focus on the clinical effects and underlying mechanisms of psychological stress (in the context of genomics, environmental factors and lifestyle choices) on dysfunctional immune responses involved in various diseases including allergic rhinitis and asthma and, most recently, COVID-19. He also studies the immunomodulatory effects of new therapeutic agents for allergy and asthma and, the effectiveness of an integrative approach to allergy and asthma care using botanicals and natural products. He has published over 250 peer reviewed articles, reviews and book chapters. He is an active speaker in regional, national and international venues. He has extensive editorial experience and recently completed his 16-year term as Editor-in-chief of the Annals of Allergy, Asthma and Immunology. He currently serves as President elect and will become President of the American College of Allergy, Asthma and Immunology in November 2023.

Clinical Trials For Botanicals And Other Natural Products: Developing Paradigms For Efficient, Sound Evaluations And Indications

Marshall, GD

University of Mississippi Medical Center, MS, USA

The use of botanicals and other natural products for health maintenance and disease management has been reported since antiquity. There is little doubt that continued use of these products in a scientifically sound, clinically relevant fashion should still be considered today even in the context of modern advanced medical technology. However, given that many of these products would not raise significant revenue if marketed because of their abundance and low manufacturing costs, financial restraints often prevent scientifically sound , relevant clinical trials from being conducted. Additionally, particularly when used for health maintenance indications, regulatory constraints make generation of extensive and sometimes unnecessary safety data necessary. Accordingly, a functional collaborative paradigm for research that defines the biological activities, chemical interactions (for drug-NP interaction) and reliable biomarker for desired effects should be designed and implemented for future development of clinical indications – both therapeutic and salutogenic.

Andrea Bugarcic

Senior Lecturer, National Centre for Naturopathic Medicine at Southern Cross University

Education: University of Auckland PhD (Virology), MSc (Virology)

Research Interests: Understanding synergistic cellular actions of herbal medicines in bacterial infections (biofilms) and Parkinson's Disease using the backdrop of traditional evidence, contemporary herbal medicine practice and complex co-culture cellular models. Developed a tradition/research/practice nexus framework for a more focused and relevant pre-clinical research that is transferable to any disease/condition/infection context.

Editorial and peer reviewer duties: Special issue Editor for Cells (Focus on Cellular Parkinson's Disease — From Gut to Brain) and peer reviewer for several journals including, Advances in Integrative Medicine, Nutrients, Molecules and Cells.

Traditional Evidence And Pre-Clinical Research - Alignment, Limitations And Opportunities

Bugarcic A[1], Steel A[2], Foley H[2], Geldard C[1], Imtiaz I[1], Oliviera E[1], Wardle J[1]

[1]National Centre for Naturopathic Medicine, Southern Cross University, Lismore, Australia, [2]Australian Research Centre in Complementary and Integrative Medicine, University of Technology, Sydney, Australia

The World Health Organisation (WHO) defines traditional medicine as the "sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness" (World Health Organization, 2018). Traditional herbal treatments, substantial part of traditional medicine across all traditional medicine systems, were prepared through the use of whole herb(s) and/or parts of plants and in different forms, including decoctions, teas, tinctures, powders, and poultices which remained the main preparation methods until the 18th century (Fridlender et al., 2015; Ogbonna et al., 2012). While traditional evidence offers an avenue for exploring approaches to disease, it is also often misinterpreted and used in a non-traditional, reductionist way to develop new pharmaceuticals and products. Researchers across the world create compound libraries using fractionation approaches - compounds that are then screened simple pre-clinical biological assays. While this bio-fractionation approach can lead to development of new drugs, it ignores the complexity and chemical synergy of medicinal plants and their traditional medicinal use resulting in expensive, lengthy and often ineffective drug development processes and criticism of medicinal plants effectiveness in the applicable disease state.

To address alignment between traditional knowledge and pre-clinical research with the ultimate view of drug development process that still aligns with the current staged approach, we have developed a tradition-research nexus framework that considers not just medicinal plant complexity and their use but also extends pre-clinical research into using more complex *in vitro* models. Tradition-research nexus seeks to first understand traditional knowledge and design appropriate co-culture/primary in vitro models to ultimately test medicinal plants in the way that they were used using multiple biological assays. Current presentation will describe the framework and its implementation using 3 different drug development projects currently underway in our laboratory - cancer, UTI and Parkinson's Disease drug development. Presentation will also discuss limitations and opportunities of using this approach - is framework flexible to capture all available traditional knowledge, how is traditional knowledge appraised, how do we account for plant complexity and possible synergy, what are intellectual property issues to consider, are in vitro models robust and reproducible, is the overall approach aligned to the current staged approach for drug development, what are the implication of natural products industry and how does this benefit custodians of the traditional knowledge?

Tahir Maqbool Mir

Senior R&D Biologist, University of Mississippi

Tahir Maqbool Mir is a Senior research and development biologist with over 10 years of experience in toxicology and preclinical research. He currently works at the National Center for Natural Products Research, University of Mississippi, where he has developed a broad scientific and medical knowledge in in-vitro and preclinical research areas. Tahir is known for his extensive expertise in toxicology, carcinogenesis, chemoprevention, pharmacology, infectious diseases, and metabolic disorders. He is a highly motivated self-starter who has successfully managed multiple projects simultaneously throughout his career.

Prior to his current role, Tahir worked as a Postdoctoral Research Associate at the University of Mississippi from 2014 - 2019. During this time, he developed numerous in-vivo models for different diseases, including diabetes, MRSA, Cryptococcus, and H1N1 infection models. His work has contributed significantly to the advancement of the fields of toxicology and preclinical research.

Tahir holds a bachelor's degree in biochemistry from University of Kashmir, India, and Masters and PhD in Toxicology from Hamdard University, New Delhi, India in 2014. Tahir's academic pursuits have centered around investigating the fundamental mechanisms underlying toxicity and cancer chemoprevention. Tahir has received numerous awards including Gold medal awarded by Society of Toxicology, India for his contributions to toxicology research. His significant contributions to the field are evidenced by more than 50 peer-reviewed publications and 03 book chapters with more than 2000 citations.

Immulina Enhances Host Resilience Against Influenza Virus-Induced Illness In A Prodromal Mouse Model: Part A – Change In Lung-Body Weight Ratio, Cytokines And Lung Histopathology

Mir TM[a], Zhang J[a], Khan SI[a], Khan IA[a], Marshall GD[b], Pugh ND[a], Ashfaq MK[a]

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Influenza is the most common health problem that targets the respiratory system with an estimated 30,000 to 40,000 annual deaths in the United States alone. Since the modern flu vaccine program has moderated but not eliminated infection risk, enhancement of host antiviral immune resilience using botanical-derived supplements may provide an important complementary approach that is inexpensive, safe, and readily available to the public. The University of Mississippi Botanical Dietary Supplements Research Center is focused on investigating the use of Immulina, an extract of *Limnospira* (formally *Arthrospira*), as an immune-based antiviral resilience promotor against influenza. Three non-lethal mouse models were established to evaluate the utility of oral administration of Immulina against influenza A virus-induced illness and whether the effect was solely prophylactic, prodromal, therapeutic or a combination of these mechanisms.

Presented here are results from the research investigating the effect of Immulina on increasing resilience against influenza A (IfA) viral infection in the prodromal model for both male and female mice. Administration of Immulina (25, 50 and 100mg/kg) or vehicle was initiated on the day of IfA infection (2 hours post-exposure) and continued once daily for 15 days. The results indicate that Immulina-fed IfA exposed mice exhibited significantly less weight loss and reduction of lung-body weight ratio as compared to the infected control group. In lung homogenate samples, levels of 8 cytokines (GM-CSF, IL-2, IL-6, IL-10, IFN- γ, IL-12, IL-17A, IL-21) were increased in Immulina exposed mice, with significant increases generally starting at days 5 and 7 post-infection for male and female mice, respectively. Histologic evaluation of lung samples indicated an overall reduction in severity of infection in treatment mice (parameters measured included pulmonary pneumonia, interstitial inflammation, bronchial inflammation, and alveolar hyperplasia). Based on results from this model, Immulina may have utility for enhancing antiviral immune resilience when consumption is started during the prodromal period of a viral infection (subject has been infected but is still asymptomatic).

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Kashif Shamim

Postdoctoral Research Associate, National Centre for Natural Products Research, University of Mississippi

Dr. Kashif Shamim is a postdoctoral research associate at the National Center for Natural Products Research (NCNPR) within the School of Pharmacy at the University of Mississippi. He holds a bachelor's degree in microbiology from Wilson College at Mumbai University, India, a master's degree in microbiology from the Department of Microbiology at Goa University, India, and a Ph.D. in microbiology from the same institution. Dr. Shamim's research interests include molecular biology, genetic engineering, and enzymology. He has authored 11 research articles and one book chapter, with his work receiving more than 200 citations.

In his master's dissertation, Dr. Shamim worked on metal resistance bacterial isolates, which resulted in his first research publication in the international journal "Environmental Monitoring and Assessment." For his doctorate, he worked on "metagenomics for the isolation of protease enzyme." Dr. Shamim has received numerous honors and awards, including the Maulana Azad National Fellowship by UGC, Govt. of India in 2011 for Ph.D. research. He has also been selected to attend a training program on "Marine bacterial diversity" at CSIR-CSMCRI institute in Bhavnagar, Gujarat, India, and served as the organizing secretary for the National Conference of Young Researchers (NCYR-2017) at Goa University.

Currently, Dr. Shamim is working on the effect of natural products on bacterial and fungal organisms and studying the immunomodulatory effect of Immulina (a commercial extract of *Arthrospira)* in antiviral resilience mouse models at the NCNPR. With his contributions, Dr. Shamim has established himself as an emerging research leader.

Immulina Enhances Host Resilience Against Influenza Virus-Induced Illness In A Prodromal Mouse Model: Part B – Changes In Viral Load And Clinical Signs Of Infection

***Shamim K*[1]**, *Mir TM*[1], *Zhang J*[1], *Khan SI*[1], *Tripathi SK*[1], *Khan IA*[1], *Marshall GD*[2], *Pugh ND*[1], *Ashfaq MK*[1]

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The University of Mississippi Botanical Dietary Supplements Research Center is performing research on the potential use of *Limnospira* (formally *Arthrospira*) to enhance resilience against influenza viral infection. *Limnospira* is a cyanobacterium that has been used as a food for centuries and more recently as a popular health supplement. A commercial extract called Immulina has been developed that concentrates the level of immunomodulatory activity due to Braun-type lipoproteins – compounds that activate immune pathways through a toll-like receptor (TLR) 2-dependent mechanism. Although oral ingestion of Immulina has been reported to exhibit a protective effect against subsequent H1N1 influenza A (IfA) viral infection using a mouse model, it is unknown whether this protection is solely prophylactic, prodromal, therapeutic or a combination of these effect.

In the current research we focus on investigating the effect of Immulina on resilience against IfA-induced illness using a prodromal nonlethal rodent model (mice were orally administered Immulina 2 hours after H1N1 IfA exposure and continued daily for 15 days). Determination of viral load in lung homogenates was performed by extraction of viral RNA followed by quantitation using real-time PCR. A statistically significant decrease in the number of viral particles was observed in both male and female mice at various timepoints post-infection at a dose of 100mg/kg, as compared to the control group. Significant reduction in viral load was also observed for Immulina-treatment at 50 and 25mg/kg on days 5 and 10 (post-infection), but for only the male mice. For clinical signs of infection, a significant reduction in all parameters (appearance, respiration and mobility) was observed for both male and female mice, generally starting at day 5 post-infection. We hypothesize that the protective effect of Immulina against IfA-induced illness is mediated through modulation of the host antiviral immune system by the TLR2 activating Braun-type lipoproteins. It is unlikely that the effect is due to direct antiviral activity within the extract since Immulina exhibited no activity when tested for *in vitro* antiviral activity against IfA.

Acknowledgments:
This work was supported by the Office of Dietary Supplements and National Center for Complementary and Integrative Health of the National Institutes of Health under Award Number U19AT010838. The content is solely the authors' responsibility and does not necessarily represent the official views of the National Institutes of Health. Additional funding was also provided by a grant from the USDA, Agricultural Research Service Specific Cooperative Agreement No. 58-6060-6-015.

Stefan Gafner

Chief Science Officer, American Botanical Council

Stefan Gafner, PhD, is currently Chief Science Officer of the American Botanical Council, an independent, nonprofit research and education organization. He is also Director of the ABC-AHP-NCNPR Botanical Adulterants Program, a large-scale collaborative program initiated by the American Botanical Council (ABC), the American Herbal Pharmacopoeia (AHP), and the National Center for Natural Product Research (NCNPR) at the University of Mississippi to educate members of the herbal and dietary supplement industry about ingredient and product adulteration. Prior to working for ABC, Gafner served as a Director of Analytical Chemistry in the R&D department of natural personal care products company Tom's of Maine.

Gafner received his degree in pharmacy at the School of Pharmacy, University of Berne, in Berne, Switzerland. He obtained a PhD in pharmaceutical sciences, with a focus on the chemistry of medicinal plants, from the University of Lausanne in Switzerland, and conducted postdoctoral research on cancer chemopreventive natural products at the University of Illinois – Chicago in the College of Pharmacy's Department of Medicinal Chemistry and Pharmacognosy. Gafner is author or co-author of over 70 peer-reviewed scientific publications and holds 5 patents. He is a member of the advisory board of the Society for Medicinal Plant and Natural Product Research (GA) and of the editorial boards of the Journal of Ethnopharmacology and Planta Medica.

The Impact Of Covid-19 On The Supply Chain And Quality Of Botanical Ingredients

Stefan Gafner[1], Nilüfer Orhan,[1] Mark Blumenthal[1], John H. Cardellina[2], Bharati Avula[3], Ikhlas A. Khan[3], Mona Hänni[4], Eike Reich[4], Roy Upton[5]

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Examples from the past show that a supply chain disruption, or a series of such disruptions, sudden spikes in consumer demand, and/or the many combinations of abrupt, unplanned changes to the supply and demand sides of commerce in botanical materials lead to an increase in adulteration and fraud. When this happens due to simultaneous interruptions of numerous ingredients based on a global pandemic, as in the case of COVID-19, it is predictable that unscrupulous suppliers and sellers of botanical (and other) ingredients will attempt to take advantage of supply shortages by manufacturers of herbal medicines and dietary supplements to sell them lower-quality or sometimes adulterated materials.

Among the botanical ingredients with the largest sales increases due to the COVID-19 pandemic are ashwagandha (*Withania somnifera*) root, elder (*Sambucus nigra*, Viburnaceae) berry, echinacea (*Echinacea purpurea* and *E. angustifolia*, Asteraceae) herb/root, and oregano (*Origanum vulgare*, Lamiaceae) herb. While adulteration of ashwagandha root and oregano herb is well documented, data on the quality of commercial elder berry and echinacea root dietary supplements is scarce. A new initiative by the ABC-AHP-NCNPR Botanical Adulterants Prevention Program attempts to assess the extent of adulteration in five popular herbal dietary supplement ingredients, including echinacea and elder. Adulteration of echinacea extracts appear to be uncommon and mostly related to the presence of undeclared *Echinacea* species. Contrarily, adulteration of elder berry extracts appears to be common. An investigation into the authenticity of 31 commercial elder berry dietary supplements sold in the United States showed that only 10 complied with the label claim. The presentation will provide details on the impact of COVID-19 on the botanical ingredient market with a focus on some of the most popular dietary supplement ingredients.

Weslee S. Glenn

Head of Innovation, Ayana Bio

Education: Caltech Post-Doctoral Fellowship (Chemical Engineering) 2013-2017; MIT Ph.D. (Chemistry) 2008-2013; Hampton University B.S. (Chemistry) 2004-2008

Research Interests: Understanding how nature (especially medicinal plants) synthesizes molecules with complex architectures from simple building blocks, manipulating biosynthesis, developing chemical tools to understand how plants respond to stress.

Honors: Environmental Advisory Commission for the City of Pasadena, California (2019-2022), UNCF/Merck Post-doctoral Fellowship (2015-2017), Ford Foundation Post-doctoral Fellowship (2014-2015), National Science Foundation Predoctoral Fellowship (2010-2013), Walter L. Hughes Graduate Fellowship in Biochemistry (2010), Henry A. Hill Fellowship (2009-2010), Chemistry/ Biology Interface Program Training Grant Institute Fellowship (2008-2009) Martin Luther King, Jr. Leadership Award (MIT, 2010), HBCU UP Scholarship (2005-2008), Hampton University Presidential Scholarship (2004-2008) Chemistry Excellence in Service Award (2008), Merck Index Excellence in Undergraduate Chemistry Award (2008), Flag Bearer for School of Science (2008), All-Virginia Collegiate Honors Council Poster Award Winner Honors Council Award (2008), Hampton University Honors Council Award (2008), ACS Award for Achievement in Physical Chemistry (2007), Beta Kappa Chi Scientific Honor Society Inductee (2006), ACS Award for Achievement in Organic Chemistry (2006), Golden Key International Honour Society (2006), Alpha Kappa Mu Honors Society (2006) Honors Council Award for Chemistry (2006), ACS Award for Freshman Achievement in Chemistry

Plant Cell Cultivation In The 21st Century

Glenn, W.

Ayana Bio

Earth will have lost six football fields' worth of arable land in the roughly five seconds it takes to read this sentence. The double bind of dwindling natural resources and a burgeoning population is a clear motivation for decisive action. Cellular cultivation has emerged as a tool to improve the production of plant-based health and wellness ingredients, which to date have relied heavily on land-intensive and extractive processes that yield unpredictable results.

Compared to traditional techniques, plant cell cultivation holds the promise of producing important molecules at consistent levels without depleting valuable resources. Although plant cell cultivation has been practiced for over a century, its full potential has yet to be realized due to various challenges that can now be addressed with state-of-the-art technologies.

This talk will frame the challenges and opportunities of plant cell cultivation, including its ability to improve ingredient quality, remedy supply chain issues, and address nutritional deficiencies.

Andrew Horwitz

Vice President Research and Development, Inscripta

Research Interests: Major research interests are in the areas of natural products and how to achieve their production in microbial hosts such as baker's yeast to create scalable and sustainable supply chains. PhD work focused on the biochemistry of transcriptional regulation by the BRCA1 breast and ovarian tumor suppressor. Postdoctoral work emphasized forward genetic engineering in S. cerevisiae and the implementation of heterologous signaling systems like tyrosine phosphorylation as a means to understand how evolution accommodates new post-translational mutations. Industrial focus on the development of robust of new tools for accelerated strain engineering, including multiplex engineering strategies employing a range of designer nucleases. Experience spanning product selection through strain development (with a focus on enzyme discovery and improvement) and scale-up.

Professional Organizations: None

Honors: Jane Coffin Childs Postdoctoral Fellow, 2006-2011

Editorial Duties: None

Biomanufacturing: Scalable Access To Rare And Powerful Natural Products

Horwitz, A

Sestina Bio

Over 400,000 natural products have been identified, with potential and realized applications from medicine to flavors and fragrances. Traditional sourcing via extraction can be problematic from the perspective of cost, purity and sustainability. By contrast, biomanufacturing can provide scalable and sustainable access, assuming that a range of technical challenges can be overcome. Bakuchiol, a phytoretinoid with a history of use in traditional Chinese and Ayurvedic medicine, is an excellent example of such a target and the associated challenges. In late 2021, our team set out to achieve production in *S. cerevisiae* via strain engineering. To achieve commercially feasible strain performance in 1 year, we employed our Genoscaler™ platform – a unique and tech advantaged combination of pathway discovery, enzyme improvement, and extensive whole genome editing.

Stephanie (Stiffy) Hice

Regulatory Review Scientist and Microbiology Reviewer

Originally from Milwaukee, WI, Dr. Stiffy Hice received their BS in Biological Science, with minors in Printmaking and Psychology, from the University of Tulsa in 2014; and their PhD in Food Science and Technology with a certificate in Food Safety and Defense from Iowa State University in 2019. After graduating from Iowa State University, Dr. Hice joined the U.S. Food and Drug Administration (FDA) in 2019 as a Regulatory Review Scientist and Microbiology Reviewer in the Division of Food Ingredients (DFI) within the Office of Food Additive Safety (OFAS). Dr. Hice has managed the review of numerous Generally Recognized as Safe (GRAS) notices—with particular emphasis on microbial-derived ingredients, bacteriophage preparations and live microbial cultures—as well as approval of direct food additive and color additive petitions that have been submitted to the Center for Food Safety and Applied Nutrition (CFSAN) at FDA. As a Regulatory Review Scientist, one of Dr. Hice's primary duties is managing both GRAS evaluation teams and petition review teams. Many submissions have robust regulatory and scientific considerations, which must be evaluated to: (1) issue a response letter regarding the safety conclusions made by the submitter of a GRAS notice, or (2) approve a food or color additive in response to a petition. As a Microbiology Reviewer, Dr. Hice is charged with evaluating the microbiological safety of ingredients intended for use in conventional foods. Dr. Hice is also a member of several workgroups, including the Cultured Meat Premarket Consultation Working Group and the DFI Infant Formula Working Group.

OFAS Pre-Market Review Programs: An Introduction To Food Additives, Color Additives, And GRAS Ingredients

Hice, S[1]
[1]U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Food Additive Safety

In the U.S., laws governing food and food ingredients fall under the Federal Food, Drug, & Cosmetic Act (FD&C Act). The FD&C Act gives the Food and Drug Administration (FDA) the authority to oversee the safety of the U.S. food supply and establishes the framework for assuring the safety of ingredients added to conventional food. An important aspect of food safety, the evaluation of ingredients added to conventional food helps to safeguard the U.S. food supply by ensuring that ingredients are safe before they are added to foods marketed to consumers. The regulatory standards for food ingredients in the U.S. are robust, relying on multiple elements, including a substance's proposed use and use level, the manufacturing process, dietary exposure, and relevant safety data and information to reach a conclusion of safe use. However, there are multiple premarket pathways for ingredients added to conventional food, depending on the intended use of the ingredient as well as the data and information in support of the safe use of a substance.
This presentation seeks to elucidate three frameworks for food ingredient regulation in the U.S.: food additives, color additives, and substances that are generally recognized as safe (GRAS) for their intended use in conventional food, as there are common misconceptions regarding the requirements of these different regulatory pathways. FDA regularly engages in outreach to help inform food ingredient manufacturers and other food safety professionals of the similarities and differences between the regulatory requirements of these three frameworks, so that food ingredient manufacturers are better able to understand and meet these requirements and help to ensure the safety of the food supply.

Ranjit Puranik

Managing Director of Shree Dhootapapeshwar Ltd.

Managing Director of Shree Dhootapapeshwar Ltd., a family led enterprise of 5 generations involved in manufacturing of Ayurved healthcare formulations for over 150 years. He also serves as President of Ayurvidya Prasarak Mandal, a 70-year Ayurved college and teaching hospital campus. He has represented the AYUSH Industry cause for the past 22 years in many forums related with Ayurveda, medicinal plants and regulatory reform. Mr. Puranik has also been a vocal spokesperson for the better recognition and acceptance of traditional medicine and in particular the classical syntax as represented in Ayurved and serves on the Ayurved Committee of American Herbal Products Association & is founder Director in AYUSH Export Promotional Council. As Trustee of All India Ayurveda Congress and World Ayurveda Foundation, he is involved with active advocacy for all matters within the realm of Ayurved.

Achieving Environmental Targets In Ayurved Manufacturing: ZEND – Zero Emissions & Nil Discharge In Ayurved Industry

Puranik, Ranjit[1]

[1]Shree Dhootapapeshwar Ltd

Ayurved manufacturing came about as an industry sometime in mid-1860's. Since then, it has been a source of a whole range of Ayurved medicines supporting the practitioner with a wide range of Ayurved medicines. Traditional medicine practice includes a large range of formulations using over 1000 medicinal plants coupled with a major dependance on the use of minerals. Ayurved being a practice which has not seen much change since its inception has very set protocols in prescription and manufacturing. Formal education in Ayurved sciences, prosperity, stability and greater communication in erstwhile South Asian principalities created a robust knowledge sharing network. This ensured the practice remained steadfastly traditional and updated all across South Asia. The Ayurved practitioners had their own organization which ensured knowledge and experience has been uniformly updated throughout their schools and dispensaries meting out primary health care to the population. Political changes in 72 odd principalities that made up South Asia, did not affect the traditional practice of Ayurved whose reliance on firm basic principles ensured that education, knowledge and internship was never affected beyond a reset. A robust trade of medicinal plants and minerals within South Asia prevailed as did strong sourcing trade channels from far off regions of Persia, Afghanistan, Tibet and South-East Asia. This scheme of operations in Ayurved and core principles of diagnosis, medicine administration, surgery at times and manufacturing of formulations ensured a widespread uniformity on a bed rock of standardized processes. With a growing population and burden of primary health care which was fast becoming a public health program the advent of Ayurved industry was but natural. Ayurved Physicians known to manufacture their own formulations could not cope with their own needs given the health challenges across.

Since the mid 1800's there have been many changes in the manner society has viewed the largesse nature offers. Massive strides in technology, communication and resultant consumerism have seen a scale up in all industry across the world. Stability led to prosperity and abuse of environmental capacity in resetting an equilibrium between Man and his Universe. We see a phase of abuse that has led us to subscribe to tenets like – Climate change, sustainability and are fast heading towards a One Health paradigm. Ayurved industry has also been impacted with such environmental policies and their impact would need a see a change in the manner the industry conducts its manufacturing. Pollution control norms have seen revolutionary strides in enforcement and almost all aspects of traditional approach to manufacturing will need a reset to a new Good Manufacturing Practice.

Even more stringent norms are yet to come, which is obvious in every forecast view – a control of Emissions, heading towards Nil discharge and an internal churn of manufacturing ethos to merge traditional processes with expected norms. We briefly explore the achievements, challenges and future compliance threshold the Ayurved industry would have to cope within a not-so-distant future.

Narayanam Srikanth

Deputy Director General, CCRAS, Ministry of Ayush , Govt. of India

Dr. Narayanam Srikanth, BAMS,University of Health Sciences, Andhra Pradesh (Gold Medallist in Ophth),M.D, Bangalore University; Ph.D, Tilak Maharastra Vidya Peeth, Pune; Post Doctorial Fellow(Immunology and Molecular Biology),Centre for International Research in Immunology & Disease, School of Medicine, University of California Los Angeles: (UCLA), USA; Fellow- AIRTP-Advanced International Research and Training Program-University of California ,Los Angeles, USA.

Presently working as Deputy Director General, Central Council for Research in Ayurvedic Sciences (CCRAS),Ministry of AYUSH, Government of India, New Delhi, India engaged in formulating, coordinating, implementing and monitoring various research program including, clinical research, drug development, literary research, pharmacology research, phyto-chemical research, medicinal plant research, research oriented public health care program such as THCRP, NPCDCS program etc.

He published 332 research papers in reputed International and National Scientific Journals, Conference Proceedings etc. and authored and edited 119 Books, Monographs and technical reports and also contributed for development of about 14 Policy documents and Guidelines including the national ethical guidelines for biomedical research in human participants published by ICMR and possess 3 patents to his credit. He has honored with 8 awards including dedicated work in the field of Ayurveda by Kesari Maharashtra Trust and NIMI award for excellence in Ayurvedic Shalakya practices by Association Ayurvedic profession of North America etc. He is investigator and coordinator of several national and international research projects and coordinator for National programs, engaged in formulation, planning, coordination, execution monitoring of Research activities including Collaborative Research, International collaboration, Projects supported by WHO etc. (about 300 research projects).

Research And Development Initiatives Of Ministry Of Ayush

Narayanam Srikanth

CCRAS, Ministry of Ayush , Govt. of India

Sayeed Ahmad

Jamia Hamdard

Albert Einstien College of Medicine New York, USA, Postdoc, 2011-12; Jamia Hamdard, New Delhi, India, Ph D (Pharmacognosy and Phytochemistry), 2002-2005; Jamia Hamdard, New Delhi, India, M. Pharm. (Pharmacognosy and Phytochemistry), 2000-2002; Jamia Hamdard, New Delhi, India, B. Pharm. (Pharmaceutical Sciences), 1996-2000.

Metabolomics, Chromatographic analysis including LCMS, HPTLC, HPLC and GCMS etc for targeted and untargeted metabolites in biological systems, quality control of Indian medicinal plants and traditional formulations, qualitative and quantitative analysis of markers, standardization of botanical dietary supplements and traditional herbal medicines; monograph of medicinal plants and formulations for development of Pharmacopoeia and standards for medicinal plants, in silico, in vitro and in vivo biological screening for biological activities etc.

CST-UP Young Scientist Award (2008-09), DST BOYSCAST (2009-10), AICTE Career Award (2009-10), Dr. P.D. Sethi Memorial Award 2013 & 2015, Al Ameen College of Pharmacy Award 2014 & 2016, Prof. M. L. Khorana IJPS Award 2016, UGC Research Award (2016), SFE Young Ethnopharmacologist Award 2017, INSA bilateral Exchange fellowship, INSA, Delhi, 2018, SFE Special Recognition Award 2020, STE Meritorious Award for Excellence in Research & Academics (2022), Member Phytopharmaceuticals in Indian Pharmacopeial Commission 2022; Member Scientific Boards of HPTLC Association & Journal of Planar Chromatography & Modern TLC 2022-till date; Member Unani Pharmacopeial sub-committee, Ministry of AYUSH, Govt of India; Board Member of International Society of Ethnopharmacology since 2020- till date; Member (Pharmacognosy) of USP's Botanical South Asia Expert Panel of USP Botanical Dietary Supplements and Herbal Medicines (2021-till date), Member (Pharmacognosy) National Unani Pharmacopeial Committee (UPC) (2017-2022)

Metabolomic Profiling Of Traditional Unani Medicine For Scientific Validation Of Traditional Claims

Sayeed Ahmad

Director, Centre of Excellence in Unani Medicine (Pharmacognosy and Pharmacology) & Bioactive Natural Product Laboratory, Department of Pharmacognosy and Phytochemistry, School of Pharmaceutical Education & Research, Jamia Hamdard, New Delhi, India

The traditional Unani medicine originated in Greek and developed in India relied on natural healing based on principles of harmony and balances. Similar to other Ayush medicine, Unani medicines are processed as per classical literature and used singly or compounded with other substances to achieve synergistic, antagonistic or detoxifying effects. The Indian traditional medicine (Ayush medicine) has long history of safe use and consists of Ayurveda, Yoga, Naturopathy, Unani, Siddha, Sowa rigpa and Homeopathy systems of medicine.

Modern analytical techniques such as LC-MS, GC-MS and NMR are the most specified techniques in addition to HPLC, UPLC and HPTLC to validate the Ayush medicine for their standardization and authenticity by evaluating their bioactive metabolites followed by network pharmacology studies. Further, high resolution LCMS/MS based fingerprinting and dereplication of metabolites present in bioactive botanicals and in traditional herbal formulations have been used not only for metabolite profiling for quality control but also for mechanistic networking and pharmacokinetics as well as toxicity evaluation of these Traditional medicines. We have used LCMS, GCMS and TLC-MS hyphenated bioautographic techniques for scientific validation of traditional claims of different Traditional Unani medicines used for different chronic disorders through network pharmacology and experimental approaches. It has been observed that metabolomics with network pharmacology may have a great future in quality-based drug development from natural sources as well as for scientific validation of traditional claims.

Acknowledgments:
Keywords: Metabolomics, Quality control, Traditional Unani Medicine, Ethnopharmacology, Network Pharmacology

Nicole Stevens

Scientific Consultant for dōTERRA International

Nicole Stevens has been conducting research with essential oils for more than 20 years. She has worked in quality control laboratories in the nutraceutical industry as well as academic research laboratories at the University of Utah and the University of Nevada Las Vegas Cancer Research Institute. In addition to research, she has taught courses in chemistry and biochemistry at Brigham Young University – Idaho and University of Nevada Las Vegas. Nicole has served as a scientific consultant for dōTERRA International since the company formed in 2008 and joined the corporate team in 2015 as an essential oil formulator and researcher. Currently she serves as Director of Clinical Research at dōTERRA. Her main field of research is essential oil biochemistry relating to human therapeutic application, along with many other aspects of essential oil science.

Nicole holds a Bachelor of Arts degree in Technical Writing and a Master of Science degree in Botany, both from Brigham Young University. She earned her doctorate degree in Biochemistry and Molecular Biology from the University of Miami Miller School of Medicine. She's currently working on a second master's degree in Public Health from Purdue University. Nicole holds a Certified Principal Investigator (CPI) accreditation with the Association of Clinical Research Professionals, and a Certified Clinical Research Professional (CCRP) endorsement with the Society of Clinical Research Associates. She is also a Certified Phlebotomy Technician (CPT) with IV specialization, a Certified Electrocardiography Technician (CET) and a Certified Clinical Medical Assistant (CCMA).

Effects Of A Novel Botanical Supplement On Glycemic Variability And Postprandial Glucose Response

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Mulberry leaf extract high in the iminosugar 1-deoxynojirimycin (DNJ) has been shown in previous studies to inhibit glycosidase enzyme activity. A novel supplement including mulberry leaf extract, berberine and cinnamon extract was evaluated in a two-cohort study using endpoints of glycemic variability, postprandial glucose response, fasting glucose, fasting insulin, and safety markers. In the first cohort (n=15), these endpoints were determined over two weeks by continuous glucose monitoring (CGM) and blood/urine analyses in healthy adults. Approximately half of the participants (n=7) took a dosage of 250 mg prior to each meal, and the other participants (n=8) took 500 mg before each meal. This cohort also included a standardized high-carbohydrate meal for breakfast. Following an interim analysis, the supplement was evaluated for the same endpoints during an additional two months in a second cohort of healthy volunteers (n=30).

The first cohort demonstrated a significant difference in the glucose coefficient of variation between supplement and placebo (p=0.0440). Participants taking the 500 mg dosage showed larger decrease in postprandial glucose levels than participants taking the 250 mg dose (p=0.033), so the 500 mg dose was continued into the second cohort.

Participants in the second cohort were randomly assigned to take 500 mg dose of supplement or placebo before each meal for 1 month, then cross over to the other treatment for 1 month. Postprandial glucose levels were significantly decreased in participants taking the supplement compared to placebo (p=0.001). Overall glucose variability was significantly different between supplement and placebo (p=0.0238). Fasting glucose and fasting insulin were not significantly different. Safety markers such as liver enzymes were not significantly affected, and no serious adverse events occurred.

This novel supplement demonstrated significant potential for postprandial glucose modulation. Additional studies will evaluate the supplement to determine long-term efficacy in various cultural, ethnic, and real-world contexts.

Acknowledgments:
We gratefully acknowledge the efforts of Alex DaBell and his team for formulation of this supplement; Cecile Bascoul and her team for compiling background safety information; Andrea Melton for clinical research support; and Karissa Jolley for data gathering and organization.

Mei Wang

Research Chemist at the NPUR Unit, ARS, United States Department of Agriculture

A research chemist at the Natural Product Utilization Research Unit, Agricultural Research Service, United States Department of Agriculture. She received a B.S. in chemistry from Nankai University, Tianjin, China in 1988 and a Ph.D. in analytical chemistry from the University of Mississippi in 2006. She joined the National Center for Natural Products Research (NCNPR), University of Mississippi in 2010 as a postdoc and was promoted to the position of research scientist in 2015. Prior to joining NCNPR, she received her postdoc training at the Department of Chemistry and Biochemistry, University of Mississippi and industrial experience as a research scientist at Perkin Elmer.

Dr. Wang is an analytical chemist with a wealth of experience in natural products analysis and bioactive natural products discovery. Her skill set covers a wide spectrum of chromatographic and spectroscopic techniques that have been successfully utilized in the analysis, isolation, and structure elucidation of natural products with biological activities in her work over the past 20 years. In particular, she excels at designing and implementing innovative analytical methods to identify bioactive compounds from complex natural products mixtures. Her accomplishments are reflected in more than 150 peer-reviewed publications, application notes, and numerous conference presentations.

A Novel Approach For Lavender Essential Oil Quality Assessment Using GC/MS, NMR And Chemometrics

Wang M[1,2], Zhao J[1], Ali Z[1], Avonto C[1], Ikhlas A. Khan [1,3]

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Currently, the quality of lavender (*Lavandula angustifolia* Mill.) essential oil (LEO) is defined and regulated on the basis of the standards and methods established by various authoritative organizations. Due to the complexity of LEO, these existing standards and methods are not sufficient to protect LEO from adulteration. With increasing awareness of both adulteration and poor LEO quality, it has become necessary to develop reliable methods for LEO quality assessment and adulteration detection. After a comprehensive study, involving a large set of LEO samples (n=72) analyzed by multiple techniques (GC/MS, GC/Q-ToF, NMR, and chemometric analysis), a new approach named Q-Index, was proposed in this study. Fourteen marker compounds, along with *trans*-furano linalool oxide acetate (an indicator of synthetic compound adulteration in LEO), were identified. These marker compounds played significant roles in discriminating the adulterated samples from the authentic LEOs. Calculation of the Q-Index value using the identified marker compounds permitted the detection of the fraudulent samples. It was demonstrated that all of the authentic LEOs exhibited high Q-Index values ($\geq$100), whereas the adulterated samples displayed low Q-Index values (<100). The NMR-based chemometric analysis, which served as an independent and complementary approach to the GC/MS and Q-Index methods, was applied to all of the samples in order to assess the validity of the Q-Index method. Overall, the results obtained from different methods were in good agreement. Moreover, compared to the NMR method, the Q-Index approach showed greater sensitivity when detecting the LEO adulteration associated with the addition of synthetic compounds. Results of this study demonstrated that the Q-Index method could be successfully used for LEO quality assessment and adulteration detection. This new approach is simple, robust, and efficient. If implemented, it may have significant potential to improve quality control for the LEO industry.

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Cécile Bascoul, M.S., Ph.D.

Director of Product Safety

As director of Product Safety at doTERRA, Cécile's research is focused on safety and toxicology of essential oils, specific constituents, potential contaminants and natural complex substance ingredients for cosmetic and nutritional use. Her team at doTERRA acts as scientific support specialized in toxicology and product safety from the product development to release and post-market surveillance. Altogether, Cécile has almost 20 years of experience in clinical and pre-clinical research, from academia, as well as the pharmaceutical, cosmetic and nutraceutical industries.

Cécile first trained as Laboratory Technician in Biology and Biotechnology (BTS ANBIOTEH) and then passed her Masters in Biotechnology from École Supérieure d'Ingénieurs de Luminy (ESIL), in France. She obtained her Ph.D. in Biosciences from Cardiff University, UK, where she also completed her postdoctoral research in collaboration with a local dietary supplement research company (Obsidian Research). Her work focused on the effects of omega-3 fatty acids and other dietary supplements in degenerative diseases.

Prior to joining doTERRA, Cécile managed pre-clinical studies and early-stage clinical trials for the development of new topical analgesics at a small pharmaceutical company, Vapogenix, in Houston, TX. Her past work experience also includes various research positions at Pierre Fabre Dermo-Cosmétiques, Laboratoires Boiron and CNRS in France, AstraZeneca and Q-Chip in the UK.

Cécile enjoys mentoring junior scientists, helping others achieve their life goals, and working with bright, diverse and dedicated teams. She is passionate about lifelong learning, continuous improvement and delivering high quality and safe products.

Eucalyptus Essential Oil: A Safety Assessment And Causality Evaluation Of Published Case Reports

Diana I. Saavedra[1], Aaron Vinson[1], Joe Dawson[1], Sara Shah[1], Shane Beck[1], Cécile Bascoul[1]

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Eucalyptus essential oil (EO) and preparations containing eucalyptus EO have been used in traditional medicine for centuries for the treatment of respiratory illnesses such as cold, influenza and sinus congestion. Research, including clinical trials, has been carried out to evaluate the efficacy of eucalyptus alleviating symptoms of such conditions. However, eucalyptus EO and preparations with eucalyptus EO have also been associated with rare cases of CNS depression and seizures. The case reports reviewed showed evidence of CNS depression and/or seizure in patients from all ages (<1- to 74-year-old) with different doses of eucalyptus EO (0.18 mL to 1000 mL). Most of the adverse events were in children; some of them reacting to small doses (4 drops of EO or about 0.24 mL), ingested, inhaled or after topical application. Most children who developed seizures did not have a history of seizures before the event. The main constituent of eucalyptus EO is 1,8-cineole (about 65% to 84% 1,8 cineole for *eucalyptus globulus* EO, one of the most commonly used eucalyptus species in commercially available products). Camphor is also often present in preparations used to alleviate respiratory symptoms.

A literature review was done to better understand the CNS effects of eucalyptus EO, 1,8-cineole, and camphor. Contradictory information of whether eucalyptus EO, 1,8-cineole, or camphor induce seizures was found. In 2014, Tisserand reported that seizures represented only 2% of adverse events related to eucalyptus EO, however, 1,8-cineole was not believed to be the cause due to its CNS depressant effect. Other case reports as well as *in vitro* and *in vivo* research showed a different outcome, with seizures being reported in human adults exposed to eucalyptus EO, and animals exposed to 1,8-cineole. *In vivo* and *in vitro* research also point to an increased risk of seizures after exposure to camphor. We did not find information about the chirality of camphor and how it impacts its effects in the CNS response, although no adverse events related to CNS response or seizures were found for blue tansy EO which contains L-(-)-camphor.

The goal of this research is to expand our knowledge of eucalyptus EO, its main constituent 1,8-cineole, and camphor, along with other essential oils containing these compounds to better understand potential side effects, improve usage indications, and evaluate the necessity of potential warnings on product labels. One cannot exclude other factors such as potential adulteration or contamination of the essential oils incriminated in case reports. Further investigations are warranted to determine the composition of the specific products used by patients experiencing the seizures. More research is needed to evaluate the data and understand the case reports.

David Vaillencourt

Founder of The GMP Collective

David Vaillencourt, M.Sc., a passionate leader in the cannabis industry, is dedicated to advancing safe access to quality therapeutic solutions. As the founder of The GMP Collective, he has spearheaded the development of industry best practices and supply chain solutions. Serving as Vice Chair of ASTM International D37 on Cannabis, David shapes product safety standards development to enable trade. His expertise in international regulatory systems advocates for increased global accessibility, benefiting researchers and professionals alike.

Medicinal Cannabis And Protecting Public Health And Safety

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David Vaillencourt, M.Sc., CEO of The GMP Collective, Vice Chair of ASTM International's Committee D37 on Cannabis

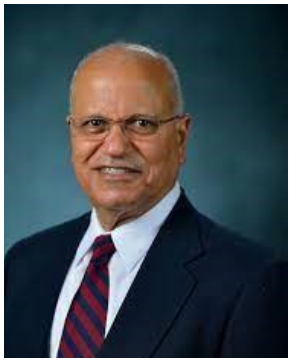
Mahmoud Elsohly, Ph.D., Research Professor, National Center for Natural Products Research, University of Mississippi

Larry Walker, Ph.D., Director Emeritus of the National Center for Natural Products Research, Research Professor Emeritus in the Research Institute of Pharmaceutical Sciences, Professor Emeritus of Pharmacology. University of Mississippi

Nandakumara Sarma, Ph.D., Director of Dietary Supplements and Herbal Medicines, US Pharmacopeia

Medical cannabis programs in the United States are operated by state regulatory agencies and vary widely in their design, oversight, and operation. For most programs, the assessment of risk and benefit outcomes has been limited. To help improve these programs, pharmacopeias, standards development organizations, academic researchers, and industry trade groups have created forums to gather data, create best practices, and develop quality standards. This panel will focus on how these groups approach cannabis quality and the several challenges they face in performing research and producing standards that put patient safety first.

The speakers will analyze the gaps between legislation, regulatory policies, and the needs of patients when it comes to cannabis product quality. The presentation will highlight issues in the cannabis industry, including ensuring safety, monitoring for contamination, quantifying cannabinoids, and the rising presence of intoxicating synthetic cannabinoids in the marketplace. The panel will also discuss dose and route of administration, research design needs in the structuring, gathering and analysis of data, and assessing patient outcomes. The quality considerations for cannabis-derived products in clinical research will also be discussed. The final portion of our panel will be reserved for questions and discussion with the audience.



Mahmoud ElSohly

Research Professor at The NCNPR, University of Mississippi

A Research Professor at NCNPR, & Professor of Pharmaceutics and Drug Delivery, School of Pharmacy, University of Mississippi (UM) & the Director of the (NIDA) Marijuana Project at UM. He is also the President and Laboratory Director of ElSohly Laboratories Incorporated, an analytical forensic drug testing and product development laboratory. He received his undergraduate and Masters from Cairo University, Cairo, Egypt and his Ph.D. in 1975 from the University of Pittsburgh, School of Pharmacy, Pittsburgh, PA. He has been with the University of Mississippi since 1975 and has been Director of the NIDA Marijuana Project since 1981. He has over 40 years' experience working with the isolation of natural products (notably cannabis secondary metabolites), synthetic, analytical and forensic chemistry. He has more than 40 patents and over 400 publications in these areas of science. He is also a member of many organizations such as American Society of Pharmacognosy, American Chemical Society, American Academy of Forensic Sciences, Society of Forensic Toxicologist, International Cannabinoids Research Society, International Association of Cannabinoid Medicines to name a few and received numerous awards. These include but not limited to Lifetime Achievement Award from the International Cannabinoid Research Society (ICRS), Special Award for his Major Contributions to the Re-introduction of Cannabis as a Medicine, from the International Association for Cannabinoid Medicines (IACM), Alexander O. Gettler Award from the American Academy of Forensic Sciences (AAFS), University of Mississippi's Distinguished Research and Creative Achievement Award, Legacy Laureate Award from the University of Pittsburgh, and UM School of Pharmacy Researcher of the Year Award.

He has been Director of the NIDA Marijuana Project at the University of Mississippi for over 40 years and is considered one of the leading authorities in Cannabis Research. He has developed several cannabis-based products for the treatment of a variety of conditions.

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Robert Welch

Director, National Center for Cannabis Research and Education, University of Mississippi

Robert Welch is Director of the National Center for Cannabis Research and Education and Research Associate Professor in the Research Institute of Pharmaceutical Sciences at the University of Mississippi. He just joined the University on April 20, 2023. A Mississippi native, he completed undergraduate coursework at the University of Mississippi and obtained his PharmD from the UM School of Pharmacy in 2002. He completed a pharmacy practice residency at North Mississippi Medical Center, working in both hospital and retail pharmacy thereafter. Robert joined the pharmaceutical industry in 2008 as a Medical Science Liaison and has worked with clinical trials sites and the medical community in immunology, diabetes, obesity, Parkinson's Disease, multiple sclerosis, sleep disorders, oncology and epilepsy. Dr. Welch most recently worked for GW Pharmaceuticals 2017-2023. During that time, he helped develop clinical trial protocols with cannabidiol, working with large institutions and epilepsy centers, such as UAB, which helped garner FDA approval for Epidiolex (cannabidiol oral solution), which was the first and only FDA-approved plant-based cannabinoid medicine. In addition to this work, he educated medical professionals, providers, payer groups, pharmacists and advocacy organizations on the science of cannabinoids.

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Nandakumara (Nandu) Sarma

Director, Dietary Supplements and Herbal Medicines USP

Dr. Nandakumara (Nandu) Sarma is Director, Dietary Supplements and Herbal Medicines at US Pharmacopeia (USP) responsible for strategy and external stakeholder engagement for new and innovative projects, working with global stakeholders and expert volunteers in the development of quality standards (monographs and general chapters) for dietary supplements and herbal medicines that are published in the USP Dietary Supplements Compendium and the Herbal Medicine Compendium.

Before joining USP 2006, he was a post-doctoral fellow at National Cancer Institute, Bethesda, and Thomas Jefferson University, Philadelphia and was a Senior Scientific Officer at The Himalaya Drug Company, India. His research experience includes isolation and analysis of active components of botanicals and their biologic activity. He published more than 25 scientific articles in peer-reviewed journals. Dr. Sarma holds a Pharmacist degree and a Ph.D. in pharmaceutical sciences (pharmacognosy) from Banaras Hindu University, India.

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