

18th Annual OXFORD ICSB

April 9th - 12th 2018

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



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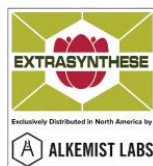
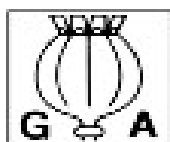
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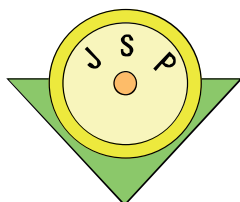
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2018 ICSB Exhibitors:



Special thanks to our co-sponsoring organizations and friends:



This conference is supported by 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). It is co-sponsored by 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); Hunan University, China; the Korean Society of Pharmacognosy (KSP) and the Japanese Society of Pharmacognosy (JSP).



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THE UNIVERSITY of
MISSISSIPPI

NATIONAL CENTER FOR NATURAL PRODUCTS RESEARCH

April 9, 2018

Dear Friends,

On behalf of the National Center for Natural Products Research, School of Pharmacy, and the University of Mississippi, we would like to welcome you to the “18th International Conference on the Science of Botanicals.” 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. The upcoming year’s meeting will explore the topic of synergy between natural products and human health. To this end, we will review, discuss, and explore the confluence of current research topics related to natural products research and development as well as topics related to safety, quality and regulatory aspects. Further information regarding this conference can also be found at www.oxfordICSB.org. This conference is supported by 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). It is co-sponsored by 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; The Vietnam Academy of Science and Technology (VAST).

We are excited to present a program featuring a roster of internationally recognized experts and researchers in the field of botanicals. We wish to extend our thanks to our speakers for their willingness to participate in and contribute to the success of this meeting.

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,

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

A DIVISION OF THE RESEARCH INSTITUTE OF PHARMACEUTICAL SCIENCES, SCHOOL OF PHARMACY

Thad Cochran Research Center | P.O. Box 1848 | University, MS 38677-1848 | (662) 915-1005 | Fax: (662) 915-1006 | www.olemiss.edu

Organizing Committee

Cara Welch, Ph.D.

Senior Advisor, Division of Dietary Supplement Programs, CFSAN, FDA

Ikhlas Khan, Ph.D.

Director, NCNPR,
The University of Mississippi.

Larry A. Walker, Ph.D.

Emeritus Director, NCNPR,
The University of Mississippi.

Mark Blumenthal

Executive Director
American Botanical Council.

Loren Israelsen, J.D.

Executive Director
United Natural Products Alliance.

Rick Kingston, Ph.D.

President,
Safety Call International

Scientific Program Committee

Cindy Angerhofer, Ph.D.

Executive Director, Botanical Research
Aveda, Minneapolis-St. Paul, MN, USA

Joseph M. Betz, Ph.D.

Office of Dietary Supplements of NIH.

Wolfgang Blaschek, Ph.D.

Professor, Pharmaceutical Biology
University of Kiel

De-an Guo, Ph.D.

Director, Shanghai Research Center for
TCM Modernization
SIMM/CAS

Rudolf Bauer, Ph.D.

Institute of Pharmaceutical Sciences
Department of Pharmacognosy
Karl-Franzens-Universitaet Graz.

John Cardellina II, Ph.D.

Distinguished Scientist - Chemistry,
Technical Innovation Center, ReevesGroup
Consultations

K. Hüsnü C. Baser, Ph.D.

Professor, Head of the Department of
Pharmacognosy, Anadolu University,
Eskisehir, Turkey.

Paula Brown, Ph.D.

Director of Applied Research, Natural
Health & Food Products Research Group.
British Columbia Institute of Technology

Sibyl Swift, Ph.D.

Special Assistant, FDA, Office of Dietary
Supplement Programs.

Stephen O. Duke, Ph.D.

Research Leader, USDA, ARS, NPURU.

Mahmoud A. ElSohly, Ph.D.

Research Professor NCNPR, Professor
of Pharmaceutics, The University
of Mississippi.

Edward J. Fletcher

COO/Botanicals Division,
Strategic Sourcing, Inc.

Craig Hopp, Ph.D.

Program Officer, NCCAM, NIH

Jinwoong Kim, Ph.D.

Seoul National University, South Korea.

A. Douglas Kinghorn, Ph.D., D.Sc.

Jack L. Beal Professor and Chair,
Ohio State University,
College of Pharmacy.

Brigitte Kopp, PhD

Professor of Pharmacognosy, Department
of Pharmacognosy, University of
Vienna, Austria.

G.N. Qazi, Ph.D.

Vice Chancellor
Jamia Hamdard, India.

Steven Musser, Ph.D.

Director, Office of Regulatory Science,
CFSAN, FDA.

Amar Chittiboyina, Ph.D.

Assistant Director, NCNPR,
University of Mississippi

Rachel Mata, Ph.D.

Department of Pharmacy,
National Autonomous University
of Mexico.

Robin J. Marles, Ph.D.

Director, Bureau of Clinical Trials and
Health Science NHPD, Health Products
and Food Branch, Health Canada

Douglas "Duffy" MacKay, N.D.

Vice President, Scientific & Regulatory
Affairs, Council for Responsible
Nutrition (CRN)

James McChesney, Ph.D.

Ironstone, Inc.

Dan Fabricant, Ph.D.

Natural Products Association

Amy Roe, Ph.D., DABT

The Proctor & Gamble Company

David S. Pasco, Ph.D.

Associate Director, NCNPR
The University of Mississippi.

Guido F. Pauli, Ph.D.

Associate Professor of Pharmacognosy
University of Illinois at Chicago

Eike Reich, Ph.D.

CAMAG Laboratory, Muttenz, Switzerland

Andre Santos, Ph.D.

Americas Market Development Manager
Agilent Technologies, Andover, MA.

Roy Upton

Executive Director, American Herbal
Pharmacopoeia.

Ram Vishwakarma, Ph.D.

Director, IIIM, Jammu.

Jimmy Yuk, Ph.D.

Senior Business Development Manager
Waters Corporation, Milford, MA

Daniel S. Marsman, DVM PhD

Head, Product Safety, Global
Product Stewardship
P&G Health Care, Worldwide



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DAY 1 (Monday, April 9)

8:00 – 9:00 Open onsite registration – Oxford Conference Center (OCC) Lobby

9:00-10:00 Opening Session - OCC Auditorium

Welcome on behalf of the University of Mississippi and the School of Pharmacy

- Joseph Gladden, Interim Vice Chancellor, Research & Sponsored Programs, University of Mississippi
- David Allen, Dean and Executive Director, School of Pharmacy, University of Mississippi

Welcome and Introductory Remarks from Organizers

- Ikhlas Khan, Director, National Center for Natural Products Research (NCNPR), University of Mississippi

Introduction of Special Guest and Keynote Speaker

- Larry Walker, Director Emeritus, National Center for Natural Products Research (NCNPR), University of Mississippi

Special Guest

- Steven Tave, Director, Office of Dietary Supplement Programs; CFSAN/FDA

Keynote Address

- John Finley, National Program Leader for Human Nutrition, USDA

10:00 - 10:30

Break

SESSION 1: "Update and Future Perspectives from the FDA" OCC Auditorium

Moderator and Session Chair: Sibyl Swift, Special Assistant, Office of Dietary Supplement Programs; CFSAN/FDA

10:30-11:50 **Karen Hatwell**, Senior Advisor for Chemistry, Office of the Center Director; CFSAN/FDA

"The CFSAN Strategic Research Plan and Research Objectives"

Cara Welch, Senior Advisor, Office of Dietary Supplement Programs; CFSAN/FDA

"FDA's Dietary Supplement Program: Overview and Update"

Shontell Wright, Chemist, Office of Dietary Supplements Programs; CFSAN/FDA

"The Secret to Successfully Identifying your Botanical NDI"

Conference Photograph

Meet at OCC side patio across from Cedar Room Dining Hall.

12:00 - 1:00

Lunch

SESSION 2a: "The P&T Dilemma: Identifying, assessing and adding natural products to institutional formularies. Probiotics and other case examples." OCC Auditorium

Moderator and Session Chair: Rick Kingston, President of Regulatory and Scientific Affairs, SafetyCall & Corey Hilmas, Senior VP of Scientific & Regulatory Affairs, NPA

1:00-1:25 **Carla Peterman Williams**, Assistant Director of Pharmacy Clinical Services, University of Maryland Medical Center
"The P&T Dilemma: Identifying, assessing and adding natural products to institutional formularies. Probiotics and other case examples"

1:25-1:50 **Mark Cope**, Applied Nutrition Manager, DuPont
"Health Benefits of Probiotics: From Innovation to Efficacy"

1:50-2:15 **Tyler Daniels**, Scientist, Thorne Research, Inc.
"Botanicals worthy of formulary inclusion"

2:15-2:35 **Dan Fabricant**, President and CEO, Natural Products Association

2:35 - 3:00

Break

SESSION 2b: "Quality Assessment" OCC Magnolia Room

Moderator and Session Chair: Amit Chandra, Manager Analytical Sciences-Chromatography Group, Amway Corporation

1:00-1:30 **Melissa Daoust**, QC Scientist, Traditional Medicinals, Inc.

"Chemical identity crisis (interpreting the unexpected): botanical ingredient case studies through the lens of HPTLC in the quality control lab and implications regarding conformance"

1:30-2:00 **Kirsten Tripplett**, QC Senior Scientist, Traditional Medicinals, Inc.

"Applying Macro-and Microscopic identification methods to multi-ingredient botanical dietary supplement finished products"

2:00-2:30 **Maxleene Sandasi**, Post-Doctoral Associate, Tshwane University of Technology

"Hyperspectral imaging: a potential tool for the quality control of herbal products"

2:30 - 3:00

Break

SESSION 3a: “Safety Assessment Of Botanicals: ‘Green Tea’” OCC Magnolia Room

3:00-3:25 **Paolo Morazzoni**, Scientific Advisor, Indena S.p.A.

“Curcuminoid-drug interactions: a first transversal clinical-based investigation”

3:25-3:50 **Bill Gurley**, Professor, University of Arkansas for Medical Science

“A preclinical safety assessment of the dietary supplement OxyElite Pro (new formula) using various mouse strains”

3:50-4:15 **Igor Koturbash**, Associate Professor, University of Arkansas for Medical Sciences

“Assessment of green tea extract hepatotoxicity in a mouse model”

4:15-4:40 **Hellen Oketch-Rabah**, Senior Scientific Liaison, U.S. Pharmacopeia Convention

“Green Tea Extract and Hepatotoxicity- Progress of work by USP GTEH Expert Panel”

Moderator and Session Chair: Xing-Cong Li, Principal Scientist, University of Mississippi

3:00-3:20 **Jeffrey Langland**, Chair, CINR, Southwest College of Naturopathic Medicine Center for Integrative Naturopathic Research

“*Echinacea purpurea*: Deciphering the Controversy behind Its Medicinal Properties”

3:20-3:40 **Mohammad Sarwar Alam**, Professor, Jamia Hamdard

"Antidiabetic effect of three new compounds isolated from the active methanolic fraction obtained from the roots of *Trapa natans* L."

3:40-4:00 **James Harnly**, Research Leader, Food Composition and Methods Development Lab US Department of Agriculture

“Chemical and genetic characterization of Maca (Lepidium meyenii) and its variance using a systematic analytical approach”

4:00-4:20 **Wei Wang**, Professor, Hunan University of Chinese Medicine

"Diverse Phytochemicals from Chinese Medicine and Hunan Ethnomedicine"

4:20-4:40 Sayeed Ahmad, Professor, Jamia Hamdard

“Hypoglycemic potential of aqueous extract of *Butea monspesia* flower: A medicinal plant from Indian System of Medicine”

6:00 - 8:00

Reception/Mixer at Lyric Oxford (1006 Van Buren Ave, Oxford, MS 38655)

Presentation of the Award for Outstanding Contribution in Natural Product Science

NOTES:

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DAY 2 (Tuesday, April 10)

SESSION 4: "Clinical Toxicology Investigations Impacting Supplement Safety Surveillance" OCC Auditorium

Moderator and Session Chair: Larry Walker, Director Emeritus, NCNPR, University of Mississippi

8:15-8:45 **Victor Navarro**, Professor of Medicine, Einstein Healthcare Network,

"Dietary Supplement Related Liver Injury"

8:45-9:15 **Rick Kingston**, President, SaftyCall

"Poison control incident data; dietary supplement AERs and safety signals"

9:15-9:45 **Patricia Deuster**, Professor & Director, Consortium for Health and Military Performance

"Efforts in DoD to Promote Safe Dietary Supplements"

9:45 - 10:15

Break

SESSION 5a: "Prospects for Naturally Derived Cannabinoids as FDA Regulated Therapeutics" OCC Auditorium

Moderator and Session Chair: Mahmoud ElSohly, Research Professor, University of Mississippi

10:15-10:45 **Ethan Russo**, Director of Research and Development, International Cannabis and Cannabinoids Institute

"History of Cannabis as Medicine: Correlations to Modern Research"

10:45-11:15 **Eric Marsh**, Doctor, Children's Hospital of Philadelphia

"Clinical and Preclinical Data for Cannabidiol in Epilepsy: Real Signal through the Noise"

11:15-11:45 **Larry Walker**, Director Emeritus, University of Mississippi

"States' initiatives on Cannabis-derived products in the treatment of resistant childhood epilepsy: challenges and updates."

SESSION 5b: "Critical Uses of Reference Materials in Natural Products Science" OCC Magnolia Room

Moderators and Session Chairs: Joseph Betz, National Institutes of Health, Office of Dietary Supplements (NIH ODS) & Catherine Rimmer, Chemical Sciences Division, National Institute of Standards and Technology (NIST)

10:15-10:35 **Adam Kuszak**, Health Policy Analyst, Office of Dietary Supplements/National Institutes of Health

"The NIH ODS Analytical Methods and Reference Materials Program: recent activities and the road ahead"

10:35-10:55 **Paula Brown**, BC Institute of Technology, *"The critical role of reference materials in metabolomic approaches to natural products research"*

10:55-11:15 **Nadja Cech**, Associate Professor, The University of North Carolina Greensboro

"Untargeted Metabolomics for Selection of Botanical Natural Products Prior to Clinical Evaluation: The Role of Reference Materials"

11:15-11:35 **Rahul Pawar**, Research Chemist, Office of Regulatory Science/DBC/BMB FDA/Center for Food Safety and Applied Nutrition

"Sensitive and Rapid Quantitation of Three Ginkgolic Acids in Dietary Supplements of Ginkgo"

11:35-11:55 **Catherine Rimmer**, Research Chemist, National Institute of Standards and Technology

"ODS/NIST certified reference materials and Quality Assurance Programs for the botanical and natural products communities"

12:00 - 1:00

Lunch

SESSION 5b Continued: "Critical Uses of Reference Materials in Natural Products Science" - OCC Magnolia

1:00-1:20 **Holly Johnson**, Chief Science Officer, American Herbal Products Association AHPA

"Reference Materials in Botanical Authentication"

1:20-1:40 **Uma Sreenivasan**, Head of Reference Materials R&D, Cerillant Millipore Sigma

"Reference materials, primary standards, and compendial standards: when and how each are used in quality control and basic research"

1:40-2:00 **Cynthia Rider**, Toxicologist, National Toxicology Program/National Institute of Environmental Health Sciences

"Reference materials as research reagents for "biologic similarity" studies"

2:00-2:20 **Amit Chandra**, Manager, Chromatography Sciences Group, Amway

"Botanical Integrity: Significance of Fit for Purpose Tests during botanical product development process"

2:30 - 3:00

Break

DAY 2 (Tuesday, April 10)

SESSION 6 : “Big data for botanicals – outlook and recommendations” - OCC Auditorium

Moderator and Session Chair: Amy Roe, Product Safety & Regulatory Affairs, The Procter & Gamble Company

1:00-1:30 **Tim Baker**, Research Fellow, The Procter & Gamble Company

“Analytical Characterization Platform for Chemical Constituents in Botanicals”

1:30-2:00 **Donna McMillan**, Research Fellow, Central Product Safety, The Procter & Gamble Company

“Large scale botanical and phytochemical data to assist in rapid analysis for safety assessment”

2:00-2:30 **Suramya Waidyanatha**, Discipline leader for chemistry, National Institute of Environmental Health Sciences, National Institute of Health

“Naturally Complex: The National Toxicology Program Strategy for Phytochemical Characterization of Botanical Dietary Supplements for Use in Safety Assessment”

2:30 - 3:00

Break

SESSION 7a: “Natural Products and Cosmetics” - OCC Auditorium

Moderator and Session Chair: Shabana Khan, Principal Research Scientist, University of Mississippi

3:00-3:30 **Stanislav Vukmanovic**, General Health Scientist, DHHS/FDA/CFSAN/OFVM/CFSAN/OCAC/COS

“Hapten-Independent Mechanisms of Skin Sensitation”

3:30-4:00 **Linda Loretz**, Director, Safety and Regulatory Toxicology, Personal Care Product Council

“A Decision Tree Approach to Assess the Safety of Botanicals in Cosmetics”

4:00- 4:30 **Cristina Avonto**, Research Scientist, University of Mississippi

“Chemical stability and skin sensitization potential of 24 fragrance ingredients”

4:30-5:00 **Baatile Komane Mofokeng**, Graduate Student, Tshwane University of Technology

“Cosmetic applications of African seed oils: Clinical observations”

SESSION 7b: “Quality Assessment of Traditional Chinese Medicine” - OCC Magnolia

Moderator and Session Chair: Jimmy Yuk, Senior Business Development Manager, Waters Corporation

3:00-3:25 **Jinghui Wang**, Chief Pharmacist, Beijing Institute of Drug Control

“Fingerprint Study in TCM Quality Control on scientific and regulatory basis”

3:25-3:50 **Binbin Song**, Technology Consultant, Chinese Pharmacopoeia

“Build up effective quality control of herbal medicine through improving Fingerprint similarity evaluation system -- Fingerprint similarity evaluation system development and design for improvement”

3:50-4:15 **Jinle Cheng**, Chinese Pharmacist Director & Doctoral Supervisor, Guangzhou University of Chinese Medicine

“Development and quality control of Ultrafine Granular Power of TCM”

4:15-4:40 **Zhong-Zhi Qian**, Professor, Chinese Pharmacopoeia

“TCM Volume of Chinese Pharmacopoeia 2020 Edition”

4:40-5:05 **Jimmy Yuk**, Senior Business Development Manager, Waters Corporation

“Direct Visualization Of Botanicals Using Mass Spectrometry For Discovery And Quality Control”

5:30 - 8:00

Poster Session: chair - Amar Chittiboyina, University of Mississippi (OCC Oak)

7:00 - 8:00

Dinner (OCC Cedar)

NOTES:



DAY 3 (Wednesday, April 11)

SESSION 8: "Natural Product Research and Regulation in the Americas: Work Underway Across the Region" - OCC Auditorium

Moderator and Session Chair: Michael Smith, Consultant, MJS Consulting

8:30-10:00 **Matthew Bown**, Senior Policy Advisor, Health Canada

"Modernizing the Regulation of Self-Care Products in Canada"

Rosa Amelia Villar Lopez, Professor, National University of Trujillo

"Research And Regulation Of Natural Products In Peru"

Veronica Margarita Lopez Moreno, Country Representative, Health Ministry & Daniel Gallego-Perez, PAHO/WHO

"Natural Products Regulation in Nicaragua And Way Forward, A Brief Case Study"

Lucrecia Pérez de Batres, Pharmacist, Universidad de San Carlos de Guatemala

"The Central American Regulation of Natural Products"

10:00 - 10:30

Break

SESSION 9a: "Natural Products Research On TCM" - OCC Auditorium

Moderator and Session Chair: De-An Guo, Professor, Shanghai Institute of Materia Medica

10:30-11:00 **Rong-Rong He**, Professor, Jinan University

"Pharmacological evaluation of Chinese patent herbal medicine: a hard nut to crack"

11:00-11:30 **Quan-bin Han**, Professor, Hong Kong Baptist University

"The discovery, chemistry, and immunomodulating effects of a unique polysaccharide of Dendrobii Officinalis Caulis"

11:30-12:00 **De-An Guo**, Professor, Shanghai Institute of Materia Medica

"Discovery of effective combination in the exact of Ginkgo biloba"

SESSION 9b: "Future Initiatives on Dietary Supplements" - OCC Magnolia

Moderator and Session Chair: Loren Israelsen, President, UNPA

10:30-11:00 **Gloria Zhang**, Director, Herbridge Media

"Regulatory and Environmental Trends in China: Clean, Land, Air and Water"

11:00-11:30 **Loren Israelsen**, President, UNPA

"The Globalized Botanical Industry - The 5 Critical Challenges"

11:30-12:00 **Mark Blumenthal**, Founder/CEO, American Botanical Council

"Proposed BAPP Best Practices SOP for the Disposal/Destruction of Irreparably Defective Materials"

12:00 - 1:00

Lunch

SESSION 10a: Town Hall Meeting- OCC Auditorium

Moderator and Session Chair: Rick Kingston, President of Regulatory and Scientific Affairs, SafetyCall & Corey Hilmas, Senior VP of Scientific & Regulatory Affairs, NPA.

1:00-2:00

SESSION 10b: "CENAPT Workshop - Practical Implementation of Metabolomics for the Study of Botanicals" - OCC Magnolia

Moderator and Session Chair: Charlotte Simmler, Research Assistant Professor, Center for Natural Product Technologies (CENAPT), University of Illinois at Chicago

1:00-1:30 **Paula Brown**, Director of Applied Research, Natural Health & Food Products, British Columbia Institute of Technology ; *"Metabolomics Analysis as a Tool for Understanding Plant Secondary Metabolite Production and Improved Quality of Botanical-Based Products"*

1:30-2:00 **Joshua J. Kellogg**, Post-Doctoral Associate, The University of North Carolina Greensboro
"Approaches to Evaluate Botanicals via Mass Spectrometry Metabolomics"

2:00 - 3:00

Afternoon tour of the NCNPR facilities or Medicinal Plant Garden

3:00 - 9:00

ICSB Picnic - The Jefferson, 365 Highway 6 East, Oxford, MS 38655
Shuttle Leaves for the Jefferson at 3:00pm!

DAY 4, (Thursday, April 12)

SESSION 11: "International Perspectives on Botanical Research" OCC Auditorium

Moderator and Session Chair: Stefan Gafner, Chief Science Officer, American Botanical Council

- 8:30-9:00 **Jon Wardle**, Senior Lecturer Public Health, University of Technology Sydney; Australian Research Centre in Complementary and Integrative Medicine
"Trends in natural product regulation: developments from Australia and the growing translation between science and traditional claims"
- 9:00-9:30 **Alvaro Viljoen**, Professor, Tshwane University of Technology
"Synergy, a modern concept based on ancient wisdom – examples from African Traditional Medicines"
- 9:30-10:00 **Alexander Shikov**, Professor, St. Petersburg Institute of Pharmacy
"Plant species used traditionally at the interface of food and medicine (the case of Russian Pharmacopoeia)"

10:00 - 10:30

Break

SESSION 12a: "Regulatory Aspects of Botanicals"- OCC Auditorium

Moderator and Session Chair: Jinhui Dou, Vice Dean, Yiling Pharmaceutical, Inc.

- 10:30-10:55 **Robin Marles**, Senior Scientific Advisor, Health Canada
"Assessing the Safety of Botanicals, their Extracts and Isolates, in Foods: Case Studies Illustrating the Scientific Challenges"
- 10:55-11:20 **Thomas Brendler**, Founder & CEO, Plantaphile
"New novel food regulations in Europe: What has changed and what is the impact on access to the EU market?"
- 11:20-11:45 **Charles Wu**, Botanical Review Team Lead (Acting), FDA/CDER/OPQ-IO
"Challenge and Opportunity of Botanical Drug Product Approval in the U.S. -the FDA's Perspective"
- 11:45-12:10 **Yue Hua Zhou**, Deputy Office Director, Office of Traditional Chinese Medicines, CDE, CFDA

SESSION 12b: "DNA Authentications" - OCC Magnolia

Moderator and Session Chair: Sarah Handy, Research Biologist, Center for Food Safety and Applied Nutrition

- 10:30-10:55 **Pang-Chui Shaw**, Professor, Chinese University of Hong Kong
"Authentication and quality control of concentrated herbal medicine granules by molecular technology"
- 10:55-11:20 **David Erickson**, Founder & CEO, DNA4 Technologies LLC
"Genome2-ID: A bioinformatic tool for unbiased and rapid species identification using genomic scale Next Generation Sequencing data"
- 11:20-11:45 **Iffat Parveen**, Research Scientist, University of Mississippi
"Family-specific DNA Mini-barcodes for Identification of Botanicals"
- 11:45-12:10 **Santhosh Kumar**, Graduate Student, Kuvempu University
"DNA barcoding of Momordica species and assessment of adulteration in Momordica herbal products, an anti-diabetic drug"

12:10 - 1:10

Lunch

SESSION 13: "Tools to assess the quality" OCC Auditorium

Moderator and Session Chair: John Travis, Senior Research Scientist, NSF International

- 1:10-1:40 **Michael Repka**, Director Of The PII Center For Pharmaceutical Technology, University of Mississippi
"Critical Issues in the Development of Tablets and Capsules"
- 1:40-2:10 **Phil Wylie**, Sr. Research Scientist, Agilent Technologies
"The Next Chapter in the Analysis of Pesticide Residues in Cannabis using GC/Q-TOF Instrumentation"
- 2:10-2:40 **Giorgis Isaac**, Principal Scientist, Waters; *"Authentication of Botanicals and Herbal Products Using UPLC/Ion Mobility QToF-MS and a Metabolomics Approach"*
- 2:40-3:10 **Maged Sharaf**, Chair Advisory Board & Director, CAMAG Scientific Inc.
"The International HPTLC Association"
- 3:10-3:40 **Shi Qiu**, Post-Doctoral Associate, University of Mississippi; *"Ultra-high performance liquid chromatography-high resolution mass spectrometry guided characterization of new fusaricidins from Paenibacillus sp. MS 2379"*
- 3:40-4:10 **Mohammad Kamil**, Professor, Zayed Complex for Herbal Research & Traditional Medicine
"Good Medicinal Plants Practices (GMPP) -Assuring Safety, Efficacy, and Quality of Botanical Products – From Field to Firm"

Afternoon tour of NCNPR facilities or Medicinal Plant Garden

6:30pm

Closing Ceremony and Banquet (OCC Cedar)
Registration is required and available on-site.



Special Guest



Steven Tave, Director, Office of Dietary Supplement Programs; CFSAN/FDA

Steven Tave is the Director of the Office of Dietary Supplement Programs (ODSP) in FDA's Center for Food Safety and Applied Nutrition (CFSAN). He was named ODSP's first permanent Director in November 2016 after serving as Acting Director beginning in March 2016. Previously, Steve was the Acting Director of the Office of Unapproved New Drugs and Labeling Compliance in CDER's Office of Compliance, where he led a multidisciplinary staff with responsibility for operations and regulatory actions with respect to misbranded and unapproved new drugs, including compounded drugs, fraudulent drugs, homeopathic drugs, marketed unapproved drugs, and over-the-counter drugs. Steve began his career as an attorney and practiced law for almost 15 years, both as a litigator in FDA's Office of Chief Counsel and in the private sector. He received his law degree from the University of Virginia School of Law and his bachelor's degree from Northwestern University.



Key Note Speaker



John Finley, National Program Leader for Human Nutrition from USDA

John Weldon Finley, Ph.D., serves as National Program Leader for the program in Human Nutrition conducted by the USDA-Agricultural Research Service; in this role helps direct the scientific program for six Human Nutrition Research Centers. He is interested in all aspects of the food system and how to optimize a sustainable system to deliver maximal health benefits. He is also involved in efforts to develop big data systems and linkages to connect agricultural production, food processing, environmental inputs/outputs and public health for the purpose of modelling the Ag/Food/Health system and providing data to make informed choices. Dr. Finley received undergraduate degrees in Animal Science and Fine Arts from Clemson University, an MEd in Science Education from the University of Virginia and an MS and Ph.D. in Animal Nutrition from Washington State University. From 1989 to 2004 he served as a Research Chemist with the Grand Forks Human Nutrition Research Center (USDA-ARS) in North Dakota where he developed a research program around trace element metabolism and nutrition, as well as the intersection of agricultural production, nutrition and human health. He has specific interests in how agricultural production and/or processing alters the accumulation of bioactive components in plant and animal foods and how those substances impact chronic disease. Dr. Finley has also worked with the US-FDA, served as Director of Regulatory for the flavor and botanical extract company A.M. Todd, and he has held adjunct faculty positions in North Dakota and Utah. Dr. Finley has authored or co-authored more than 100 peer-reviewed scientific publications, journal articles and book chapters.



Karen Hatwell, Senior Advisor for Chemistry, Office of the Center Director; CFSAN/FDA

Karen Hatwell, Ph.D., began her career at the Food and Drug Administration in 2008 as a review chemist in first the Office of Food Additive Safety at the Center for Food Safety and Applied Nutrition and then the Office of Science at the Center for Tobacco Products. She is currently the Senior Advisor for Chemistry in the Office of the Center Director, Senior Science Advisor Staff. In this role, Dr. Hatwell helps to formulate, support, and implement short- and long-term strategy for research at CFSAN. She works on guidance supporting scientists, such as those involving manuscript clearances, improving public access to scientific publications and data, and communicating technical standard development. She is especially interested in fostering communication among researchers and between the program and research offices.

Prior to FDA, Dr. Hatwell was Associate Professor of Chemistry at Stevenson University and Visiting Assistant Professor of Chemistry at Swarthmore and Vassar Colleges. Dr. Hatwell earned her Ph.D. in Inorganic Chemistry from the University of Massachusetts, Amherst, in kinetics of metal-based polymers.



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The CFSAN Strategic Research Plan and Research Objectives



Cara Welch, Senior Advisor, Office of Dietary Supplement Programs; CFSAN/FDA

Cara Welch, Ph.D., came to the Food and Drug Administration in January as a Regulatory Special Assistant in the agency's Division of Dietary Supplement Programs. In this role, Dr. Welch works on new policies and programs involving regulatory compliance matters of significant importance to the dietary supplement industry, with particular interest in cGMP issues. Welch utilizes her chemistry background to provide guidance on assessing dietary supplement manufacturing methods, evaluating test methodologies, and reviewing different cGMP systems regarding their particular public health and regulatory vulnerabilities.

Prior to FDA, Dr. Welch was the Senior Vice President of Scientific and Regulatory Affairs at the Natural Products Association (NPA). While there, she was responsible for implementing policies in response to government initiatives in the regulatory arena; advising association members on regulatory, safety, nutrition and health issues; and overseeing the association's Natural Seal Certification and Dietary Supplement GMP Certification programs. Dr. Welch earned her Ph.D. in Medicinal Chemistry from Rutgers University working with traditional medicinal African plants under the direction of plant biologist Jim Simon. She is a member of the American Chemical Society and the American Society of Pharmacognosy.



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FDA's Dietary Supplement Program: Overview and Update



Shontell Wright, Chemist, Office of Dietary Supplements Programs; CFSAN/FDA

Shontell Wright, M.S. is a chemist in the Office of Dietary Supplements Programs. She is a member of the Evaluation and Research Staff, where she reviews new dietary ingredient (NDI) notifications, responds to consumer and industry inquiries, assist 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.



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The Secret to Successfully Identifying Your Botanical NDI



Carla Peterman Williams, Assistant Director of Pharmacy Clinical Services, University of Maryland Medical Center

Dr. Carla Williams is the Assistant Director of Pharmacy Clinical Services at the University of Maryland Medical Center (UMMC) in Baltimore, Maryland for the past 5 years. Prior to this, she held a clinical practice in the cardiac surgery intensive care unit at UMMC for 8 years. She received her Doctor of Pharmacy degree in 2003 at The University of the Sciences in Philadelphia where she also completed specialty residency training in cardiology in affiliation with The Hospital of the University of Pennsylvania in Philadelphia. Additionally, she has been Board Certified in Pharmacotherapy for the past 10 years. She is the pharmacy chair and coordinator for the local P&T Committee as well as the pharmacy representative and lead for the System P&T Committee, which consists of 13 hospitals. Additionally, she chairs the system clinical group, which looks at maintaining consistent clinical practice, development of a system formulary, and evaluating clinical financial initiatives and cost containment across the health system. She is a member of several hospital committees including Clinical Practice Council, Staff Nurse Council, and the Medication Error Adverse Drug Event Committee, amongst others. She serves as Residency Director of the PGY-2 Health System Pharmacy Administration program and has consistent involvement with both MSHP and ASHP.



The P&T Dilemma: Identifying, Assessing and Adding Natural Products to Institutional Formularies. Probiotics and Other Case Examples

Williams, C¹

¹*University Of Maryland Medical Center*

As the chair and member of the pharmacy and therapeutics committee for several years, there are continued requests for non-FDA approved agents, like supplements and natural products to be added to the formulary that pose unique challenges to the pharmacy as well as the P&T Committee. As each of these products are reviewed, they pose a marketing and technological challenge that is hard to overcome at times in that there is just limited resources on the safety and quality of these individual agents. Additionally, there are many “brands” to choose from, and there are limited resources and evidence that would support one product over another.

Ultimately, the P&T Committee is acting like the FDA, and attempting to treat these agents as drugs. Unfortunately, we do not have the data to assess the equivalency of the different products, and essentially may be going on our best guess. It is our job to ensure medication safety in our patients, and therefore requests for certain product have been denied for addition to formulary due to lack of information. However, patients are admitted today on various products, and want to continue them as inpatients which makes it challenging for pharmacists to address safety and drug interactions.

It would be very helpful to have some sense of “best practice” with these agents, or some guidance on how to evaluate them for hospital use for the very near future. These requests are increasing and are certainly becoming more popular with patients as treatment options. The committee needs some help with bridging the gap with these unique agents.



Mark Cope, Applied Nutrition Manager, DuPont

Mark Cope, PhD, has Bachelor of Science degrees in Chemistry and Mathematics as well as a PhD in Nutrition Sciences from the University of Alabama at Birmingham. Dr. Cope is currently an Applied Nutrition Manager at DuPont Nutrition & Health where he works closely with the Global Nutrition Innovation and Product Applications teams and interacts with customers to discuss nutrition science related topics associated with DuPont Nutrition & Health ingredients. He has worked in nutrition research for more than 15 years and has experience in several areas related to nutrition science including weight management and muscle recovery after exercise. Dr. Cope has been a member of American Society for Nutrition for 8 years, The Obesity Society for 12 years, and has also published several peer-reviewed papers and chapters related to nutrition, obesity and muscle health.



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Health Benefits of Probiotics: from Innovation to Efficacy



Tyler Daniels, Scientist, Thorne Research, Inc.

Tyler Daniels, Industry scientist and cGMP expert dedicated to building next generation quality systems in an evolving industry.

Looking around the dietary supplement space, I see a model where supplement companies purchase ingredients without necessarily knowing where they came from. Quality assertions are based entirely on test results. Testing is an indispensable tool, but only one of them. The future state of the industry is more vertical, more engaged, where data and supply chain harmonize such that quality is built into products by design. I am hopeful to be a catalyst for this shift.

I am also passionate about biotechnology. I would be happy if I could always maintain access to a modern sequencer, asking it questions and then translating the answers into industry practice. The technology is so powerful, those questions are always there. My latest project, in partnership with some of the most energetic people for botanical quality, is to take on the task of genetically identifying plants, which seems pretty simple until you actually try it.

Key skills: cGMP, quality systems (QA/QC), product development, supply chain management, product formulation, portfolio management, project management, laboratory management, quality auditing

Scientific competencies: Molecular biology, bioinformatics, QC microbiology, human microbiome biotechnology, analytical chemistry



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Botanicals Worthy of Formulary Inclusion



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Dan Fabricant, President and CEO, *Natural Products Association*
"TBA"



Chemical Identity Crisis (Interpreting the Unexpected): Botanical Ingredient Case Studies Through the Lens of HPTLC in The Quality Control Lab and Implications Regarding Conformance

Daoust M

Traditional Medicinals, Sebastopol, CA, USA

21 CFR 111 requires that botanical dietary supplements conform to identity and purity standards. To ensure the quality of our herbal products at Traditional Medicinals, we test our botanical ingredients to pharmacopoeial standards according to monograph methods. High Performance Thin Layer Chromatography (HPTLC) is a valuable analytical tool widely accepted across pharmacopoeia and the dietary supplement industry for verification of botanical identity, while simultaneously providing insight into purity. HPTLC, as a chemical separation technique, allows for the visualization of constituents within a botanical as a reproducible pattern of bands that act as a fingerprint by which identity may be evaluated. While the focus of evaluation of HPTLC results lies in confirming the presence of specifically identified bands, this interpretation of acceptance criteria does not emphasize the possibility that non-specified bands may also be of significance. Going beyond this limited interpretation raises the question of when to pay extra attention to non-diagnostic bands that seem aberrant in relation to past experience, while also taking into consideration the reality that a certain level of chemical variability exists within botanicals. While there are many sources of information on potential adulterants, including pharmacopoeial monographs and industry programs, there is a lack of sufficient guidance on this topic. The often-stated caveat for the evaluation of test samples, "other faint bands may be present," could allow for a contaminant or adulterant to be overlooked, especially if mixed with the botanical of correct identity. How does one determine the need to investigate further? Specific quality control cases are presented, illustrating examples of the presence of unexpected bands in otherwise conforming botanicals. Investigations into *cause* address the topics of correct species, known vs. unknown adulterants, unspecified plant parts and source of origin, as well as methods of harvest/processing. The implications of these topics as they relate to natural chemical variability vs. possibility of contamination/adulteration are discussed.



Applying Macro and Microscopic Identification Methods to Multi-ingredient Botanical Dietary Supplement Finished Products

Tripplett, K.¹

¹ Quality Control Laboratory, Traditional Medicinals, Inc, Sebastopol, CA 95472

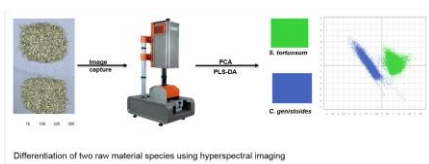
The current 21 CFR 111 code requires manufacturers of botanical dietary supplements to identify all ingredients in finished products, *using at least one appropriate identification method*. How does a manufacturer choose which identification method to apply? What if one is analyzing multi-ingredient botanical finished products? Can one, in fact, use plant morphology and anatomical techniques to determine multiple plant species at a tea-bag cut particle size, or for that matter, at the microscopic level in a powder? What if the raw material is heat-treated? Do the tissues retain their cellular integrity and same quality of information? Do pharmacopoeial monographs and classic botanical macro- and microscopic anatomy techniques provide enough resources to successfully identify botanical ingredients in multi-species finished products? Are such methods practical, efficient and cost-effective, especially for small businesses? The initial hypothesis was no, such multi-species identification could not be done; how does one create a rigorous, replicable testing method? When experiments were initiated, however, it quickly became apparent that much success could be achieved from previous experience with products consisting of 1-4 ingredients. A composition analysis of 25 different finished products with up to 10 ingredients was conducted. Recent method developments using macroscopic and microscopic (anatomical) techniques demonstrate that multiple ingredients *can be* identified with confidence, and with reduced testing times, and high replicability. Successes, failures, method development and applications to the botanical dietary industry are discussed and presented. The use of classic botanical methods of identification, examples, and their application to complex botanical finished products is demonstrated.

Hyperspectral Imaging: a Potential Tool for the Quality Control of Herbal Products

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¹Department of Pharmaceutical Sciences, ²SAMRC Herbal Drugs Research Unit, Faculty of Science, Tshwane University of Technology, Private Bag X680, Pretoria 0001, South Africa

Growing concerns over the safety and efficacy of herbal products has led researchers to focus on developing quality control protocols that enable ‘holistic’ analysis of these complex matrices. Spectroscopy-based techniques that are regarded as ‘pattern-oriented’ have gained a lot of attention in this regard. Hyperspectral imaging spectroscopy acquires both spectral (chemical) and spatial information by combining conventional spectroscopy and imaging. The technique offers comprehensive chemical profiling, it is simple, rapid, non-destructive, chemical-free, and suited for large-scale screening of material. In this study, HSI as a quality control method was used to investigate various quality aspects as demonstrated in the following three examples; 1) to differentiate between various ‘ginseng’ species and verify the botanical species present in commercial ginseng products; 2) to discriminate *Scutellaria lateriflora* (skullcap), a medicinal herb used for the management of insomnia and anxiety, from potentially hepatotoxic, adulterant ‘skullcap’ plants (*Teucrium canadense*, and *T. chamaedrys*) and to detect adulteration, and 3) to differentiate herbal tea raw materials (*Sceletium tortuosum* and *Cyclopia genistoides*) and determine the relative proportions of each raw material in tea blends. The results demonstrate that HSI successfully differentiated “ginseng” raw materials; *Panax ginseng*, *P. quinquefolius*, *P. pseudoginseng* and *Eleutherococcus senticosus*. Partial least squares discriminant analysis (PLS-DA) models accurately predicted a majority of commercial products to contain either *P. ginseng* or *P. quinquefolius* although most predictions did not match the label claims. Hyperspectral imaging was able to clearly differentiate the three ‘skullcap’ plants with a modelled chemical variation of 92.3%. Based on pixel abundance, it was possible to quantify raw material adulteration as low as 40% in spiked samples. In combination with multivariate data analysis methods, HSI revealed chemical differences between *S. tortuosum* and *C. genistoides* and quantitatively predicted raw material constituents in the tea blends. The aforementioned examples demonstrate the potential of HSI as a quality control technique that can be used for routine analysis of complex herbal products.



The authors would like to acknowledge the National Research Foundation (NRF) of South Africa, Department of Science and Technology (South Africa) and the Tshwane University of Technology for financial support.



Paolo Morazzoni, Scientific Advisor, Indena S.p.A.

Paolo Morazzoni has a degree in Biological Sciences from University of Milan. After a scientific fellowship in Biochemistry and Enzymology at Mario Negri Institute of Pharmacology of Milan (1976-1980), he worked as senior scientist in the Pharmacological Department of Invernizzi Della Beffa S.p.A. (1980-1982). He covered the role of Head of the Metabolism and Pharmacokinetic Laboratories (1983-1993) concentrating his interest on the metabolism and pharmacokinetics of pharmaceutical products of botanical origin. From 1993 to 1997, he was the Associate Scientific Director of Indena S.p.A., Milan, taking care of the development of new botanical active derivatives in different therapeutic areas including cardiovascular, CNS and oncology. From 1998 to 2016, he was the Scientific Director of Indena S.p.A. with the specific role of coordinating the research and development of new botanicals, being oncology the main area of activity. From 2017, he is Scientific Advisor of Indena S.p.A. in the area of strategic innovation and scientific assistance. Dr. Paolo Morazzoni is the author of more than 300 research articles on medical and biological issues (with particular attention to phytotherapy) and an active participant to international symposia and congresses. He is also inventor/co-inventor of more than 50 patents.



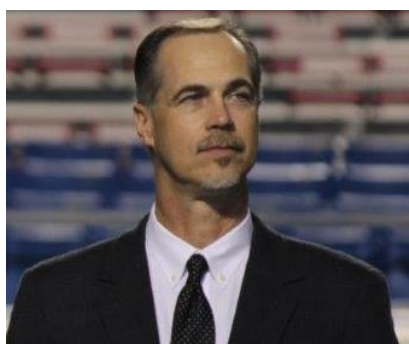
Curcuminoid-Drug Interactions: a First Transversal Clinical-Based Investigation

Morazzoni P, Riva A, Allegrini P

Indena S.p.A., Milan, Italy

Botanical-based nutraceuticals represent since many years one of the fastest growing market worldwide and relevant percentages of the population of major countries are currently every day-consumers of botanical-based products. Despite a widespread public perception that herbals are safe, increasing evidences are emerging showing that upon consumption of some specific derivatives obtained from plants (e.g.: St. John's worth, goldenseal, licorice, kava, ginkgo biloba....) pharmacological interactions can occur with both prescription and over-the-counter drugs. Nevertheless concerns about herb-drug interactions are often not based on rigorous clinical research but inferred from cellular assays, animal studies, single case report or other indirect means. Well-designed clinical studies evaluating herbal supplement-drug interactions are still a limited number and inconclusive.

Evidences from this non-interaction clinical study suggest that Meriva® does not interfere with the antiplatelet activity of the most commonly utilized agents and in addition does not alter the INR values in stable subjects assuming warfarin or dabigatran. Furthermore the concomitant treatment in subjects under LT4 does not require its dosage adjustment.



Bill Gurley, Professor, University of Arkansas for Medical Science

Bill J. Gurley, Ph.D., is a Professor of Pharmaceutical Sciences at the University of Arkansas for Medical Sciences (UAMS) College of Pharmacy, vice-chair of the UAMS Department of Pharmaceutical Sciences, and Chair of the UAMS Institutional Animal Care and Use Committee. He is a member of the American Association of Pharmaceutical Scientists, American Association of Colleges of Pharmacy, American Society of Clinical Pharmacology and Therapeutics as well as the USP's Expert Panel on Dietary Supplements. Gurley also serves on the editorial boards of *Clinical Pharmacology & Therapeutics*, and *Phytomedicine* as well as the advisory board of the American Botanical Council. He has authored more than 175 peer-reviewed publications, abstracts, and book chapters in the areas of pharmacokinetics, analytical method development, therapeutic drug monitoring, herbal dietary supplements, and herb-drug interactions. His research interests include mechanisms of herb-drug interactions, toxicity of multiple-component herbal dietary supplements, phytochemical modulation of human drug metabolizing enzymes and drug transport proteins, human phytochemical disposition, and botanical supplement use in special populations. Gurley is the inventor of Omnibalm™, a tea tree oil-containing nonprescription skin and foot care product distributed by Balm Innovations, LLC, of which he serves as the Chief Science Officer. Gurley received a B.S. in chemistry from Tennessee Technological University and a B.S. in pharmacy and Ph.D. in pharmaceuticals from the University of Tennessee Health Science Center.



A Preclinical Safety Assessment of the Dietary Supplement Oxyelite™ Pro (New Formula) Using Various Mouse Strains

Gurley BJ¹, Koturbash I², Miousse IR², Skinner CM², Lin H², Ewing LE², Williams DK³, Avula B⁴, Khan IA⁴, ElSohly MA⁵.

¹University of Arkansas for Medical Sciences, Department of Pharmaceutical Sciences, ²University of Arkansas for Medical Sciences, Department of Environmental and Occupational Health, ³University of Arkansas for Medical Sciences, Department of Biostatistics, Little Rock, AR 72205, USA, ⁴National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, The University of Mississippi, University, MS 38677, USA, ⁵ElSohly Laboratories, Inc., Oxford, MS 38655, USA.

Herbal dietary supplements have gained wide acceptance as alternatives to conventional therapeutic agents despite concerns regarding their efficacy and safety. In 2013, a spate of severe liver injuries across the United States was linked to the dietary supplement OxyELITE Pro-New Formula (OEP-NF), a multi-ingredient product marketed for weight loss and exercise performance enhancement. The principal goal of this study was to assess the hepatotoxic potential of OEP-NF in outbred and inbred mouse models. In an acute toxicity study, significant mortality was observed after administering 10X and 3X mouse-equivalent doses (MED) of OEP-NF, respectively. Increases in liver/body weight ratio, ALT and AST were observed in female B6C3F₁ mice after gavaging 2X and 1.5X MED of OEP-NF. Similar findings were observed in a 90-day feeding study. These alterations were paralleled by altered expression of gene- and microRNA-signatures of hepatotoxicity, including *Cd36*, *Nqo1*, *Aldoa*, *Txnrd1*, *Scd1* and *Ccng1*, as well as miR-122, miR-192, miR-193a and miR-125b and were most pronounced in female B6C3F₁ mice. Body weight loss, observed at week 1, was followed by weight gain throughout the feeding studies. Female NZO/HILtJ mice were fed diets containing 1X and 3X MED of OEP-NF. While body weight loss was observed during week 1, all mice in both treatment groups exhibited weight gain starting at week 2, which continued through completion of the study. Hepatotoxicity gene arrays revealed substantial dose-dependent deregulation in the expression of nearly 20 genes in the livers of OEP-fed NZO/HILtJ mice. The majority of affected genes were up-regulated and the degree of up-regulation was substantially higher compared to CD-1 and B6C3F₁ mice. A 2-week gavage study resulted in 33% mortality in NZO/ HILtJ mice, even at 1 MED of OEP-NF, potentially due to combined liver and cardiovascular toxicity. These findings bolster safety and efficacy concerns for OEP-NF, and argue strongly for implementation of pre-market toxicity studies within the dietary supplement industry.

Support for this study was provided by the United States Department of Justice.



Igor Koturbash, Associate Professor, University of Arkansas for Medical Sciences

Dr. Igor Koturbash is an Associate Professor at the Department of Environmental and Occupational 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). Dr. Koturbash completed his training as an Oak Ridge Institute for Science and Education Research (ORISE) Fellow at the National Center for Toxicological Research, US Food and Drug Administration in Jefferson, AR.

The focus of Igor's research is to understand: 1) the metabolic mechanisms of the tissue responses to environmental stressors, such as radiation, and how the diet can modulate those response; and 2) safety, efficacy and mechanisms of action of dietary supplements. He has published over 80 peer-reviewed articles and book chapters. Igor's research has received uninterrupted extramural funding since the beginning of his independent career. Dr. Koturbash is a recipient of numerous prestigious awards and honors, including an Award for Faculty Excellence in Research from UAMS and the Michael Fry Award from the Radiation Research Society.

Dr. Koturbash serves as a scientific reviewer on the Department of Defense Congressionally Directed Medical Research Programs (CDMRP), U.S. Environmental Protection Agency, National Center of Science and Technology Evaluation, JCS (Republic of Kazakhstan), and the FWF Austrian Science Fund. Igor is a current President of the South-Central Chapter of the Society of Toxicology, and serves as an Editorial Board Member for *Chemico-Biological Interactions* and as an Associate Editor for *Radiation Research*.



Assessment of Green Tea Extract Hepatotoxicity in a Mouse Model

Igor Koturbash,¹ Charles M Skinner,¹ Isabelle R Miousse,¹ Laura E Ewing,¹ Bill J Gurley,² Bharathi Avula,³ Ikhlas Khan³

¹ *Department of Environmental and Occupational Health, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA,* ² *Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA,* ³ *National Center for Natural Product Research, School of Pharmacy, University of Mississippi, University, MS 38677, USA*

Green tea extract (GTE) has been implicated as a potential causative agent in several human hepatotoxicity cases. In this study, we evaluated the hepatotoxic potential of GTE in both acute (24 h) and sub-acute (2 weeks) settings. Eight-week old male B6C3F₁ mice were gavaged with 1X, 3X, and 10X mouse equivalent doses (MED) of decaffeinated GTE in distilled water (pH = 5). In the acute study, a significant decrease in the body weight was observed in mice gavaged with 10X MED. The weights of livers and hearts, as well as liver/body weight and heart/body weight ratios, were decreased in all experimental groups, but no changes were observed in the kidneys. A modest, but statistically significant increase in plasma ALT was observed in 1X MED mice only. No changes in AST, GGT, or alkaline phosphatase were detected. After two weeks of dosing, trends towards body weight gain were noted in 1X MED mice, while no changes were observed in 3X and 10X MED mice. Similarly, trends towards liver, heart, and kidney weight and organ/body weight ratio increases were detected in 1X MED mice only. Hepatotoxicity gene expression array analysis revealed a small subset of genes differentially regulated in a dose-dependent mode in the livers of mice gavaged with GTE. Specifically, down-regulation of *Timm10b*, *L2hgdh*, *Lss*, *Mlxipl*, and *Osmr* and up-regulation of *Mcm10* were observed at both time-points. The results of this study suggest a low hepatotoxic potential for GTE in this experimental mouse model; however, further long-term studies are warranted given the observed physiological and gene expression alterations.



Green Tea Extract and Hepatotoxicity- Progress of Work by USP GTEH Expert Panel

Oketch-Rabah, Hellen¹; Rider, Cynthia V¹; Jordan, Scott¹; Roe, Amy L¹

¹ USP Green Tea Extract Hepatotoxicity Expert Panel, USP Rockville MD 20852

USP provides quality standards for commonly used botanical dietary supplements. A Label caution statement may be included in some monographs in order to mitigate a safety concern. Following a routine review of the literature on hepatotoxicity of green tea extract (GTE), the USP Dietary Supplement Admission Evaluations Joint Standard Setting Sub-committee recommended and USP sought the assistance of external experts to conduct a risk assessment on GTE. The USP Expert Panel (the Green Tea Extract Hepatotoxicity Expert Panel) was charged to review the toxicity and safety data related to GTE hepatotoxicity and to define an appropriate label cautionary statement for inclusion in the USP Powdered Decaffeinated Green Tea Extract monograph. The expert panel considered three major topic areas relevant to understanding potential hepatotoxicity of GTE: 1) chemistry, manufacturing and controls, 2) pharmacokinetics/pharmacodynamics, and 3) clinical/non-clinical data and adverse event reporting for risk assessment.

Information available on first two topics suggest that active constituents, particularly epigallocatechin gallate (EGCG) and other catechins, of GTE may be involved in hepatotoxicity, not contaminants, and suggest that taking GTE under fasting conditions increases the absorption of GTE which can lead to hepatotoxic levels of catechins. A comprehensive literature search for both clinical and non-clinical studies on GTE and major constituents published after previous USP safety review in 2008 was performed. Also obtained were human case reports, and FDA MedWatch Adverse Event Reports (AERs) related to the use of dietary supplement products containing GTE for the period January 1, 2008 to October 31, 2016.

The non-clinical data demonstrated dose-dependent hepatotoxicity in rodents and dogs, with fasted dogs being the most sensitive model (NOAEL of 40 mg/kg EGCG content). In the nine clinical studies, reviewed, one reported clear signs of hepatotoxicity while sporadic indications of possible liver effects were noted in multiple trials (e.g., intestinal distress, ALT changes). Human case reports are being reviewed by physicians from the Drug-Induced Liver Injury Network (DILIN) for causality assignment. Findings from this review were used to propose significant revision to the proposed label cautionary statement pertaining to hepatotoxicity in the USP GTE monograph which now states: *Dosage forms prepared with this article should bear the following statement: Do not take on an empty stomach. Take with food. Do not use if you have a liver problem and discontinue use and consult a healthcare practitioner if you develop symptoms of liver trouble, such as abdominal pain, dark urine, or jaundice.*



Echinacea Purpurea: Deciphering the Controversy Behind Its Medicinal Properties

Gerstel, J.¹, Turner, T.¹, Ruiz, G.¹, and Langland, J.O.^{1,2}

¹Center for Integrative Naturopathic Medicine, Southwest College of Naturopathic Medicine, Tempe, Arizona, USA 85282

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Rhinovirus infections are associated with the common cold. Symptomology and complications of rhinovirus infections are often linked to the immune response and the expression of the cytokine, IL-8. Rhinovirus complications may include chronic bronchitis, sinusitis, otitis media and asthma. *Echinacea purpurea* has historically been asserted as a therapy for rhinovirus infections, but results from clinical studies have been controversial. Many studies conclude that *Echinacea* is an effective therapeutic against the rhinovirus infections, whereas an equal number of reports claim the opposite. The purpose of our study was to investigate the biological activities of *Echinacea* based on different plant parts and various extraction methods. Results demonstrated a dramatic difference between the root and flower portions of the plant, where flower ethanol extracts enhanced immune cytokine production, while ethanol extracts of the root repressed cytokine production and inhibited viral growth. In addition, a water extract of the root led to an enhancement in rhinovirus replication. Based on our results, predictions can be made where *Echinacea* flower extracted in ethanol or root extracted in water may lead to increased symptoms if used to treat a rhinovirus infection, while root extracted in ethanol would likely decrease and improve symptoms if used to treat a rhinovirus infection. From this, we can begin to understand and decipher the controversy surrounding the therapeutic efficacy of *Echinacea* where different plant parts and extraction methods will likely produce significantly different physiological responses.



Antidiabetic Effect of Three New Compounds Isolated From the Active Methanolic Fraction Obtained from the Roots of *Trapa Natans* L.

Mohammad Sarwar Alam^{1*}, Chetna Kharbanda¹, Hinna Hamid¹, Yakub Ali¹, Saqlain Haider²

¹Department of Chemistry, Faculty of Science, Jamia Hamdard, New Delhi-110062, India

²National Center for Natural Products Research, University of Mississippi, Oxford, MS, USA.

From ancient times, *Trapa natans* L. is being used as a nutrient and is traditionally being used as remedy against diabetes, cancer, diuretic, diarrhea and many other maladies also. The authors of the present study have already reported antihyperglycemic and anti-hepatotoxic effects of ethanolic extract and its fraction obtained from the roots of *T. natans*. Extending the previous study further, the present study focuses on the isolation and identification of the active principles from the active methanolic fraction of the roots of *Trapa natans* L.

The phytochemical investigation of the active methanolic fraction of the roots of *Trapa natans* L. led to the isolation of three new compounds and two known compounds. Structures of new compounds were elucidated through extensive spectral data. Two glycosides and a flavone isolated as new compounds were evaluated for their antidiabetic potential by OGTT method and on STZ induced diabetic rat model were found to possess significant antidiabetic activity in comparison to glibenclamide. The flavone was found to be the most active compound among these three new isolated compounds.

The authors thank Dr. Seyed Ehtesham Hasnain, Vice-Chancellor, Jamia Hamdard for providing necessary facilities to the department of chemistry to carry out this work.



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**James Harnly, Research Leader, Food Composition and Methods Development Lab US
Department of Agriculture**

Research Leader
Food Composition and Methods Laboratory
Beltsville Human Nutrition Research Center
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Dr. Harnly serves as the Research Leader for Food Composition and Methods Laboratory (FCMDL), part of the Beltsville Human Nutrition Research Center of the US Department of Agriculture. His lab is tasked with the development of new analytical methods for nutrients and bioactive compounds in foods, dietary supplements, and botanical materials in support of nutrition research at USDA. Current projects in the lab include development of new methods for vitamins, metabolomics, and chemical fingerprinting of foods and botanical supplements. His personal research interest is the development of chemometric methods for the identification and authentication of botanical materials. Dr. Harnly received his BA from the University of Colorado and his PhD from the University of Maryland. He joined USDA as a research scientist in 1979 and became the Research Leader in 1997. He has served on the Board of Directors for AOAC International, the Advisory Board of the American Botanical Council, and numerous Expert Committees for US Pharmacopeia and AOAC. He served for 22 years as the US Editor for the Journal of Atomic Spectrometry for the Royal Society of Chemistry and is currently the Editor in Chief for the Journal of Food Composition and Analysis.



Chemical and Genetic Characterization of Maca (*Lepidium Meyenii*) and Its Variance Using a Systematic Analytical Approach

Harnly J¹, Geng P¹, Sun J¹, Chen P¹, Gafner S², Jeremy Stewart J³, Frame J⁴, & Meissner H⁴.

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Maca (*Lepidium meyenii*) is a tuber grown in Peru and China at elevations above 4,000 feet which has become popular throughout the world. Raw samples were collected in Peru and China and compared with commercially prepared products which have been ground, extruded, and gelatinized. The raw samples were classified on collection as white, yellow, red, or black based on their appearance and age. With hundreds of samples, complete analysis of individuals can be time consuming, expensive, and logistically impossible. With this in mind, the first step was a simple grinding and extraction of each sample prior to flow injection high resolution mass spectrometry (FIHRMS), an analysis requiring less than 5 minutes per sample. Principal component analysis (PCA) of the resulting spectral fingerprints (~1500 ions between *mz* 500-2000) produced 3 separate clusters for Peru (raw), China (raw), and commercial samples. PCA loadings identified ions key to separation of the clusters. From each cluster, 2 samples were selected for full metabolomics and next generation DNA sequencing. All six samples were genetically identified as *Lepidium meyenii* with some contamination from broccoli and sweet basil. Metabolomics revealed 3 distinctive profiles for each cluster and individual components were identified. The resulting library of ions made it possible to return to the fingerprint loadings and identify the compounds that were distributed differently in the 3 clusters. This was followed by separate PCA of the Peru (raw) and China (raw) clusters to determine systematic chemical differences with respect to color. Again, PCA led to the selection of representative samples of each color for metabolomics profiling. Thus, mass spectral fingerprint guided metabolomics and next generation genetic sequencing proved an excellent systematic approach to the characterization of a botanical supplement.

This research was supported by an Interagency Agreement with the Office of Dietary Supplements, NIH, Bethesda, MD and by a collaboration with the Waters Corporation, Milford, MA



Wei Wang, Professor, Hunan University of Chinese Medicine

Biography

Wei Wang, Ph.D, Furong Distinguished Professor, Hunan University of Chinese Medicine. Director of TCM and Ethnomedicine Innovation & Development International Laboratory. Executive editor of "***Current Traditional Medicine***".

Prof. Wang got his B.S and M.S degree in Hunan University of Chinese Medicine. He received his Ph.D degree in Peking University at 2006. He had worked in National Center for Natural Products Research, School of Pharmacy, The University of Mississippi for 5 years from 2007 to 2012 as a post-doctor and visitor scholar.

In 2012, Wei Wang went back to his hometown Changsha, and worked in Hunan University of Chinese Medicine as an associate professor. He was promoted to full professor in 2013. In 2015 he was appointed as Furong Distinguished Professor.

He and his group were interested in isolation and structure elucidation of natural products, search for new bioactive compounds from traditional Chinese medicine (TCM) or other ethnic medicine (e.g. Tujia, Miao and so on).

The second research field is quality control study of Chinese herbal medicine. His group has actively involved some monograph standards for Chinese pharmacopoeia.

The third research field is diseases related Metabolomics research, his group aimed to find some biomarkers for diseases early diagnosis and guiding clinical treatment, such as bladder cancer, breast cancer and other diseases.

Prof. Wei Wang has over 100 publications and 4 patents.



Diverse Phytochemicals from Chinese Medicine and Hunan Ethnomedicine

Wang W¹

¹TCM and Ethnomedicine Innovation & Development International Laboratory, , Sino-Pakistan TCM and Ethnomedicine Research Center, School of Pharmacy, Hunan University of Chinese Medicine, Changsha 410208, China

Hunan Province of China has several ethnic nationalities including Han, Tujia, Miao, Dong and so on. They have developed their special ethnomedicine for the prevention and treatment of kinds of disease over thousands of years. The chemistry, efficacy and quality control were carried out on several typical Chinese medicine and Hunan ethnomedicine, with some interesting results.

The work was supported by China State of TCM administration (ZYBZH-Y-HUN-23) and National Natural Science Foundation of China (81673579)



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Hypoglycemic Potential of Aqueous Extract of *Butea Monsperma* Flower: a Medicinal Plant From Indian System of Medicine

Sayeed Ahmad

Bioactive Natural Product Laboratory, School of Pharmaceutical Education and Research, Jamia Hamdard, New Delhi-110062, India

In Indian traditional system of medicine, the flower of *Butea monosperma* Lam. has been used for since long. The aim of our study was to explore the hypoglycemic properties of the aqueous extract of *B. monosperma* flower (AEBMF) and to elucidate its mechanism. The AEBMF has been tested on the activity of carbohydrate-digesting enzymes, glucose uptake in yeast cell and skeletal muscle, glucose absorption in intestine, followed by in streptozotocin induced diabetic rats and in mice fed with high-fat-diet followed by gut microbiota based metabolomic profiling. AEBMF remarkably inhibited the activity of α -amylase and α -glucosidase with improved antioxidant capacity and glucose tolerance. Percentage increase in the rate of glucose uptake into yeast cell was linear to that of a dose of extract and concentration of glucose. In STZ-induced diabetic rats, a dose of 150 mg/Kg produces a maximum fall of 47.86% in acute effect, whereas in chronic effect, it was 44.5% as compared to toxic control. The level of fasting blood glucose (FBG), lipid profiles and antioxidant marker enzymes were significantly ($P < 0.05$) ameliorated in both HFD and STZ experimental model. A total of 146 different metabolites were tentatively identified with their m/z value using UPLC-MS metabolomics. *Ex vivo* culture of gut microbe with AEBMF, resulted in the production of 15 new bioavailable and 12 non-bioavailable metabolites. Aurone, butrin, coreopsin, lupeol, monospermoside, and quercetin were the major metabolites as demonstrated by PCA and found in the blood after oral administration of AEBMF to rats. Further, docking analysis tentatively postulated the mechanism. The mean plasma concentration versus time profiles of monospermoside, coreopsin and isovaleric acid resulted in peak plasma concentration (C_{max} 19.29, 14.28 and 16.15 $\mu\text{g/mL}$) with half-life ($t_{1/2}$ 4, 2 and 1 h) for monospermoside, coreopsin and isovaleric acid, respectively. Metabolically characterized AEBMF demonstrated as good antidiabetic agent using *in vitro*, *in vivo* and *in silico* model. Hence, it can be developed as phytopharmaceuticals for the management of diabetes and can be used as adjuvants.

University Grants Commission, New Delhi, Indi



Victor Navarro, Professor of Medicine, Einstein Healthcare Network

Victor Navarro earned his Doctor of Medicine degree from the Pennsylvania State College of Medicine and completed medical residency followed by chief residency in Internal Medicine at Temple University. Thereafter, he completed his fellowship in Gastroenterology, Hepatology, and Hepatobiliary Endoscopy at Yale University, along with a fellowship training period in Liver Transplantation at the University of Nebraska. In 1994, Dr. Navarro joined the faculty of the Yale University School of Medicine as an Assistant Professor of Medicine and Epidemiology and the Director of its Liver Failure and Transplantation service. He was also the Director of the State of Connecticut Emerging Infections Program Liver Study Unit. His scholarly work while at Yale focused on the population-based epidemiology of chronic liver disease, and also the role of soluble adhesion molecules in liver transplant rejection.

Dr. Navarro joined the clinical pharmacology group at Merck Research Laboratories in 2001 while continuing as an adjunct faculty member at Yale, and in 2002 he assumed a full time faculty position with Thomas Jefferson University, Philadelphia, as Chief of Hepatology and Medical Director for Liver Transplantation. While at Jefferson, he rose to the rank of Professor of Medicine, Pharmacology and Experimental Therapeutics. His scholarly interests focused on drug and dietary supplement induced liver injury. In 2012, he joined the Einstein Healthcare Network, Philadelphia, as Chairman of the Division of Hepatology, and Medical Director for Liver Transplantation, continuing his appointment at the Jefferson Medical College as Professor of Medicine. Recently, Dr. Navarro became the founding Co-Chair for the Department of Transplantation, Albert Einstein Medical Center.

Dr. Navarro is funded by the National Institutes of Health as an investigator for the U.S. Drug Induced Liver Injury Network (DILIN). His main scholarly focus continues to be liver injury attributable to Herbal and Dietary Supplements. Dr. Navarro maintains several lines of investigation in this area and also oversees the DILIN's Repository for HDS, which houses products implicated in liver injury.



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Dietary Supplement Related Liver Injury



Rick Kingston, President, SafteyCall

Rick Kingston, PharmD, is the President, Regulatory and Scientific Affairs and Sr. Clinical Toxicologist at SafetyCall International P.L.L.C., a multidisciplinary healthcare firm of nationally recognized experts focused on providing manufacturers an outsourced option for postmarket medical surveillance, product safety assessment and evaluation, and regulatory reporting support for adverse events. His academic career spans more than 30 years at the University of Minnesota where he attained the rank of full Professor in the Department of Experimental and Clinical Pharmacology and currently serves as Clinical Professor, in the College of Pharmacy. Dr. Kingston earned his B.S in Pharmacy at the University of New Mexico, his Doctorate in Clinical Pharmacy at the University of Minnesota and completed a Post-Doctoral Fellowship in clinical toxicology and pharmacokinetics at St. Paul-Ramsey Regional Trauma Center and the University of Minnesota. He was the co-founder and Director of the Minnesota Poison Control System and its Regional Poison Control Center where he served for 18 years. He has authored more than 100 peer reviewed scientific abstracts, publications, confidential technical white papers and textbook chapters. He is co-editor of the recently published Herbal Products Toxicology and Clinical Pharmacology Second Edition published by Humana Press. He serves on numerous scientific panels, advisory boards and non-profit professional organization scientific committees advising on issues of product stewardship, science and safety. He also serves on the advisory board of the American Botanical Council as the resident expert on botanical safety. His professional experience includes a focus in the areas of clinical toxicology and pharmacology, poison control, product post-market safety surveillance, regulatory policy, drug and dietary supplement safety, and academic medicine.



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Poison Control Incident Data; Dietary Supplement AERS and Safety Signals



Patricia Deuster, Professor & Director, Consortium for Health and Military Performance

Patricia A. Deuster, PhD, MPH, is a Professor in the Department of Military and Emergency Medicine at the Uniformed Services University of the Health Sciences (USU) in Bethesda, Maryland and Director for the Consortium for Health and Military Performance (CHAMP), the Defense Center of Excellence for Human Performance Optimization. She obtained an AB in Mathematics and Computer Science and MA in Education and Physical Education from the College of William and Mary, a PhD in Nutritional Sciences and Physiology from the University of Maryland, and a MPH with an emphasis in public health and epidemiology from USU.

Dr. Deuster chairs the Department of Defense (DoD) Dietary Supplement Subcommittee, is a member of the DoD Food and Nutrition Subcommittee, serves on the DoD Human Performance Optimization Committee, the VA/DoD Health Executive Committee Women's Health Work Group, the DoD Nutrition Committee, and the DoD Population Health Working Group. She also oversees the DoD Operational Supplement Safety (OPSS) program. She is a Fellow of the American College of Sports Medicine, a Certified Nutrition Specialist, and has over 200 peer-reviewed papers and numerous book chapters and books relating to human performance with a focus on health, nutrition, dietary supplements, and total force fitness. She has conducted research in the area of sports and warrior nutrition and performance for over 30 years. Visit the CHAMP Human Performance Resource Center (hprc-online.org) and Operation Supplement Safety (OPSS.org) websites. Dr. Deuster is a member of the Order of Military Medical Merit and received the Special Operations Medical Researcher Award from the Special Operations Medical Association in 2014.

She was the author of the first U.S. Navy SEAL Nutrition Guide sponsored by U.S. Special Operations Command and, because of its success, was commissioned to update the nutrition guide for the United States Special Operations Commands (USSOCOM). Dr. Deuster has been a tennis professional, nationally ranked marathoner, qualifier for the First Women's Olympic Marathon Trials, triathlete, skydiver with over 100 jumps, and world-wide scuba diver.



Efforts in DOD to Promote Safe Dietary Supplements

Deuster PA and Lindsey AT

Consortium for Health and Military Performance, Department of Military and Emergency Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD 20814

Service members (SM) want to gain an edge to be stronger, bigger, and faster than their adversaries. Dietary and herbal supplements are a route many take. Some of these products are of concern, and marketed directly to the military. Operation Supplement Safety (OPSS), the Department of Defense's go-to program for information about dietary and herbal supplements, receives questions about products daily, analyzes questionable products, provides evidence-based information, works with providers on reporting adverse events, and tries to keep up with what industry will do next.

Questions submitted by Service Members and providers ask about dietary and herbal ingredients, whether products will cause a positive drug test, and if products are safe to take. Products analyzed have been found to contain illegal steroids, unapproved amines, Phenibut, multiple types of nootropics (e.g. racetams), sulbutiamine, DMAA, Rauwolscine, and many more. Adverse events have ranged from exertional heat injury to hepatic injury and cardiac arrest. These activities have led to great collaborations with other federal agencies, universities, the US Anti-Doping Agency, and the Drug-Induced Liver Injury Network. Maintaining awareness and active partnerships are needed to keep our Service Members safe from potentially problematic products.

We acknowledge the US Anti-Doping Agency, the Sports Medicine Research and Testing Laboratory, the National Center for Natural Products Research, our Operation Supplement Safety Staff, and our Federal partners.



Ethan Russo, Director of Research and Development, International Cannabis and Cannabinoids Institute

Ethan Russo, MD, is a board-certified neurologist, psychopharmacology researcher, and Director of Research and Development of the International Cannabis and Cannabinoids Institute (ICCI).

Previously, from 2015-2017, he was Medical Director of PHYTECS, a biotechnology company researching and developing innovative approaches targeting the human endocannabinoid system (ECS). From 2003-2014, he served as Senior Medical Advisor, medical monitor and study physician to GW Pharmaceuticals for numerous Phase I-III clinical trials of Sativex® for alleviation of cancer pain unresponsive to optimized opioid treatment and initial studies of Epidiolex® for intractable epilepsy.

He graduated from the University of Pennsylvania (Psychology), and the University of Massachusetts Medical School, before residencies in Pediatrics in Phoenix, Arizona and in Child and Adult Neurology at the University of Washington in Seattle. He was a clinical neurologist in Missoula, Montana for 20 years.

He has held faculty appointments in Pharmaceutical Sciences at the University of Montana, in Medicine at the University of Washington, and as visiting professor, Harvard University, Johns Hopkins University, and the Chinese Academy of Sciences.

He is a former president of the International Cannabinoid Research Society and former Chairman of the International Association for Cannabinoid Medicines. He serves on the Scientific Advisory Board for the American Botanical Council. He is author/editor of seven books on cannabis and medicinal herbs, and has also published numerous book chapters, and over fifty articles in neurology, pain management, cannabis, and ethnobotany. He has consulted or lectured on these topics in 38 states and Canadian provinces and 34 countries.



History of Cannabis as Medicine: Correlations to Modern Research

Russo EB

Director of Research and Development, International Cannabis and Cannabinoids Institute (ICCI), Prague, Czechia.

Cannabis sativa L. is one of the oldest plants cultivated by man, but one of the most controversial. Whether it is truly a pariah or panacea, this versatile botanical medicine has provided many new insights into human pathophysiology and pointed the way toward novel approaches to intractable medical conditions including chronic pain, spasticity, obesity, epilepsy, and cancer among others through the discovery of its unique biochemical attributes, entourage effects, and leverage of the endocannabinoid system wherein many of its components operate. This presentation will survey the history of cannabis, and its formulations highlighting how ancient and 19th century claims of its therapeutic benefits have been borne out by modern basic science and clinical trials. We will examine first mentions from Old World cultures and their pertinence for contemporary scientific investigation. Cannabis historians of the past have provided promising clues to potential treatments for a wide array of currently puzzling medical syndromes that still confound 21st century physicians and their patients.



Eric Marsh, Associate Professor, Children's Hospital of Philadelphia

Institution	Degree	Year
Haverford College	BS	01/1991
New York University	MS	05/1995
NYU School of Medicine	MD	01/1997
New York University	PHD	01/1998
New York University	NIH training grant	06/1996

Positions and Employment

- 2004 - 2005 Clinical Affiliate, Children's Hospital of Philadelphia
- 2005 - Attending Neurologist, Children's Hospital of Philadelphia
- 2009 - Assistant Professor of Neurology, Children's Hospital of Philadelphia
- 2009 - Assistant Professor of Pediatrics (Secondary), Perelman School of Medicine at University of Pennsylvania

Other Experience and Professional Memberships

- 2000 - Member, American Academy of Neurology
- 2000 - Member, Child Neurology Society
- 2003 - Member, American Epilepsy Society
- 2003 - 2012 Member, Philadelphia Medical Society
- 2003 - 2012 Member, Philadelphia County Medical Society
- 2007 - Member, Society for Neuroscience

Honors

- 1996 Graduate Student Award, Annual Neural Control of Movement Meeting
- 2000 Resident of Year Award, NYU Dept. of Pediatrics
- 2002 TOPs Scholar, Child Neurology Society
- 2004 Alavi-Dabiri Postdoctoral Fellowship Award, Children's Hospital of Philadelphia
- 2004 Merritt Putnam Award, Epilepsy Foundation Research and Clinical Training Grant
- 2005 Early Career Investigator Award, American Epilepsy Society/Milken Family Foundation
- 2007 Young Investigator Award, MDDRC, Children's Hospital of Philadelphia
- 2014 Leonard Berwick Teaching Award, Perelman School of Medicine at the University of Pennsylvania



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Clinical and Preclinical Data for Cannabidiol in Epilepsy: Real Signal Through the Noise



Larry Walker, Emeritus Director, University of Mississippi

Larry A. Walker, PhD is Emeritus Director of the National Center for Natural Products Research (NCNPR), and Professor in the Department of Pharmacology at the University of Mississippi. A native of Martin, Tennessee, his undergraduate pharmacy degree is from Mercer University (1975), and his doctorate in Pharmacology from Vanderbilt University School of Medicine in 1979, with emphasis in the areas of renal and cardiovascular pharmacology. He spent periods in postdoctoral research at the Bosch Institute for Clinical Pharmacology in Stuttgart, Germany and in the Department of Physiology at Dartmouth Medical School. He joined the faculty at the University of Mississippi as a Research Assistant Professor in 1981, and has worked for much of his career on research related to the pharmacology of natural products. In 1992, Dr. Walker assumed the role of Program Coordinator of the Drug Discovery and Development Program of the Research Institute of Pharmaceutical Sciences at the University of Mississippi. In 1995 was named Associate Director of the NCNPR. In 2001, he was named Interim Director, and selected as Director in 2002. The NCNPR has currently 85 full-time researchers in the natural products field, with programs in drug discovery, and in the chemistry and pharmacology of medicinal plants. In 2010, he also was appointed as Associate Director for Basic Science Research, Oxford campus, for the University of Mississippi Medical Center Cancer Institute.

Dr. Walker is a co-author of more than 150 papers in peer-reviewed journals in pharmacology, toxicology, and natural products discovery. He is a member of the American Society of Pharmacognosy, American Society of Pharmacology and Experimental Therapeutics, American Society of Microbiology, American Society of Tropical Medicine and Hygiene, American Association of Pharmaceutical Scientists, and the Society for Biomolecular Screening. He served as Editor-in-Chief of the Journal of Biomolecular Screening, and on the editorial boards of Phytotherapy Research and the J. of Pharmacology and Experimental Therapeutics, and sits on numerous grant review panels for the NIH and Dept. of Defense. In 2003 he received the UM School of Pharmacy's Researcher of the Year award, and in 2009 the University's Distinguished Research and Creative Achievement Award.



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**States' Initiatives on Cannabis-Derived Products in the Treatment of Resistant Childhood
Epilepsy: Challenges and Updates.**



Adam Kuszak, Health Policy Analyst, Office of Dietary Supplements/National Institutes of Health

Adam J. Kuszak is an analyst in the National Institutes of Health (NIH) Office of Dietary Supplements (ODS), and Assistant Director of the ODS Analytical Methods and Reference Materials Program. Dr. Kuszak works with 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, he works with ODS staff on several initiatives including the Dietary Supplement Label Database and the development of ODS dietary supplement Fact Sheets for health professionals. Dr. Kuszak's primary research interests are in the chemical and biological characterization of complex natural products and understanding their effects on cellular signaling networks.

Adam J. Kuszak earned his B.S. in the Pharmacology-Toxicology Program at the University of Wisconsin – Madison, and his Ph.D. from the Department of Pharmacology at the University of Michigan Medical School. Dr. Kuszak completed his postdoctoral training at the National Institute of Diabetes and Digestive and Kidney Diseases, and first joined the ODS as an American Association for the Advancement of Science (AAAS) Science & Technology Policy Fellow in 2014.



The NIH ODS Analytical Methods and Reference Materials Program: Recent Activities and The Road Ahead

Kuszak AJ¹ and Betz JM¹

¹Office of Dietary Supplements, National Institutes of Health, Bethesda, MD, USA

The NIH Office of Dietary Supplements (ODS) Analytical Methods and Reference Materials (AMRM) Program supports the development of tools that permit the verification of dietary ingredient identity and the measurement of constituents and contaminants in botanical raw materials and finished dietary supplement products. AMRM goals are accomplished through funding and collaborative activities with dietary supplement stakeholders across academic research institutions, manufacturers and industry trade groups, third-party testing and standard-setting groups, and Federal agency communities. AMRM funds the National Institute of Standards and Technology (NIST) to produce Standard Reference Materials® (SRM), and to administer Quality Assurance Programs (QAP) which help laboratories improve through the assessment of method performance and identification of sources of measurement bias. AMRM supports analytical method development and validation by funding NIH grants and research at the U.S. Department of Agriculture, as well as through a Stakeholder Panel on Dietary Supplements convened by AOAC International. AMRM accomplishments include 12 funded NIH grants, over 170 peer-review publications, 19 AOAC Methods of Analysis, 30 SRMs, and 26 QAP exercises. The AMRM Program underwent its third External Expert Review in August 2017, and this presentation will outline how ODS is looking to further prioritize reference material development and dissemination, and increase educational outreach for the dietary supplement and botanical research communities.



Paula Brown, Director of Applied Research, Natural Health & Food Products, British Columbia Institute of Tech

Canada Research Chair, Phytoanalytics

Adjunct Professor, Department of Chemistry, University of British Columbia

Adjunct Professor, Gosling Research Institute for Plant Preservation, University of Guelph

Director of Applied Research, BC Institute of Technology (BCIT)

Burnaby, British Columbia, Canada

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Paula has supported the natural health & food product industry for close to two decades by conducting applied research at BCIT on product quality, safety and efficacy. Supported by grant funding and Industry contracts BCIT has engaged in projects focused on health policy, regulatory affairs, product formulation, botanical authentication, analytical method development and validation, chemometrics and therapeutic monitoring for preclinical and clinical studies. Dr. Brown was appointed Fellow of the AOAC in 2009 after serving 5 years as General Referee and 6 years on the Dietary Supplement Task Force. She has served on 14 AOAC Expert Review Panels, directed 4 collaborative studies on botanicals, published numerous validation studies, and taught method development and validation workshops for Health Canada, the American Society for Pharmacognosy, the United States Pharmacopoeia, and the NHP Research Society of Canada. In 2009, she was appointed to the American Botanical Council Advisory Committee, the inaugural Natural Health Products Program Advisory Committee for Health Canada, and became Chair of NSF's Joint Committee for Dietary Supplements. In 2017, she joined the USP Expert Committee for Botanical Dietary Supplements and Traditional Medicines and the American Herbal Pharmacopoeia Advisory Board. She is currently the President of the NHP Research Society of Canada, Dietary Supplement & Traditional Medicine Section Editor for Journal of the AOAC International, and holds the Canada Research Chair for Phytoanalytics.



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The Critical Role of Reference Materials in Metabolomic Approaches to Natural Products Research



Nadja Cech, Associate Professor, University of North Carolina Greensboro

Dr. Nadja Cech is Patricia A. Sullivan Distinguished Professor of Chemistry at the University of North Carolina, Greensboro (UNCG). Her PhD training is in mass spectrometry, and for the last 16 years, she has applied this expertise to solve challenging problems in natural products research, largely supported with funding from the National Institutes of Health (National Center for Complementary and Integrative Health, NCCIH). Work in the Cech group centers around the development of strategies to address synergy and complexity in the biological activity of botanical extracts. Dr. Cech's interests in this area stem from a long history of involvement in alternative medicine; her family owns and operates one of the largest medicinal herb seed companies in the country, and she spent her childhood working on their farm. Dr. Cech supervises a research group of sixteen students and postdoctoral research associates. She is the recipient of the 2011 Jack L. Beal Award for Best Paper in the Journal of Natural Products by a Young Investigator, and the 2017 Thomas Norwood Award for Undergraduate Research Mentorship. Dr. Cech a member of the research team for the NCCIH-funded Center of Excellence for Natural Product Drug Interaction, and Co-Director of the Medicinal Chemistry Collaborative (<https://mcsquared.uncg.edu/>).



Untargeted Metabolomics for Selection of Botanical Natural Products Prior to Clinical Evaluation: the Role of Reference Materials

Cech, N. B., Kellogg, J. J., Caesar, L. K., Britton, E. R.

University of North Carolina at Greensboro, Department of Chemistry and Biochemistry

Countless studies have been devoted to the scientific evaluation of the safety and/or efficacy of botanical natural products. Investigators involved in such studies face a unique set of challenges. Natural products differ from their pharmaceutical counterparts in that they are typically complex mixtures, for which the identities and quantities of components present are not known. To further complicate matters, the composition of these mixtures will vary depending on source material and method of preparation, and mislabelling or intentional adulteration occurs in commercial products. Investigators evaluating biological activity of complex botanical natural products must choose from a myriad of potential preparations, which may vary greatly in composition. Our research group has developed untargeted mass spectrometry metabolomics approaches to compare similarity among commercial botanical natural products, and to identify putative active constituents of complex mixtures. These strategies involve profiling botanical mixtures using ultraperformance chromatography coupled to high resolving power mass spectrometry. The resulting chemical data is then integrated with biological assay data using biochemometric data analysis strategies. Several case studies will be presented illustrating how this approach can be applied, including for the identification of compounds from the botanical green (*Camellia sinensis*) that inhibit drug metabolizing enzymes. For these investigations, it has been particularly helpful to utilize reference materials from the National Institute of Standards and Technology.

These studies were conducted with support from the Center for Excellence in Natural Product Drug Interaction Studies (NaPDI), which is funded by a cooperative agreement with the National Center for Complementary and Integrative Health (NCCIH), a component of the National Institutes of Health (U54 AT008909) and by R01 AT006860, also from NCCIH.



Rahul Pawar, Research Chemist, Office of Regulatory Science/DBC/BMB FDA/Center for Food Safety and Applied Nutrition

Dr. Rahul Pawar was awarded a PhD. in Natural Products from the National Institute of Pharmaceutical Education and Research (NIPER), India in 2003. He pursued postdoctoral research at the National Center for Natural Products Research (NCNPR) at the University of Mississippi from 2003-2007. He is currently working at CFSAN /FDA and serves as the Office of Regulatory Science's Research Coordinator for dietary supplements. His research focuses on development of analytical methods for determination of dietary supplement quality.



Sensitive and Rapid Quantitation of Three Ginkgolic Acids in Dietary Supplements of Ginkgo

Jing Li and Rahul S. Pawar

Office of Regulatory Science, Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration, 5001 Campus Drive, College Park, MD 20740, USA

Ginkgo biloba-containing products are among the top-selling dietary supplements in Europe and the United States. Ginkgolic acids (GAs) from *G. biloba* leaf are potentially hazardous constituents due to their allergenic and carcinogenic properties. The United States and European Pharmacopeias have adopted an acceptable concentration of GAs of 5 µg/g in dried extracts of *G. biloba* leaves.

The study was conducted to optimize the extraction method for GAs and to develop a rapid and simple high performance liquid chromatography-diode array detection (HPLC/DAD) method for the determination of GAs in ginkgo-containing dietary supplements. We compared the extraction efficiency of GAs using a conventional methanol extraction and a QuEChERS (Quick Easy Cheap Effective Rugged and Safe) procedure. HPLC/DAD detection was used to quantitate three major GAs (i.e., GA13:0, 15:1, and 17:1) in extracts of ginkgo-containing dietary supplements. We determined that the QuEChERS method efficiently extracted GAs from ginkgo-containing dietary supplements. Extraction yields were three times higher than those resulting from use of conventional methanol extraction. The use of a Kinetex Biphenyl column with a gradient mobile phase of acetonitrile and water, both containing 0.1% formic acid, provided adequate chromatographic separation. The HPLC/DAD method was validated and found to be applicable for the routine analysis of GAs in Ginkgo-containing dietary supplements. Eighteen (18) of the 30 products analyzed contained more than 5 µg/g of total GAs.



Catherine Rimmer, Research Chemist, National Institute of Standards and Technology

Catherine Rimmer received her Ph.D. in analytical chemistry from Florida State University and completed a National Research Council postdoctoral fellowship at the National Institute of Standards and Technology (NIST). In addition to co-coordinating a dietary supplement quality assurance program she is the program coordinator for dietary supplement reference materials at NIST. Her specific interests are related to natural products analysis, authentication of natural products, and the use of liquid chromatography and mass spectrometry for complex matrices.



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**ODS/NIST Certified Reference Materials and Quality Assurance Programs for the Botanical
and Natural Products Communities**



Holly Johnson, Chief Science Officer, American Herbal Products Association AHPA

Holly E. Johnson Ph.D., is the Chief Science Officer for the American Herbal Products Association (AHPA). She previously served for three years as Laboratory Director for Alkemist Labs, an ISO 17025 accredited natural products testing lab specializing in botanical dietary supplements. Dr. Johnson took her Ph.D. in Pharmacognosy at the College of Pharmacy, University of Illinois – Chicago (UIC), under renowned Pharmacognosist and researcher Dr. Norman Farnsworth. Holly was awarded a National Institutes for Health (NIH) Fellowship and trained at the UIC/NIH Center for Botanical Dietary Supplements. She was a Postdoctoral Research Fellow at the Institute for EthnoMedicine studying the etiology of neurodegenerative disease, and also worked for Waters Corporation conducting technical training and regulatory consulting for pharmaceutical and supplements companies. She is currently a Research Associate with the National Tropical Botanical Garden and serves on AOAC working groups, stakeholders panels and expert review panels for Foods and Dietary Supplements. She is a member of the United States Pharmacopeia's (USP) Medical Cannabis Expert Panel, the Editorial Board of the Journal of AOAC International, and she serves on the Advisory Boards of the American Botanical Council and the American Herbal Pharmacopeia. Holly has over 20 years experience working with natural products & botanicals and spent many happy years conducting research on medicinal plants and giving courses at the University of Hawaii.



Reference Materials for Botanical Authentication

Holly E. Johnson, Ph.D.
Chief Science Officer
American Herbal Products Association

With the current trend in globalization of the botanical supply chain, brand holders and manufacturers are increasingly trading in powdered and/or extracted dietary ingredients, as opposed to purchasing more morphologically intact plant materials. Vertical integration and cultivating robust relationships with farmers are practices established by some companies, but are not the current norm in the industry. This situation has highlighted the need for more scientifically valid fit for purpose methods for botanical identity that are appropriate for the myriad materials in commerce. Botanical reference materials play a key role in development and validation of such methods; challenges will be discussed.



Uma Sreenivasan, Head of Reference Materials R&D, Cerillant Millipore Sigma

Uma Sreenivasan is Head of R&D for Cerillant™ Reference Materials in MilliporeSigma. She leads a team responsible for product development and certification of small and large molecule reference standards for clinical, forensic, dietary, and pharmaceutical applications. Ms. Sreenivasan has extensive experience in bio-organic, synthetic and analytical chemistry, operations, and management. Since 2000, she has served in various roles as Manager of Synthesis Operations, Analytical Laboratory Manager, and Chief Science Advisor overseeing technical issues relating to Cerillant products. In 2013, as VP Production & R&D she had oversight of manufacturing and development operations. The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.



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**Reference Materials, Primary Standards, and Compendial Standards: When and How Each
Are Used in Quality Control and Basic Research**



Cynthia Rider, Toxicologist, National Toxicology Program/National Institute of Environmental Health Sciences

Cynthia Rider, PhD, DABT is a toxicologist with the National Toxicology Program (NTP), National Institute of Environmental Health Sciences (NIEHS), where she serves as project leader for a diverse portfolio of testing programs including polycyclic aromatic compounds, botanical dietary supplements (e.g., *Ginkgo biloba* extract, *Garcinia cambogia*), and industrial chemicals. In this capacity, she leads multi-disciplinary study design teams in developing research programs to address critical data gaps and inform risk assessment. Dr. Rider's research interests are in evaluating and refining methods to predict mixture toxicity based on data from components or whole reference mixtures. She co-chairs the NIEHS Combined Exposure/Mixtures working group tasked with advancing mixtures research throughout the Institute. Dr. Rider received her B.S. from Tulane University and her Ph.D. from North Carolina State University in Environmental Toxicology (2005). She completed postdoctoral training in the Reproductive Toxicology Branch of the EPA and Duke University, Nicholas School of the Environment, and became a Diplomate of the American Board of Toxicology in 2011.



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Reference Materials as Research Reagents for “Biologic Similarity” Studies



Amit Chandra, Manager, Chromatography Sciences Group, Amway

Dr. Amit Chandra is the Distinguished Scientist and an R&D Manager at Dept of Analytical Sciences, Amway Corporation. He is a world class subject matter expert in the area of botanicals, dietary supplements, nutraceuticals and cosmeceuticals. Dr. Chandra is a phytochemist with a doctorate in Natural Products Chemistry. He has over 30 years of experience in academia and industry in this area. Amit's area of focus at Amway- Nutrilite is focused on discovery, development and support areas of health and beauty products (dietary supplements, food and beverage, cosmetics, skin and personal care). His research has gained him more than 80 publications / presentations in international peer reviewed journals and scientific societies worldwide and 18 patents in his career so far. He is very focused and active on the scientific areas that relate to deliver authentic, safe and efficacious botanicals as part of dietary supplements. Amit's passion is to evolve the traditional botanical medicine that has already proven to work based on folklore using current technology that addresses consistency in quality and authenticity. Dr. Chandra also participates and serves as an expert member in international scientific societies and organizations such as ACS (American Chemical Society), AOAC (International Association of Analytical Communities), ASP (American Society of Pharmacognosy), CRN (Council for Responsible Nutrition), ABC (American Botanical Council) and AHPA (American Herbal Products Association), NCNPR (National center for Natural Products Research) to name a few. He also performs peer reviews of scientific papers published in top rated natural products Journals such as Journal of Agriculture and Food Chemistry, Journal of Natural Products and Journal of Chromatography.



Botanical Integrity: Significance of Fit for Purpose Tests During Botanical Product Development Process

Chandra, A.

Department of Analytical Sciences; Amway R&D, Amway R&D , Ada, Michigan, USA

Presentation will focus on the concept and utility of the available analytical methods and their “fit for purpose” status for evaluating quality of botanical extracts. Examples will be cited for impact in botanical quality assessments by using fit for purpose methods and vice versa during QbD process. It will be emphasized that the evaluation / identity of botanical genus and species and botanical extracts are two different things and there is no one universal analytical test that can do it all. DNA bar coding could be an appropriate test for verifying genus and species in intact botanicals (aka botanical ID) while phytochemical fingerprinting should be the method of choice for evaluating identity and authenticity of processed botanical extracts. DNA barcoding cannot differentiate between plant part within the same species while phytochemical fingerprinting can. DNA barcoding is a generic test while phytochemical fingerprint is dependent of experimental conditions applied for specific botanicals as focuses on unique phytochemicals in that preparation (botanical extract). Phytochemical fingerprinting is recommended as a method for choice for tracking economically motivated adulteration in botanical extracts. Real time case studies will be shared on commercial economically motivated adulteration of botanical extracts (such as Ginkgo biloba leaf and Bilberry fruit extracts) using phytochemical fingerprint as “fit for purpose” method. Importance of working / partnering with industry and regulatory authorities by sharing results / findings, on an international platform and raising awareness via education will be emphasized as a good practice to stop botanical adulteration in the industry. General guidelines for designing experiments for studying economically motivated adulteration in botanicals (in general) with perspective on fit for purpose methods will also be discussed. Emphasis will be on creating and following QbD processes during product development.

Department of Analytical Sciences, Amway R&D



Tim Baker, Research Fellow, The Procter & Gamble Company

Tim Baker received a B.S. in Chemistry from Canisius College (Buffalo, NY) in 1979. After working several years at contract labs using GC-MS to quantitate environmental pollutants, he returned to school and obtained a Ph.D. in Analytical Chemistry (with Paul Vouros at Northeastern University, Boston, MA), specializing in mass spectrometry.

Tim joined Procter & Gamble's Health & Personal Care Technology Division at Miami Valley Laboratories, near Cincinnati Ohio, in 1990. After several years in that division, and then in the over-the-counter medicines business (Oral Care and Personal Health Care), he joined the pharmaceutical discovery effort in P&G Pharmaceuticals, in 1995. During over a decade working in P&GP, Tim acquired expertise supporting pharmacokinetic and *in vitro* studies using HPLC-MS/MS. He also supported metabolite identification studies and was an early practitioner of high resolution mass spectrometry for that and similar efforts.

With the formation of a corporate Analytical resource, Tim led the Quantitative HPLC-MS Lab, supporting all of P&G's businesses. In 2009 Tim formed the Qualitative MS Lab, and this group continues to support all of P&G with identifications of metabolites, biomarkers, impurities, degradation products, contaminants, adulterants, color bodies, malodor agents, oligomeric mixtures, raw materials and natural products. Tim's group has a great deal of experience characterizing complex mixtures using a variety of chromatographic approaches (UHPLC, SFC, GC, GCxGC) coupled with high resolution mass spectrometry.

Tim is currently a Research Fellow in Corporate Functions Analytical with nearly 200 internal and external publications and presentations. An avid skier, Tim has been married to Mary Lou for over 26 years, and they have three daughters (Kelsey, Rachel, and Sydney).



Analytical Characterization Platform for Chemical Constituents in Botanicals

Baker TR¹, Sica VS¹, Pulliam CJ¹, Britton ER², Price JM¹

¹The Procter & Gamble Company, Mason, OH 45040

²University of North Carolina at Greensboro, Greensboro, NC 27402

An approach for chemical constituent characterization and comparison has been developed and utilized for the analysis of numerous botanicals. The methodology utilizes chromatographic separation using UHPLC, followed by detection with three complementary detectors. Following separation of the botanical constituents, the eluents are first analyzed by a photo diode array UV detector. This provides information about analytes with chromophores and often allows comparison to vendor HPLC/UV data. Next the post-column eluent is split and analyzed by charged aerosol detection (CAD) and high-resolution mass spectrometry (HRMS). CAD is a universal detector that provides quantitative results, even in the absence of standards of the constituents. HRMS detection, in positive and negative ion mode and with MS/MS, allows identification of the chemical constituents. The experimental requirements, advantages and limitations of this approach will be explained. Experiments using this approach have been utilized to compile chemical constituent identification (CCID) data sets which enable in silico toxicological assessments of botanicals. These assessments eliminate or guide in vitro and in vivo safety studies. Additionally, this approach allows rapid comparison of similar materials for batch or vendor comparison. Furthermore, the approach has been customized to enable systematic comparison of botanical constituents as a function of different extraction solvents (aqueous, ethanolic and supercritical CO₂). Examples of these comparisons, from several different plants, will be shown.



Donna McMillan, Research Fellow, Central Product Safety, The Procter & Gamble Company

Donna McMillan has a BS in Microbiology with a minor in Chemistry from the University of Central Florida, an MS in Pharmacodynamics and Toxicology and PhD in Pharmaceutical Sciences, both from the University of Nebraska Medical Center, Omaha. She did postdoctoral research in the Department of Pharmacology & Toxicology, College of Pharmacy, University of Arizona, Tucson.

Donna originally joined Procter & Gamble's Health & Personal Care Product Development Division. In her time with P&G, she has provided human safety assessments for such diverse products as Peridex (a prescription mouthrinse), Scope, Crest dentifrice, Crest Whitestrips, the flavors used in P&G Health Care products and Gillette/The Art of Shaving products. Donna was a member of the P&G Corporate Institutional Review Board from 1999 to 2009 (when it was decommissioned). In 2007, Donna assumed leadership of the P&G Botanical/Natural Substance Human Safety Expert Team. Her current responsibilities also include human safety support for Hair Care Technology projects.

Donna is a Research Fellow in the Beauty Global Product Stewardship organization with numerous internal and external publications and presentations. Donna has been a Board-certified toxicologist (Diplomate, American Board of Toxicology) since 1990. She has been on the Board of Directors for the Lloyd Library in Cincinnati since 2011. Memberships to scientific organizations include the Society of Toxicology and the American Society of Pharmacognosy.



Large Scale Botanical and Phytochemical Data to Assist in Rapid Analysis for Safety Assessment

McMillan DA

The Procter & Gamble Company, Mason, OH 45040, USA

The presence of botanicals and other natural substances in consumer products has become an important consumer criterion for the purchase of many product categories. Botanicals are complex mixtures and classical toxicological data are often lacking. While some botanicals are used broadly by humans as food, flavors/spices, or medicines, other botanicals are known to cause various toxic effects. The combination of these uncertainties makes safety assessment for botanicals a challenging task.

The first example of using a large-scale data set for safety assessment is the development of a botanical TTC. The Threshold of Toxicologic Concern (TTC) is used to support the presence of single chemicals, without full toxicological characterization, when they are used at low exposure levels in consumer products. The first TTC exposure limit of 0.15µg/day (0.0025 µg/kg bw/day) was adjusted using the concentration data of over 50 genotoxic/DNA reactive and carcinogenic chemical constituents found in about 1000 plant species (over 2800 observations) to adjust the TTC for botanicals.

When botanical exposure from a consumer product is higher than the TTC and a history of safe human use cannot be established or published data on the botanical indicate the possibility of a safety issue, the next step is to request chemical constituent identification (CCID). The second example of managing a large-scale data set for safety assessment will be to describe the botanical safety assessment tool developed by P&G specifically to handle the hundreds of chemical constituents identified in the CCID analysis.



Suramya Waidyanatha, Discipline leader for chemistry, National Institute of Environmental Health Sciences, National Institute of Health

Suramya Waidyanatha, received her Ph. D. in 1991 in Analytical Chemistry at University of Maine, ME; her M.S. in 1987 in Biochemistry at University of Illinois at Chicago, Chicago, IL; her B. Sc. (Honors) in 1984 in Chemistry at University of Colombo, Sri Lanka.

2012-present-Discipline Leader for Chemistry, Division of the NTP, NIEHS, NIH, Research Triangle Park, NC; 2010-present-Group Leader, Chemistry & ADME Resources Group (CARG), Program Operations Branch, Division of the NTP, NIEHS, NIH; 2008-Present-Discipline Leader for ADME, Division of the NTP, NIEHS, NIH; 2008-Present-Project Officer/Contracting Officer's Technical Representative/Contracting Officer's Representative, Division of the NTP, NIEHS, NIH; 2008-present-Visiting Scholar, Department of Environmental Sciences & Engineering, Gillings School of Global Public Health, University of North Carolina at Chapel Hill

Professional Organizations: Society of Toxicology-American; Society for Mass Spectrometry; International Society for the Study of Xenobiotics; American Chemical Society-North Carolina; Section of the American Chemical Society; RTP Drug Metabolism Discussion Group.

NIEHS/NTP Activities:

- NTP Toxicokinetics Faculty Chair (2008-present)
- NTP Acquisition Plan Review Committee (2010-present)
- NTP Protocol Approval Committee (2010-Present)
- NTP Report on Carcinogens NIEHS Internal reviewer (2013-present)
- Women Scientist Advisor (2011-2013)
- NTP Report on Carcinogens NIEHS/NTP Scientific Review Group (NSRG) (2008-2012)
- NIEHS Strategic Planning/Exposome Faculty Member (2012-present)
- Tox 21 Chemical Selection Working Group
- Dietary Supplement Prioritization for Prevention of Toxic Compounds Working Group

Her NIEHS Honors and Awards:

- NIH Merit Award (2016) For exceptional work in support of the NTP mission, performed to an impressively high standard with unwavering collegiality.
- NIH Merit Award (2014) For sustained efforts to ensure continuous high-quality analytical chemistry support.
- NIH Director's Award (2014) In recognition of extraordinary vision, effort, creativity, and scientific leadership during the implementation of the Toxicology in the 21st Century (Tox21) Interagency effort.

Journal Reviewer: Chemical Research in Toxicology Chemico-Biological, Interactions Drug Metabolism and Disposition Journal of Chromatography, Toxicology and Applied Pharmacology, Toxicology Letters, & Xenobiotica



Naturally Complex: the National Toxicology Program Strategy for Phytochemical Characterization of Botanical Dietary Supplements for Use in Safety Assessment

Waidyanatha S, Mutlu E, Ryan K and Rider CV

Division of the National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA

Botanical dietary supplements (BDS) are complex mixtures containing one or more botanical ingredient(s). The National Toxicology Program (NTP) has been investigating the toxicity of BDS in rodent models following both short- and long-term exposure to generate data to evaluate safety/toxicity of these products. However, because of the variability and complexity of these products and the multitude of products in the marketplace, designing sound research approaches to generate high quality data for human safety assessment has been challenging. One of the key challenges includes selection of a representative lot and accurate identification and thorough characterization prior to use in testing. To date, there aren't any established strategies for selection of a representative lot, and often the data on phytochemical composition is inadequate. In addition, each BDS is unique, and in our experience, presents different challenges and decisions in the process leading to safety/toxicity assessment. To develop a potential strategy, case studies with *Echinacea purpurea* and black cohosh extracts will be presented. In each case, bulk lots from multiple vendors, along with vouchered reference material and finished products, were procured and analyzed using a combination of untargeted and targeted chemistry approaches and chemometric methods. This case study demonstrated that a combination of untargeted and targeted analytical chemistry approaches can be applied to determine the: 1) authenticity of lot 2) contaminants present 3) identification and/or quantitation of the known and unknown fraction, and 4) stability of active and/or marker compounds during storage and/or testing.



Stanislav Vukmanovic, MD, PhD

EDUCATION:

1984- M.D., Belgrade University School of Medicine

1991- PhD (Immunology) Belgrade University School of Medicine

TRAINING:

1988- 1990 Visiting fellow- Imperial Cancer Research Fund, Tumor Immunology Unit, University College London, London, UK

1991- 1993 Senior Research Associate- Howard Hughes Medical Institute, Department of Immunology, U. of Washington, Seattle, WA

PROFESSIONAL EXPERIENCE:

- 2015 (July)-pres. General Health Scientist (July 2015-September 2016), Acting Team Lead (September 2016- January 2017), and Team Lead (January 2017-present), Division of Cosmetics, Office of Cosmetics and Colors, CFSAN, FDA, College Park, MD.
- 2015 (March-July) Scientific Review Officer, National Cancer Institute, NIH, Bethesda, MD.
- 2003-2014 Senior Investigator (tenure), Children's Research Institute, Children's National Medical Center, Washington, DC.
Center for Cancer and Immunology Research, (2003-2010) and Sheikh Zayed Institute for Pediatric Surgical Innovation (2010-2014)
Academic Appointment: Associate Professor (2003-2006) and Full Professor (2006-2014), Departments of Pediatrics and Microbiology, Immunology and Tropical Medicine, George Washington University School of Medicine.
- 1993-2003 Assistant (1993-2000) and Associate (2000-2003) Professor (tenured in 2003), Division of Immunology, Department of Pathology, NYU School of Medicine, New York, NY.
- 1988-1992 Assistant Professor, Institute of Microbiology and Immunology, Belgrade University School of Medicine.

PUBLICATIONS:

Total 84 (72 listed in PubMed).

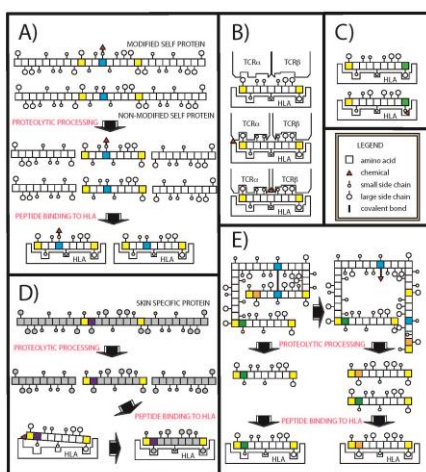
Hapten-Independent Mechanisms of Skin Sensitization

Vukmanovic S¹, Schutte R², Zhang X², An N¹ & Ostrov D²

¹ Division of Cosmetics, Office of Cosmetics and Colors, CFSAN, FDA, College Park, MD

² Department of Pathology, Immunology and Laboratory Medicine, University of Florida College of Medicine, Gainesville, FL

There is a considerable interest in development of alternative (in vitro, in chemico and in silico) testing for skin sensitization. These methods are based on the Adverse Outcome Pathway (AOP) of skin sensitization published by the Organisation for Economic Co-operation and Development in 2012. The AOP lists haptenation (covalent modification) of epidermal proteins and immune response to modified self-proteins as the mechanism leading to skin sensitization. However, results of existing alternative methods do not match the in vivo sensitization potential for about 20% of tested chemicals, suggesting that additional mechanisms of skin sensitization may exist. We will review existing evidence for these hapten-independent mechanisms of skin sensitization. Novel alternative assays based on hapten-independent mechanisms of skin sensitization need to be designed, to increase the predictive power of alternative testing for assessment of skin sensitization potential.





Linda J. Loretz, Ph.D., DABT, is currently Director, Safety and Regulatory Toxicology at the Personal Care Products Council. In this position, she is responsible for safety and toxicology issues related to cosmetic ingredients and products, which includes preparation and review of safety assessments; coordination and monitoring of toxicology studies; preparation of comments to regulatory agencies on issues of concern to the industry; and communication of safety developments relevant to the industry. She has worked at the Council (formerly the Cosmetic, Toiletry, and Fragrance Association) since 1997.

Prior to joining the Council, Dr. Loretz worked at the Pillsbury Company where she was responsible for toxicology and regulatory issues related to food products, including ingredient safety and labeling, chemical residue/contaminant issues, and management of food allergens. She has also worked for the Monsanto Company, developing toxicological databases for pesticide safety assessments and registration.

Dr. Loretz received her B.S. in Biochemistry from the University of California-Davis, and a Ph.D. in Toxicology from the University of Wisconsin-Madison, where she was a National Science Foundation Fellow. She is a Diplomate of the American Board of Toxicology and a member of the Society of Toxicology, and has authored numerous journal articles and other scientific publications.



A Decision Tree Approach to Assess the Safety of Botanicals in Cosmetics

Loretz L, Personal Care Products Council, Washington DC, 20036

Botanical ingredients are widely used in cosmetics. These include extracts, hydrolysates, juices, powders, resins, saps, and seedcakes. While the concentrations used are generally low, the complexity and variability of these mixtures can make their safety assessment challenging. To address this issue, a decision tree for the safety assessment of botanical cosmetic ingredients was developed by cosmetic industry scientists as a guidance tool for finished product manufacturers. The decision tree is a set of scientific recommendations for gathering data and information. The approach takes into account how cosmetic exposure compares to exposure from traditional uses; chemical characterization; available safety data; and local (dermal) tolerance. The guidance tool is intended to provide a flexible approach given the wide variety of botanical ingredients that may be used. The components of the decision tree for use in cosmetic safety assessment will be described.

The Cosmetic Ingredient Review (CIR) Science and Support Committee of the Personal Care Products Council

Dr. Thomas Re, L'Oreal USA (retired)



Cristina Avonto, Ph. D., Research Scientist, National Center for Natural Products Research

Dr. Avonto joined Dr. Ikhlas Khan's research team as a natural products chemist in 2011. Her current work is focused on the safety of natural products and botanicals in cosmetics and dietary supplements, with a special emphasis on development and application of non-animal methods for skin sensitization risk assessment. As part of her research at the National Center for Natural Products Research, she was involved in the *ex-novo* development of two *in chemico* methods to identify and characterize electrophilic compounds as potential skin sensitizers. Her professional experience also includes the isolation and characterization of secondary metabolites from plant sources, as well as authentication and analytical profiling of plant extracts, cosmetic preparations and dietary supplements.

Dr. Avonto received her Ph. D. in Science of Bioactive Substances in 2010 from the University of Eastern Piedmont "Amedeo Avogadro" (Italy), where she worked on the isolation and chemical derivatization of natural products targeting chemo-sensorial receptors of biomedical relevance. She focused on the importance of electrophilicity in targeting nociceptors of biomedical importance (such as TRPA1) and on the development of an NMR method to identify reversible Michael acceptors as potential anticancer agents. She also worked on the synthesis of triterpene derivatives as antidiabetogenic compounds.

She received her Master of Science in Industrial Biotechnology in 2007 from the University of Milano-Bicocca (Italy) and her Bachelor of Science in 2004 from the University of Eastern Piedmont "Amedeo Avogadro", where she worked in the isolation of potential anti-malarial compounds from *Mirtus communis*.

Dr. Avonto has one patent pending and published over 20 research papers and over 30 poster presentations. She is a member of the Society of Toxicology and American Chemical Society, and served as reviewer for several international scientific journals.



Chemical Stability and Skin Sensitization Potential Of 24 Fragrance Ingredients

Cristina Avonto,¹ Amar G. Chittiboyina,¹ Mei Wang,¹ Stanislav Vukmanovic² and Ikhlas A. Khan^{1,2}

¹National Center for Natural Products Research; ²Division of Pharmacognosy, Department of BioMolecular Sciences; School of Pharmacy, University of Mississippi, University, MS 38677, USA.

Contact with fragrance ingredients is one of the most common causes of adverse reactions such as allergic contact dermatitis (ACD). Due to their widespread use in cosmetic, toiletry and personal care products, avoiding exposure to fragrance ingredients is almost impossible. In such scenarios, identification of the source of a particular hazard can sometimes be a daunting task as some compounds are ubiquitously present in a plethora of products, typically as complex mixtures/formulations. Based on large population epidemiological data, 24 pure fragrance ingredients and 2 natural extracts have been identified as frequently recognized allergens.

Skin sensitizers are usually electrophilic in nature and capable of covalently binding to skin proteins. Non-animal methods, such as *in chemico* methods, can provide a useful tool to predict the ability of skin allergens to bind to biological nucleophiles.

Interestingly, 13 of the 24 compounds identified as being the most recurrent fragrance allergens do not contain potentially reactive mechanistic domains. It has been hypothesized that some form of chemical or biological activation may be involved in the generation of the reactive compound(s) causing ACD adverse reactions.

The high throughput screening based on dansyl cysteamine (HTS-DCYA) method was here applied to the investigation of chemical reactivity of the 24 pure fragrance ingredients. The 24 chemicals were then subjected to forced degradation studies and changes in chemical reactivity upon degradation were studied. The details on applicability of alternative *in-chemico* methods for assessing the sensitization potential of pre/pro-haptens, stability and reactivity will be presented.



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Cosmetic Applications of African Seed Oils: Clinical Observations

Komane B¹, Alvaro Viljoen A ¹⁻², Ilze Vermaak I ¹⁻² & Summers B ³

¹Department of Pharmaceutical Sciences, Tshwane University of Technology, Private Bag X680, Pretoria 0001, South Africa, ²SAMRC Herbal Drugs Research Unit, Faculty of Science, Tshwane University of Technology, Private Bag X680, Pretoria 0001, South Africa. ³Photobiology Laboratory, School of Pharmacy, Sefako Makgatho Health Sciences University, P.O. Box 218, MEDUNSA, 0204, South Africa.

African seed oils such as *Sclerocarya birrea* (Marula), *Adansonia digitata* (Baobab) and *Citrullus lanatus* (Kalahari melon) are popularly included in commercially available cosmetic products based on traditional uses. However, the cosmetic value claims of these oils have not been substantiated through scientific studies. The fatty acid content of seed oils are of significant value in cosmetic product formulations and are considered the most important quality parameter. In this study, chemical profile of fatty acids present in the seed oils was conducted using comprehensive two dimensional analysis (GCxGC-MS). A clinical study to validate claims of beneficence of these oils was piloted on twenty Caucasian female participants ($n=20$). An irritancy patch test was conducted using Marula, Baobab and Kalahari melon. De-ionised water and 1% sodium lauryl sulphate were used as negative and positive controls respectively. Corneometer® and Aquaflux® were used as measuring instruments for moisture retention and moisture loss respectively. Two dimensional gas chromatograph results indicated that eighteen fatty acids were detected in Marula oil with oleic acid identified as the major fatty acid (19.8-89.1%) while in Baobab oil twenty-four fatty acids were detected with linoleic (28.0-55.6%) and oleic acid (14.0-39.6%) as principal fatty acids. Kalahari melon oil major fatty acid was linoleic acid ranging from 71.2-72.5 %. The clinical results revealed that Marula, Baobab and Kalahari melon oils are non-irritant ($p<0.001$), with hydrating properties ($p<0.001$) when applied to a lipid-dry (xerosis) skin and moisturising ($p<0.001$) when applied to normal skin. These findings may be linked to the easy absorption of the oils into the skin due to the presence of oleic acid which is regularly included in cosmetic products and pharmaceutical formulations as an excipient for trans-dermal application as well as linoleic acid known to be an effective alternative treatment for atopic eczema due to its anti-inflammatory activity. It can be concluded that African seed oils (Marula, Baobab and Kalahari melon) used in cosmetic products may be beneficial to the skin due to their non-irritating, soothing, hydrating and moisturising properties with moderate prevention of trans-epidermal waterloss which may alleviate premature-aging.

Prof. A.M. Viljoen, Dr. I. Vermaak, and Prof. B Summers

Faculty Science: Department of Pharmaceutical Science



Jinghui Wang, Chief Pharmacist, Beijing Institute of Drug Control

Jinghui Wang, Chief Pharmacist of Beijing institute of drug control, now is working at ChP-Waters Joint Open Lab. She was devoting herself in TCM standard related work such as drug control, new drug approval, drug standard studies. She has participated in several national and regional TCM research program including National Programs for Science and Technology Development, National Science and Technology Major Project for "Major New Drugs Innovation and Development" etc. In past years, she has drafted over 33 TCM standards, 10 of which were included in Chinese Pharmacopeia or approved by SFDA. Until now, she has published over 40 papers, 4 patents, and awarded the Beijing Scientific and Technological Advancement Prize 5 times. Especially, as project leader, she participated in the standard research program of ginkgo leave product, drafted the fingerprint standard of ginkgo leave extracts, and promoted the standard to be international advanced.



Fingerprint Study in TCM Quality Control on Scientific and Regulatory Basis

Wang, Jinghui,

Beijing Institute Of Drug Control

Fingerprint was firstly used in the quality control of TCM injections in 2002. It has been used to evaluate the quality equivalency of chemical components in TCM material or products via chromatography or spectrum analysis. Fingerprint reflects both the chemical feature in its entirety and the variation of every chemical component, and it can be used for identification and quantification of multiple components simultaneously. Therefore, Fingerprint is perfect match the idea of “holism” in traditional Chinese medicine theory, and is suitable to systematical control the quality of TCM in its entirety.

This Report demonstrated how to produce a usable Fingerprint on the basis of extensive research. Especially, it illustrated how to identify the chemical components and how to establish the fingerprint method.



Binbin Song, Technology Consultant, Chinese Pharmacopoeia

Song Binbin, Female, Master of Pharmacy, after graduating from Shenyang Pharmaceutical University, experienced in lab management, drug analysis and data integrity etc through working in research institutions and chemical analysis laboratories, Song Binbin joined in the Chinese Pharmacopoeia-Water Joint Open Laboratory as technology consultant in 2015, in this role, She participate in many projects for quality standard research such as antimicrobial content in eye drops, and participated in the drafting Guideline of "different particle size column method" conversion in <China Pharmacopoeia Analysis and Testing technology Guide> , which have published as Guideline for industry.



Build Up Effective Quality Control of Herbal Medicine Through Improving Fingerprint Similarity Evaluation System -- Fingerprint Similarity Evaluation System Development and Design for Improvement

Song, Binbin

Chinese Pharmacopoeia, Beijing, China

"Fingerprint similarity evaluation system" can comprehensively reflect the feature of the synergy of multiple – components, as well as chemical characteristics, components distribution in TCM, which is an effective quality control method to ensure the consistency of Chinese medicine products. This system is based on the idea of Chinese medicine, and connects to thoughts of quality control, component analysis, mathematical model, chemometrics and software, it helps to establish a reasonable similarity value in fingerprint development and evaluate the similarity level compare with the standard spectrum.

The Improvements of this system are mainly including: combine with the latest analysis, detection technology as well as data management requirements, make it more universal, practicable and compatible; strengthen identification ability, for the specific chromatographic peaks, add weights to make the similarity more scientific; establish new function of multidimensional fingerprint, as well as spectral matching; build up the library of fingerprint and develop the English version of system and so on.

In the future, Internet technology can be jointed, hope it can turn into an internationalized quality evaluation system genuinely.



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Development and Quality Control of Ultrafine Granular Power of TCM

Cheng, Jinle

Guangzhou University of Chinese Medicine, Guangzhou City, Guangdong Province, People's Republic of China

“Inheriting” and “innovating” are the key issues to the modernization of TCM prepared slices. The lecture will focus on the recent development of TCM prepared slices including: chemical component research, key problems in modernization, cutting-edge of modern research. The speech will also discuss the concept of Ultrafine Granular Power of Herbal, the major improvements it has been made for the modernization of TCM prepared slices, and the achievements in recent scientific research and industrialization.



Zhong-Zhi Qian, Professor, Chinese Pharmacopoeia

Prof. Zhong-zhi Qian, born on January 30 of 1953, is professor of pharmacy and Ph.D. Student supervisor. Received Master of Science Degree from Heilongjiang University of Chinese Medicine. He is visiting Professor of Kumamoto University in Japan.

He focused on the research and management of standardization of traditional Chinese medicine for more than 40 years. He has successively served as Director of Chinese Medicine Standardization Division, Director of Business Comprehensive Division, Chief Scientist of the Chinese Pharmacopoeia Commission, and Executive Director of the Chinese Pharmacopoeia / Waters Joint Open Laboratory. He enjoyed special allowances from the State Council. Received the second prize in National Science and Technology Progress Award in 2016. The 8th and 9th Committee member, the 10th and 11th Executive Committee member of Chinese Pharmacopoeia. Expert Committee member in 2005-2015, and Chair of Botanical Dietary Supplement and Herbal Medicine Expert Committee of United States Pharmacopoeia. Adjunct professor and Ph.D. Student supervisor of Shenyang Pharmaceutical University, Heilongjiang University of Traditional Chinese Medicine, Chinese Academy of Traditional Chinese Medicine, Chinese Academy of Medical Sciences Institute of Medicinal Plant.



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Qian, Zong-zhi

Committee of Chinese Pharmacopoeia, Beijing, China, 100061

Strategy and syllabus of Chinese Pharmacopoeia 2020 for volume of Traditional Chinese Medicine will be introduced. The lecture will focus on the background, guiding ideology and overall goal of Chinese Pharmacopoeia 2020. ChP 2020 (Volume I, TCMs) emphasizes on improving the application of ChP as the core role for evaluation of TCM standard system, especially TCM clinical treatment-oriented standard for evaluation of TCM efficacy, and strengthening internationalization and lead the formulation of international TCM standards.



**Dr. Jimmy Yuk, Senior Manager, Metabolomics Business Development
Waters Corporation, Milford, MA**

Dr. Jimmy Yuk is the Senior Manager for Metabolomics Business Development at Waters Corporation.

In this role, Dr. Yuk develops novel analytical methodologies using liquid chromatography-mass spectrometry (LC/MS) to understand the complexities of natural products. Dr. Yuk collaborates with many academic and industry leaders to investigate challenging natural product research questions to further the analytical knowledge in this field. Dr. Yuk's research expertise for the past 10 years has been in the area of chemometrics especially in the area of targeted and non-targeted approaches.

Prior to Waters, Dr. Yuk worked as a research scientist in R&D for Bruker Biospin. He has written analytical methods and publications focusing on metabolomic approaches in natural products using NMR spectroscopy. He has published various research articles and co-authored two book chapters in the utilization of NMR spectroscopy for the quality control of natural products in the industry.

Jimmy has presented his work in many international conferences and is actively involved in various natural products professional affiliations such as the American Society of Pharmacognosy (ASP), Metabolomics Society, and is a statistics committee member for the Association of Analytical Communities (AOAC). Dr. Yuk obtained his B.Sc in Biological Chemistry and his Ph.D. in Analytical Environmental Chemistry from the University of Toronto. During his Ph.D., he developed metabolomic approaches in complex environmental mixtures using NMR, GC-MS and hyphenated LC-NMR-SPE-MS technologies.



Direct Visualization of Botanicals Using Mass Spectrometry for Discovery and Quality Control

Jimmy Yuk, and Giorgis Isaac

Waters Corporation, 34 Maple Street, Milford, MA 01757

Ambient mass spectrometry provides a comprehensive approach for obtaining rapid chemical profiles and also spatial distribution of a large variety of endogenous and exogenous analytes from a natural product without sample extraction or addition of any external label. Distribution of molecules in natural products (botanicals, microbial, and traditional medicines) can provide an understanding of spatial metabolomics, sample-environment interactions, and aid in compound screening. For example, location information of medically important compounds within a natural product will strengthen fundamental understanding of their metabolic origins, as well as, improve their extraction. For quality control, a detailed chemical profile of natural product can give valuable insight to a natural product's geographical origin or species-specific information. Molecular images provided by MS are complementary to the structural information provided by optical microscopy.

Here, we share advances in ambient mass spectrometry such as multimodal molecular imaging of natural products using desorption electrospray ionization (DESI) and Rapid Evaporative Ionization Mass Spectrometry™ (REIMS™) for various botanical studies. From understanding the distribution of ginsenosides in *panax ginseng* to conducting rapid identification of different herbs using multivariate modeling of the chemical profiles, ambient mass spectrometry can be a very powerful analytical technique for natural product discovery and quality control.



Matthew Bown, Senior Policy Advisor, Health Canada

Matthew Bown began working with Health Canada immediately following his graduation from Dalhousie University with a Masters in Public Administration. Matthew's early career was as an analyst with the Health Products and Food Branch Inspectorate, later working as a senior analyst on files such as legislation renewal, natural health product compliance, active pharmaceutical ingredients, and anti-counterfeiting/border policies.

After eight years, Matthew left the Inspectorate to serve as the manager of risk issues for the Natural and Non-Prescription Health Products Directorate. This included aspects of risk communication, product classification and supporting border admissibility decisions.

Following this, Matthew joined the Marketed Health Products Directorate as the associate director of policy, supporting the development of summary safety reviews, risk communications and other aspects of risk management.

Matthew then returned to Natural and Non-Prescription Health Products Directorate as the Senior Policy Advisor on the development of the Self-Care Framework, leading on policy development and stakeholder engagement.



Modernizing the Regulation of Self-Care Products in Canada

Matthew Bown
Natural and Non-Prescription Health Products Directorate
Health Canada

Health Canada is looking to modernize its approach to regulating self-care products. Self-care products are available for purchase without a prescription and include cosmetics, natural health products and non-prescription drugs. Canadians use self-care products every day to maintain health, treat minor ailments and improve appearance. Lipstick, vitamins, sunscreen and pain relievers are examples of self-care products.

The goals of this regulatory modernization are to align the levels of oversight with risk to the consumer, and to help consumers make better informed decisions. While many self-care products are low risk, the regulatory oversight for each category is very different, including requirements for product labelling. To ensure that the new approach is informed by a broad range of perspectives, Health Canada has consulted extensively with Canadians, including consumer groups, academia, health professionals and industry.

Health Canada is taking a phased approach, with plans to introduce key regulatory changes over the next two years. First, in the fall of 2018, Health Canada will introduce targeted amendments to the *Natural Health Products Regulations* to improve labelling of natural health products, including a facts table. These changes are intended to better support consumers in selecting and safely using a product. Second, in early 2019, Health Canada will introduce targeted amendments to the *Food and Drug Regulations* to align regulatory oversight of non-prescription drugs with the risk of the product, including the creation of expedited pathways for lower-risk products. The goal is to focus oversight where it will most benefit Canadians, based on evidence and the risk of the product.

While these first two projects are underway, Health Canada will continue to develop plans for further improvements to how self-care products are regulated, which will follow over the coming years.



Rosa Amelia Villar Lopez, Professor, National University of Trujillo

Amelia Villar Lopez, Healthcare Professional, Pharmaceutical Chemist for 34 years. Broad experience in Public Health as well as important experience in management, public administration and regulatory affairs in health and medicines. National and International Consultant in health, pharmaceutical and educational issues. Professor for more than 30 years, teaching pharmacology and pharmacotherapy. Contributed in medicinal plants researches and different drugs group's researches, but her important cooperation has been improving access to medicines in the Peruvian public health. It's also important to mention her influence in health professionals education, training human resources with different perspectives of health. Participates as guest speaker in multiple national and international events.

Career Path:

- National Dean of the Pharmaceutical Chemical Peruvian Board - Period 2016 – 2017
- Technical Coordinator for the International Project 'Alliance for Transparency in Medicines – MeTA Peru', coordinated by the World Health Organization and financed by the British Government (June-2015 to January-2016)
- National Advisor for Medicines and Health Technologies at the Pan American Health Organization - Peru (2009-2014)
- General Director of Medicines, Supplies and Drugs (DIGEMID) (June-2005 to January 2007)
- National Executive Director for Access and Use of Medicines - DIGEMID, Ministry of Health. (May 2002-May 2004)
- University Teacher in the Pharmacy and Biochemistry Faculty from the National University of Trujillo (Pre and Post-grade) (Feb 1986 to May 2010) and nowadays teacher at the Post-graduate Unit of the Pharmacy and Biochemistry Faculty from the Major National University of San Marcos (2012 to present)
- Commission Member for the National Drug Formulary - MINSA. Elaborating the National Drug Formulary for years 2002, 2005, 2008 and 2011.

Academic Background:

- Professional Title: Pharmacist- Chemist, graduated from the National University of Trujillo.
- Post-graduate studies: Master's Degree in Higher Education – National University of Trujillo, Master studies in Science - mention in Pharmacology – National University of Trujillo, Doctorate studies in Pharmacy and Biochemistry – Major National University of San Marcos, Doctorate studies in Public Health – National University of Federico Villareal.
- Postgraduate studies in the Institute of Education of London University, England.



Research and Regulation of Natural Products in Peru

Villar A¹, Villar M², Astahuamán D², Robles R³

¹ Unidad de Postgrado de la Facultad de Farmacia y Bioquímica de la Universidad Nacional Mayor de San Marcos

² Gerencia de Medicina Complementaria de la Seguridad Social del Perú

³ Centro Nacional de Documentación e Información del Medicamento (CENADIM), Dirección General de Medicamentos, Insumos y Drogas -DIGEMID, Ministerio de Salud del Perú

Peru presents approximately 25,000 plant species of which 1,400 are described as medicinal. Several ethnobotanical studies have been conducted, recording the traditional knowledge of Peruvian communities, as well as the management of useful plants, and conservation strategies, among others. Although it is not an obligation, it is important to highlight the economic importance and the return to communities of the benefits associated with intellectual property and the protection of biodiversity.

There are few clinical studies with medicinal plants in terms of efficacy and safety. However, some preliminary studies have been reported with some species, such as *Uncaria tomentosa* (Willd. ex Schult.) DC., used in osteoarthritis and in rheumatoid arthritis, *Smilax sonchifolius* (Poepp.) H. Rob., used as hypoglycemic, and *Lepidium meyenii* Walp. (maca), used in postmenopausal problems. The cultivation of these plants represents an economic income to the population. Currently Peruvian companies have the support of the PeruBiodiverso Project that is working directly with the main research entities, producers and governments.

Despite the development of modern phytochemical research, scientific knowledge about all Peruvian medicinal plants is still incomplete. In this context, Peruvian government has established a legal framework for the provision of safety of botanicals, as well as for the research and for the regular production of phytopharmaceuticals. Currently, Peru has 11 acts, 4 supreme acts and two ministerial resolutions, a decision of the CAN (Comunidad Andina de Naciones) among other laws. An innovative experience has been developed in the Social Health Insurance (EsSalud) that has developed a complete program of Complementary Medicine. They have created the "Natural Pharmacy" with a focus on medicinal plants and their therapeutic function. They elaborate phytotherapeutic preparations, floral therapies and homeopathic, including pharmaceutical care and pharmacovigilance, to control the patient's response. About 68% of patients who uses these therapies as a complement have been reported to decrease the use of synthetic medicines.

In the course of the last decades, Peru has had a significant increase in the number of scientific investigations. However, their complexity requires other harmonized approaches in new methodologies that allow the use of basic tools with advanced features for the complexity inherent in the health problems of people. The use of medicinal plants and phytotherapy are of paramount importance in the medical practices of the high Andean areas.



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Natural Products Regulation in Nicaragua and Way Forward, a Brief Case Study

Veronica Margarita Lopez Moreno, Country Representative, Health Ministry & Daniel Gallego-Perez, PAHO/WHO



Lucrecia Pérez de Batres, Pharmacist, Universidad de San Carlos de Guatemala

Lucrecia de Batres graduated from University of San Carlos de Guatemala with degree in both Pharmacy and Archeology. For the past 30 years, she has been involved in the research and industrial production of natural medicinal products focusing on 1) legislation concerning natural medicinal and phyto-cosmetic products in Central America, and 2) the history of the use and application of medicinal plants and natural cosmetics in ancient Mesoamerica (stretching from modern Central Mexico through Central America), particularly how these applications have been transmitted as ancestral knowledge and are understood and used in the present by current Maya communities in Guatemala.

As an industrial pharmacist, she has worked as a director of production, as well as in quality control and research and development for new products, in addition to serving as the coordinator for sanitary registration and a quality assurance for several pharmaceutical laboratories that manufacture natural medicinal products, natural cosmetics, and dietary supplements.

In Guatemala, she has served as a representative of the Pharmaceutical Technical Advisory Group of Asociación Pro Industria Farmacéutica (APIFAR), and represented the natural medicinal, cosmetics, and pharmaceutical products industries before the National Technical Committee for Medicines during the negotiation process of Central American Customs Union. She was on the Advisory Committee of Natural Medicinal Products (CAPRONAT) for the Regulation and Control of Pharmaceutical and Related Products, for Department for the Ministry of Health, and is currently Vice President of the Phytotherapy and Natural Products Association of Guatemala (AFITOGUA).

Lucrecia de Batres has presented on natural medicinal products and related topics at several international conferences including: the Technological Forum of Chemistry and Pharmacy TecnoQuimiva (2013), the Congress of Pharmaceutical Products in Bogotá (2013), the National Congress of Chemical and Pharmaceutical Sciences, El Salvador (2014), and the Congress of Pharmaceutical Sciences, Honduras (2015). She has attended international trainings on natural products including those organized by the Social Security Institute (IMSS) and Mexican Society of Phytotherapy in Mexico City, UNIDO, in Havana, the Faculty of Biochemical and Pharmaceutical Sciences of the National University of Rosario, in Argentina and the Faculty of Pharmacy at the Fluminense Federal University, in Brazil.

She has also organized multiple academic events related to the legislation and development of new products, phytotherapy, industrial production, and quality control of natural medicinal products and phytocosmetics, including the First Central American Congress on Natural Medicinal Products (2015) in cooperation with Galileo University and University of San Carlos de Guatemala, attended by 200 professionals and students from Mexico, Central America, Germany, Argentina, Panama, Cuba, Antilles and Spain. She is currently planning events for pharmacists and pharmacology students in Guatemala including a workshop about the challenges of formulating natural medicinal products, phytocosmetics, and dietary supplements planned for June and a forum to discuss the technical aspects involved in the medical use of *Cannabis* in October.



Central American Regulation Concerning Natural Medicines and Personal Care Products

de Batres, L
University of San Carlos de Guatemala

The Organization of Central American States (ODECA) was established in 1951 to promote integration and cooperation among all Central American countries. ODECA created the General Treaty for Central American Economic Integration, signed in 1960, which established free trade for all products originating in the region. Between 1993 and 2013, Panama, Belize and the Dominican Republic also became members of ODECA. These three countries became part of the Economic Integration System known as SICA. Within SICA, the Secretariat for Central American Economic Integration (SIECA) is charged with providing technical support to member states and enforcing regulations in order to promote economic unity and ensure the correct application of regulations arising from economic integration processes. In addition to organizing meetings, SIECA also works to carry out studies on behalf of or in conjunction with member countries, as well as those assigned by the Ministers' Council for Economic Integration (COMIECO).

COMIECO has issued several resolutions that have enacted Central American Technical Regulations (RTCA, by its Spanish acronym) governing synthetic pharmaceuticals, hygienic products, pesticides, cosmetics, and natural medicinal products. These regulations (RTCA) enforce good manufacturing practices, labeling standards, and quality verification, and confer sanitary registration. By observing these regulations, manufacturing companies of Central America can be recognized in all countries of the region as having been awarded sanitary registration for all their products. This paper details the situation concerning the legislation of natural medicinal products in Central America and briefly outlines the legislation emanating from the Central American "Unión Aduanera" (customs unions) concerning cosmetics and personal care products with natural ingredients.



Pharmacological Evaluation of Chinese Patent Herbal Medicine: A Hard Nut to Crack

Rong-Rong He*, Chang Yan

Guangdong Engineering Research Center of Chinese Medicine & Disease Susceptibility, Jinan University, Guangzhou 510632, China

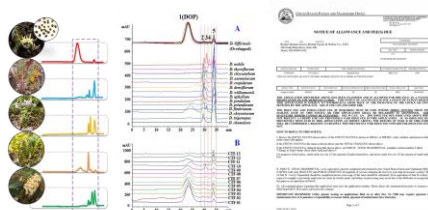
Traditional Chinese medicine (TCM) has evolved over thousands of years in China, and it is also widely used worldwide. Chinese patent medicines (CPM) are mainly herbal medicines, and more than 1000 kinds of CPM are clinically used in China at present. However, there is challenge that the effectiveness of CPM are difficult to evaluate with conventional pharmacological methods. The therapeutic philosophies of TCM are different from Western Medicine. In our studies, the research strategy we employed is setting disease susceptible animal models for pharmacological effectiveness evaluation of CPM. One case is that a mouse model by using restraint stress plus viral infection, which is more conducive to simulate the clinical features of susceptible population and evaluate the activities of Chinese herbal medicine. Our results demonstrated that stress-induced corticosterone (CORT), a stressor sensor, increased the morbidity and the mortality of virus-infected mice loaded with restraint stress. Stress was found decreased IFN- β responses by increasing expression of Mfn2, and accordingly decreased mitochondrial antiviral signaling (MAVS) aggregates in the host cells. We successfully evaluated the anti-influenza activities of different types of CPM, like Qingre Xiaoning Capsule, KangBingDu Oral Liquid, Reduning Injection, etc.

The Discovery, Chemistry, and Immunomodulating Effects of a Unique Polysaccharide of *Dendrobii Officinalis Caulis*

Li-Feng Li*, Hong-Bing Liu*, Quan-Wei Zhang, Zhi-Peng Li, Ting-Long Wong, Hau-Yee Fung, Ai-Ping Lu, Quan-Bin Han

School of Chinese Medicine, Hong Kong Baptist University, Hong Kong, China

The quality control of many saccharide-rich Chinese Medicines remains a challenge due to lack of proper chemical markers. *Dendrobii Officinalis Caulis* (DOC), the dried herb of *Dendrobium officinale*, one of the most expensive Chinese herb materials, is a good case. In our study, we compared the molecular size distribution pattern of DOC samples from GAP farms, commercial samples from market, and 20+ other *Dendrobium* species, and established a chemical marker for the authentication of DOC. This chemical marker, named DOP, is identified to be a glucomannan with a large molecular size beyond 400K, by using chemical and spectral analysis. We further proved its anti-fatigue and anti-tumor activities using mice models. Investigations on its digestion properties verified that DOP is hardly absorbable and is mainly digested in large intestine, in other words by microbiota. Its bioactivities are associated with its modulatory effect on gut microbiota.



This study was supported by HKSAR Innovation and Technology Fund (ITF), Tier 3, ITS/311/09, General Research Fund (12100615, 22100014), Health Medical Research Fund (11122531), National Natural Sciences Foundation in China (81473341), and Hong Kong Baptist University (RC-start up grant, MPCF-001-2014/2015, and FRG2/14-15/028).



De-An Guo, Professor, Shanghai Institute of Materia Medica

Dr. De-an Guo serves as director of the Shanghai Research Center for TCM Modernization at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences. He received his Ph.D. Degree of Pharmacognosy at Beijing Medical University in 1990. He engaged in his postdoctoral research at the Department of Chemistry and Biochemistry, Texas Tech University, (1993-1996). His major research interest is focused on the standardization and modernization of Chinese herbal medicines. He has received a number of international, national and ministerial awards such as National Natural Science Award, Norman Farnsworth Excellence in Botanical Research Award, etc. He is currently the president of GP-TCM Research Association (London) and chair or expert committee members of Chinese Pharmacopoeia, United States Pharmacopoeia and European Pharmacopoeia. At present, he is Editor-in-chief, vice editor or editorial board member of 18 international journals. To date, he has published 560 papers including 380 SCI articles with over 6000 SCI citations.



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Discovery of Effective Combination in the Exact of Ginkgo Biloba



Gloria Zhang, Director, Herbridge Media

Gloria Zhang

1999-2003 Traditional Chinese Medicine Major in Jilin University.

2003-2005 Researcher at BGG

2005-2007 Industry Analyzer in Healthoo.com

2008- Now Created Herbridge Media

Sharing the TCM ,New Herbal active ingredients news to health industry readers.

Promote China natural ingredients innovative and development

Holding China Natural Ingredients Industry Conference every October.

Lauch the market magazine <Asiacetical Insights>

Widely recognized By China professional health industry.



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Regulatory and Environmental Trends in China: Clean, Land, Air and Water



Loren Israelsen, President, UNPA

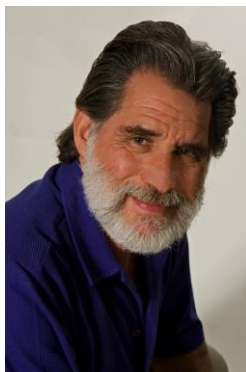
Loren Israelsen, is President and Founder of the United Natural Products Alliance (UNPA). He has been deeply involved in the commercial, political, and regulatory issues facing the global dietary supplement industry since 1980. On the commercial side, he served as general counsel and president of Nature's Way Products, Inc. Much of his career has involved creating and supporting efforts to allow broad access to dietary supplements, together with the systems to assure product quality, safety, and benefit.

Mr. Israelsen has authored over 150 articles and/or book chapters and has lectured in over 30 countries on dietary supplement and functional food issues. Currently, his greatest areas of interest are the growing presence of synthetic biology in the natural products industry, personalized nutrition, preservation of the cultural knowledge on which the natural products industry is founded, and securing seat upgrades on Delta Airlines.



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The Globalized Botanical Industry - The 5 Critical Challenges



Mark Blumenthal, Executive Director, American Botanical Council

Mark Blumenthal is the Founder and Executive Director of the American Botanical Council (ABC), the leading independent, nonprofit organization dedicated to disseminating accurate, reliable, and responsible information on herbs and medicinal plants. He is the Editor/Publisher of HerbalGram, an international, peer-reviewed quarterly journal. For six years he was 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." Mark is the Senior Editor of the English translation of The Complete German Commission E Monographs—Therapeutic Guide to Herbal Medicines (1998), Herbal Medicine: Expanded Commission E Monographs (2000), The ABC Clinical Guide to Herbs (2003), and co-author of Rational Phytotherapy, 5th edition (2004). He has appeared on over 400 radio and television shows and has written over 500 articles, reviews and book chapters for many major publications. In 2010 he was awarded the prestigious Tyler Prize in honor of the late Purdue Professor Varro E. Tyler from the American Society of Pharmacognosy. In 2008 he was awarded the "Natural Legacy" award from Natural Foods Merchandiser magazine and he has also been named to Natural Health Magazine's Hall of Fame Award for "...opening America's eye to the healing powers of herbs." He has been a leader in the concerns for more rational regulations of herbal and natural product manufacturing, and education on plant-based medicines for over 36 years.



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**Proposed Bapp Best Practices Sop for the Disposal/Destruction of
Irreparably Defective Materials**



Paula Brown, Director of Applied Research, Natural Health & Food Products, British Columbia Institute of Technology

Canada Research Chair, Phytoanalytics

Adjunct Professor, Department of Chemistry, University of British Columbia

Adjunct Professor, Gosling Research Institute for Plant Preservation, University of Guelph

Director of Applied Research, BC Institute of Technology (BCIT)

Burnaby, British Columbia, Canada

Paula.Brown@bcit.ca Tel: 604.412.7484

Biography: Paula has supported the natural health & food product industry for close to two decades by conducting applied research at BCIT on product quality, safety and efficacy. Supported by grant funding and Industry contracts BCIT has engaged in projects focused on health policy, regulatory affairs, product formulation, botanical authentication, analytical method development and validation, chemometrics and therapeutic monitoring for preclinical and clinical studies. Dr. Brown was appointed Fellow of the AOAC in 2009 after serving 5 years as General Referee and 6 years on the Dietary Supplement Task Force. She has served on 14 AOAC Expert Review Panels, directed 4 collaborative studies on botanicals, published numerous validation studies, and taught method development and validation workshops for Health Canada, the American Society for Pharmacognosy, the United States Pharmacopoeia, and the NHP Research Society of Canada. In 2009, she was appointed to the American Botanical Council Advisory Committee, the inaugural Natural Health Products Program Advisory Committee for Health Canada, and became Chair of NSF's Joint Committee for Dietary Supplements. In 2017, she joined the USP Expert Committee for Botanical Dietary Supplements and Traditional Medicines and the American Herbal Pharmacopoeia Advisory Board. She is currently the President of the NHP Research Society of Canada, Dietary Supplement & Traditional Medicine Section Editor for Journal of the AOAC International, and holds the Canada Research Chair for Phytoanalytics.



Metabolomics Analysis as a Tool for Understanding Plant Secondary Metabolite Production and Improved Quality of Botanical-Based Products

Brown, P. N.

BC Institute of Technology, Burnaby, British Columbia, Canada

In response to their environment, plants produce a phytochemical arsenal in order to communicate and to withstand abiotic and biotic pressures. The average plant tissue contains upwards of 30,000 phytochemicals, consequently the vast majority of approaches used to study plant chemistry are reductionist, only targeting specific classes of compounds, often are selected for ease of detection or isolation. Metabolomics is the qualitative and quantitative analysis of all metabolites present in a biological sample. By providing researchers with a phytochemical snapshot of all existing metabolites present in a sample, metabolomics has allowed researchers to study plant primary and secondary metabolism in ways that were never done before. A standard metabolomics data set contains vast amounts of information and key factors in using the data effectively are experimental design, availability of reference materials, sample preparation and selection of statistical analyses performed. This presentation will discuss and demonstrate some of the recent tools developed for analysis and interpretation of plant metabolite data for authentication of botanicals, improving the safety and efficacy of products and discovery of new metabolites and pathways. Collectively, metabolomic tools represent an entirely new approach to both quality control and phytochemical discovery.



Joshua J. Kellogg, Post-Doctoral Associate, The University of North Carolina Greensboro

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Biography: Joshua is passionate about the unique realm of natural products, medicinal plants, and botanical dietary supplements, especially its interdisciplinary essence, at the interface of botany, agriculture, chemistry, and medicine. Josh received his doctorate from North Carolina State University under the mentorship of Dr. Mary Ann Lila. His dissertation research focused on the phytochemistry of ethnobotanically-relevant Alaskan seaweed and wild berries, and their ability to mitigate hyperglycemia and inflammation. He is currently a postdoctoral research fellow at the University of North Carolina at Greensboro in Dr. Nadja Cech's research group. Josh has worked in translating analytical metabolomic methods to the natural products and dietary supplements realm. He has developed biochemometric workflows to identify bioactive metabolites from complex mixtures, and has also worked in establishing and improving the analytical capacity of metabolomics analyses.

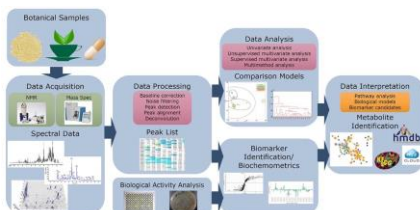


Approaches to Evaluate Botanicals Via Mass Spectrometry Metabolomics

Kellogg, JJ¹, Wallace, ED¹, Kvalheim, OM², Paine, MF³, Oberlies, NH¹, Cech, NB¹

¹University of North Carolina at Greensboro, Department of Chemistry & Biochemistry, Greensboro NC, ²University of Bergen, Department of Chemistry, Bergen, Norway, ³Washington State University, College of Pharmacy, Department of Pharmaceutical Sciences, Spokane, WA

The number of Americans utilizing dietary supplements has risen to well over 50% of the population, with sales nearly tripling during the 20 years since passage of the Dietary Supplement Health and Education Act. In many cases, these dietary supplements are prepared from botanical sources in the form of extracts, teas, capsules, or tinctures. Investigators involved in studies of botanical dietary supplements face a unique set of challenges as they are typically complex mixtures, for which the identities and quantities of components present may not be fully known, and the composition of which can vary greatly depending on the method of preparation or source material used. Two common designs for studies of botanicals investigate comparisons amongst multiple samples or seek to identify bioactive principles from a complex matrix. Our work has focused on the development of mass spectrometry-based metabolomic approaches for analysis of complex mixtures. Herein, **we present a series of methods for botanical natural product analysis**: defining the scope of the study and ensuring beforehand that the hypotheses are clearly defined; obtaining study materials, whether via collection, purchase, or contract manufacture; authentication of the material by a relevant methodology; sample preparation prior to instrumental analysis; analytical methodologies available for metabolomics; data processing and integration, statistical analysis; and quantitation and biomarker identification. These analytical approaches are appropriate for both comparison studies as well as a **biochemometric workflow** to investigate potential bioactive principles. As part of this workshop, we will discuss the practical application of these methods, as well as potential pitfalls, challenges, and issues for consideration, and provide suggestions for addressing them.



Acknowledgements: The authors would like to acknowledge Dr. Daniel Todd, director of the Triad Mass Spectrometry Facility at UNCG, for his expertise in mass spectrometry analysis. Research reported in this work was supported in part by NCCIH/NIH awards U54 AT008909 (NaPDI, Center of Excellence for Natural Product Drug Interaction Research) and 1R01 AT006860.



Jon Wardle, Senior Lecturer Public Health, University of Technology Sydney; Australian Research Centre in Complementary and Integrative Medicine

Dr Jon Wardle has clinical backgrounds in nursing and naturopathy and heads the Regulatory, Legislative and Policy Stream at the Australian Research Centre in Complementary and Integrative Medicine, Faculty of Health, University of Technology Sydney, where he holds a prestigious Australian National Health and Medical Research Council Research Translation Fellowship. In addition to his clinical qualifications, Jon also has postgraduate qualifications in public health (including a doctorate from the University of Queensland), law and health economics and holds visiting positions at the Schools of Medicine at University of Washington and Boston University. Jon has published more than 100 peer-reviewed journal articles and over 20 academic book chapters. Jon works on the editorial board of eight international academic journals, including serving as the Editor-in-Chief of the journals *International Journal of Naturopathic Medicine* and *Advances in Integrative Medicine*. Jon is also co-editor of *Clinical Naturopathy: an Evidence-Based Guide to Practice*, published by Churchill Livingstone now used as a core naturopathic teaching text in over a dozen countries. Jon is actively involved in research and policy at the interface of public health and traditional medicines. Jon is co-convenor of the *Public Health Association of Australia's* Research Advisory Committee as well as the PHAA's Complementary Medicine Special Interest Group, and he has led several *World Federation of Public Health Association* initiatives on traditional medicines. Jon currently serves as Secretary-General of the *World Naturopathic Federation*, an organisation that represents naturopathic medicine at international organisations such as the *World Health Organization*. Jon has worked on traditional medicine, public health and primary health care policy and regulatory initiatives with numerous governments, non-government organisations and international bodies. Jon is passionate about both protecting and embracing traditional knowledge and fostering innovative research, and believes that by combining both can optimal public health outcomes be achieved.



Trends in Natural Product Regulation: Developments from Australia and the Growing Translation Between Science and Traditional Claims

Jon Wardle¹

¹Australian Research Centre in Complementary and Integrative Medicine, Faculty of Health, University of Technology Sydney, Sydney, Australia

Australia is considered an early adopter of the recognition of traditional and complementary medicine products and practices through legislation and regulation. In 2018, the most significant reforms to natural products regulation in decades were passed as amendments to the *Therapeutic Goods Act 1989*. These reforms - aimed at improving patient access to new medicines in a timely manner and encouraging industry innovation – transform the way in which therapeutic goods will be regulated in Australia.

Whilst the reforms are varied, several areas are particularly relevant to natural products. Overseas regulator reports will now be accepted in addition to *de novo* evidence for natural products, access to higher-level health claims will be available via a “third listing pathway” for complementary medicines and permitted indications will include a wide range of traditional, as well as scientific claims.

The third listing pathway requires low-risk products substantiate higher-level claims with scientific evidence, but not to the same extent as required for registered medicines (such as pharmaceutical drugs). Specificity clauses also allow for better intellectual property protections for product sponsors. These reforms are expected to drive innovation and research in the complementary medicines sector, as well as offer consumers a more informed indication of natural product effectiveness.

These reforms have also highlighted governmental support for recognition of traditional knowledge as a valid source of evidence. Whilst inclusion of traditional indications has been controversial, the government has supported their inclusion citing obligations under the World Health Organization and international legal and policy norms, which increasingly recognise traditional evidence. This has led to a need to be able to 'translate' evidence from scientific and traditional evidence into appropriate product claims, which has served as a catalyst for scholarly, research and commercial interest in identifying the most effective methods by which to ensure appropriate use of traditional indications.

This presentation will update the audience on recent reforms in Australia, highlight what they mean for product sponsors in Australia and overseas, and examine how these developments are expected to interplay with the global regulatory and legislative landscape.



Alvaro Viljoen, Professor, Tshwane University of Technology

Alvaro Viljoen, Born in 1969, Pretoria South Africa. Completed a BSc, BSc Hons. (*cum laude*) and MSc (*cum laude*) in Botany at Stellenbosch University. In 1994 Alvaro commenced with a PhD at the University of Johannesburg on the chemotaxonomy of the genus *Aloe*. In July 2005 he was appointed as a research fellow in the Department of Pharmaceutical Sciences, Tshwane University of Technology (Pretoria). More than seventy post-graduate students have graduated under his supervision since 2002. His research interest is the phytochemistry and biological activity of medicinal and aromatic plants indigenous to South Africa. He has authored / co-authored >220 peer reviewed papers mostly on the phytochemical exploration and biological activity of indigenous medicinal and aromatic plants. He has been elected on to the editorial board of the Journal of Essential Oil Research (Francis & Taylor), Phytochemistry Letters (Elsevier), he is the Editor-in-Chief of Journal of Ethnopharmacology (Elsevier) and reviewing-editor for South African Journal of Botany (Elsevier). In October 2013 Alvaro was awarded the National Research Chair in Phytomedicine a position which he holds concurrently as Director of the MRC Herbal Drugs Research Unit in South Africa.

www.alvaroviljoen.com



Synergy, a Modern Concept Based on Ancient Wisdom – Examples from African Traditional Medicines

Viljoen A^{1, 2}, Sandasi M¹ & Van Vuuren S³

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One of the biggest misconceptions in modern medicine was that all complex diseases could be treated with a “one-molecule-one-target” approach. Some of the most challenging and stubborn infectious conditions such as malaria and tuberculosis are now routinely treated with a combination-therapy approach. Combination therapy has been an integral concept of ancient healing modalities such as African Traditional Medicines, Ayurveda, and Chinese Traditional Medicines, etc. Taking leads from traditional practices we have explored the possible interaction and/or synergy at various levels:

1. Combining different plant species e.g. *Artemisia afra* and *Lippia javanica*
2. Combining different plant parts e.g. leaves and bark of *Croton gratissimus*

These studies clearly confirm the synergistic/additive interactions which prompted us to further explore synergy at a chemical level. Several examples will be presented illustrating the intricate interaction leading to enhanced biological activity. The powerful application of metabolomics to explore synergy will be demonstrated through our work on essential oil constituents.

Although synergy has become a “buzz word” in phytomedicine literature, most studies hint (or grasp) at synergy to try and explain results obtained with few studies proving and validating claims of synergy. A bibliometric survey has however shown a revival of synergy research which may become an important strategy in future plant-based pharmacological studies.

The authors are grateful for the financial support of the National Research Foundation (South Africa), Department of Science and Technology (South Africa), Tshwane University of Technology and University of the Witwatersrand.



Alexander Shikov, Professor, St. Petersburg Institute of Pharmacy

Professor Dr. Alexander Shikov studied pharmacy at the Saint-Petersburg State Chemical Pharmaceutical Academy; 1995 graduation as Ph.D. at the same Academy; 1995 – 1998 Associate Professor at the Saint-Petersburg State Chemical Pharmaceutical Academy; Independent expert of Institute of Standardization of Scientific Center of Expertise and Governmental Control of Medicinal Preparation of the Ministry of Public Health of Russian Federation in 2002 – 2003, since 2004 he is full professor of pharmaceutical science at Saint-Petersburg State Chemical Pharmaceutical Academy, Russia and since 2008 he is deputy of General Director of Saint-Petersburg Institute of Pharmacy, Russia. His research interests are in the natural product chemistry, pharmacology, and pharmaceutical formulations with natural products. He has published over 200 research papers. Currently he is Associate Editor of Journal of Ethnopharmacology and member of editorial board of Phytomedicine; Chinese Herbal Medicines; Chinese Journal of Natural Medicines; Synergy, and World Journal of Traditional Chinese Medicine. Prof. Shikov is expert of Russian Academy of Science and member of Specialty Committee: Society for TCM Pharmaceutical Analysis (WFCMS-World Federation of Chinese Medicine Societies) from 2010.



Plant Species Used Traditionally at the Interface of Food and Medicine (The Case of Russian Pharmacopoeia)

Shikov AN, Pozharitskaya ON, Makarov VG

St-Petersburg Institute of Pharmacy, Leningrad Region, Vsevolozhsky District, 188663, Kuzmolovo P 245, Russia

Plants are excellent sources of active phytochemicals with importance in the prevention of different diseases and are gaining rapid recognition globally. Many medicinal plants may also have direct nutritional benefits of which we know little. Where the boundary between food and medicine?

The multinational population of Russia has used plants both in daily diet and for self-medication however these traditions has remained mostly unknown in other regions. The large majority of species referred in the Russian Pharmacopoeia are known to have been used as food by local population in Russia. These edible plants have a wide range of pharmacological properties: antihelminthic, anti-inflammatory, astringent, bitterness and choleric, cardiovascular, diaphoretic, diuretic, expectorant, haemostatic, polyvitamin, sedative, spasmolytic, and tonic. These plants are used in next food categories: beverages, bread surrogates, green vegetables and potherbs, plants used for preserves, seasonings and spices, sweets, tea and coffee substitutes, wild berries and fruits. The improvement of economic and living standards has changed people's concept of lifestyle and they pay more attention to health food. This type of food not only serves to provide nutrition but also can be a source for prevention and cure of various diseases and become a large popularity. The utilization of knowledge about beneficial pharmacological effects of edible plants is one of probably safe and effective way for development of new health food.



**Assessing the Safety of Botanicals, Their Extracts, and Isolates in Foods: Case Studies
Illustrating the Scientific Challenges**

Marles RJ¹ and Jennifer Barber¹

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Foods as vehicles for the consumption of potentially bioactive or nutritive botanicals, their extracts and isolates, present distinctly different scientific challenges from dosage forms with the same ingredient consumed as dietary supplements or natural health products. One key consideration is the evidence for a history of safe use of a novel botanical ingredient as a food in a sufficiently large population over a long enough time, keeping in mind that exposure from consumption of a traditional herbal medicine is usually substantially less than a food consumed *ad libitum* without limitations for vulnerable subpopulations. We also need to consider whether they would replace existing foods; supplements are generally consumed in addition to the usual diet. The food matrix may have direct and indirect (e.g., via the gastrointestinal microflora) effects on the absorption, metabolism, distribution and excretion of the botanical component. Botanicals may also have been subject to conventional breeding, genetic modifications, or processing that has changed their properties. Foods do not usually carry labeling with directions for use, dosage, and cautions. Specific non-proprietary cases will be used to illustrate the challenges for regulators to have no objection to the proposed marketing of botanicals in foods as safe for consumption.



New Novel Food Regulations in Europe: What Has Changed and What is the Impact on Access to the EU Market?

Brendler T^{1,2,3}

¹Plantaphile, 710 Park Ave, Collingswood, NJ 08108, USA; ²Department of Botany and Plant Biotechnology, University of Johannesburg, South Africa; ³Traditional Medicinals Inc., 1400 Valley House Dr Ste 120, Rohnert Park, CA 94928, USA

As per January 2018, long-expected and long-debated changes to the regulations governing access of novel foods to the European marketplace have come into effect. The new legislation (EU) 2015/2283 lifts the assessment burden off national authorities in favor of a centralized approach and thus provides for a streamlined and potentially more speedy and effective procedure. It also expands the scope of what is considered a novel food and it holds a major paradigm shift in that it considers traditional food use in the country of origin alongside a flawless safety profile to be a suitable evidence base for an authorization. The new assessment approach is multi-tiered and invokes toxicological and other safety data only when and where deemed necessary. A move away from applicant-specific authorizations comes with its own pros and cons: while adding a novel food to a new Union List eases the burden on applicants by making authorizations generic, it at the same time limits the protection of proprietary product-specific data leading to a first-time approval. It is too early to ascertain the impact of the new regulation on both the central regulator's workload and the ease with which novel foods will reach the EU market henceforth, however, the inherent acknowledgment of traditional use in the food category is a major opportunity for traditional foods originating outside Europe.



Challenge and Opportunity of Botanical Drug Product Approval in the U.S.: The FDA's Perspective

Charles Wu, Jing Li, Cassandra Taylor and Katherine Tyner

Office of Pharmaceutical Science, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, Maryland

Botanicals are important sources of new drug discovery and development. FDA received over 700 botanical investigational new drug applications (IND) and pre-IND meeting requests (PIND) until 2017. Despite the increasing interest in investigating botanical mixtures as new drugs from sponsors around the world, only two botanical new drug applications have been approved in the US, Veregen® in 2006 and Fulyzaq® in 2012.

In this presentation, we analyzed these INDs containing a wide variety of botanical raw materials (single vs. multiple herbs), with various previous human experience, and originated from broad geographic regions and we also discussed the opportunities and challenges for botanical new drug development. The data showed that the indications cover almost every review divisions of the FDA, from cancer prevention/treatment, mitigating common warts to pain relief as proposed for early phase I/II trials. About 2% of total INDs have stockpiled enough clinical, nonclinical, and quality control data to advance to well-designed Phase 3 clinical trials. Given the nature of the botanicals with chemical and biological complexity, the therapeutic and quality consistency remains a great challenge from the Agency's regulatory and scientific perspective.

With accumulated experience and knowledge on botanical drug products, FDA published the revised Botanical Drug Development-Guidance for Industry in December of 2016 to address the challenging issues for later phase trial and provided further recommendations to better facilitate botanical drug development.



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Yue Hua Zhou, Deputy Office Director, *Office of Traditional Chinese Medicines, CDE, CFDA*



Pang-Chui Shaw, Professor, Chinese University of Hong Kong

Professor Pang-Chui Shaw obtained his Ph.D degree from Imperial College, University of London, UK. He is now Director of Li Dak Sum Yip Yio Chin R & D Centre for Chinese Medicine and Professor and Director of Biochemistry Programme, School of Life Sciences at the Chinese University of Hong Kong. He also serves as Chairman of the Endangered Species Advisory Committee, Agriculture, Fisheries and Conservation Department of the Hong Kong SAR. His research focuses on the authentication, quality control and pharmacological studies of Chinese medicinal material. He has published more than 220 refereed articles, three books and has obtained four USA and four Chinese patents.



Authentication and Quality Control of Concentrated Herbal Medicine Granules by Molecular Technology

Lo YT & Shaw PC

LDS YYC R&D Centre for Chinese Medicine, Institute of Chinese Medicine and School of Life Sciences, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China

Concentrated herbal medicine granules (CCMG) offer patients a convenient option for traditional therapy. However, with morphological and microscopic characteristics lost, it is difficult to authenticate and control the quality of these medicinal products. This study aimed to develop effective and universal methods for species identification and quantification. Species-specific primers which amplified DNA fragments in *Mesobuthus martensii* and *Zaocys dhumnades* CCMG with sizes less than 200 bp were found to be effective for species identification from the adulterants. On the other hand, polymerase chain reaction (PCR) amplification of full-length DNA barcode in processed products is difficult because of severe DNA fragmentation. In order to develop a universal method for species identification, an adaptor ligation-mediated PCR protocol was derived. The specially designed adaptor with asymmetric strands and terminal modification avoided amplification of non-target DNA sequences. Sets of target DNA fragments from *Angelica sinensis* and *Panax notoginseng* CCMG were ligated with the adaptors, amplified by an adaptor primer with a single universal barcode primer to obtain partial internal transcribed spacer 2 (ITS2) sequence, and identified by DNA sequencing. Besides species authentication, determination of the constituent species amount in multi-herb products is important for quality control. Quantitative PCR (qPCR) was used to determine the amount of *Whitmania pigra* and *Zaocys dhumnades* CCMG in mixture solution. Results showed that reproducible quantification results could be obtained (1) using a modified DNA extraction protocol, (2) amongst DNA extracted from the same batch of CCMG and (3) amongst different batches of CCMG from the same company. The above studies extended the application of DNA techniques to concentrated herbal medicine granules and may be further developed for quality assurance and regulatory compliance in the CCMG industry.



David Erickson, Founder & CEO, DNA4 Technologies LLC

Dr David Erickson received his PhD in Botany from the University of Georgia where he studied population and evolutionary genetics. He then completed postdoctoral training at the University of Maryland and the Smithsonian Institution studying quantitative and evolutionary genetics respectively. He then helped establish and run the plant DNA barcode program at the Smithsonian's National Museum of Natural History. In 2015 Dr Erickson founded the biotech company DNA4 Technologies, where they have developed innovative methods for the use of DNA data to resolved the taxonomic identity of natural products in commercial use.



Genome2-ID: A Bioinformatic Tool for Unbiased and Rapid Species Identification Using Genomic Scale Next Generation Sequencing Data

Erickson, DL¹ and Gustafson K²

¹ DNA4 Technologies LLC, bwtech@UMBC Research & Technology Park. Baltimore, MD 21227, USA

² The Nature's Bounty Corporation, Nutrition and Scientific Affairs, Ronkonkoma, NY 11779

As the cost of Next Generation DNA sequencing (NGS) continues to fall, new tools are needed to interpret the massive quantities of data that can be recovered from a sample. Genome2-ID is a bioinformatics tool that automates the use of NGS data to generate accurate and precise identifications of the species content in natural products. We review the background of similar approaches, how they are increasingly used in clinical environments, and compare Genome2-ID to historical methods of DNA based species identification. The performance of Genome2-ID when applied to a range of products is summarized, and an introduction to the publically available online data analysis portal hosting Genome2-ID is given.

This research has been supported by Amy Acher and Pawel Rudzinski of The Nature's Bounty Corporation, Andrea Ottesen and Sara Handy of the Food and Drug Administration, John Spouge of the National Institutes of Health, and Meaghan Parker of the World Resources Institute. Kevin Chu and Shu Zhang of DNA4 Technologies have also made critical contributions to the development and testing of Genome2-ID.



Iffat Parveen, Research Scientist, University of Mississippi

Iffat Parveen, Ph.D., is a Research Scientist working at the National Center for Natural Products Research at the University of Mississippi. Parveen received B.S. and M.S. in Botany from University of Delhi and Ph.D. in Botany with a specialization in Plant Molecular Biology from Department of Botany, University of Delhi, India. She recently completed her Post- Doctoral research studies at the National Center for Natural Products Research, University of Mississippi, USA. Parveen's research areas of interests are plant molecular biology and biochemistry. Her current projects includes isolation and molecular characterization of genes involved in terpenes and tri-terpenes biosynthetic pathways of medicinally important plants and the authentication and identification of plants using various molecular marker techniques technique including DNA Barcoding. She has 10 peer-reviewed publications and 15 published abstracts to her credit.



Family-Specific DNA Mini-Barcodes for Identification of Botanicals

At the molecular level, plant species can be identified using DNA loci either from nuclear or plastid genome with easily available universal oligonucleotides, a technique called DNA barcoding. However, this is possible when single-species plant material is present but may not work on a mixture of plants species. Another disadvantage is that using universal oligonucleotides is of limited help especially if the adulterating material is present in low quantities. On the other hand, if using the species-specific oligonucleotides, they could only detect a single specific adulterating plant material and consequently the unexpected adulterants may go undetected. Therefore, we designed degenerated oligonucleotides from different gene regions of the nuclear genome that can bind to a variety of genera from one particular family and not to other genera belonging to different plant families. These family-specific oligonucleotides were able to amplify a diagnostic PCR product from the size range of 80-200 bp. The small sized products falls in the category of a desired mini-barcode size to be used for damaged/fragmented DNA and Next Generation Sequencing.



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DNA Barcoding of *Momordica* Species and Assessment of Adulteration in *Momordica* Herbal Products, an Anti-Diabetic Drug

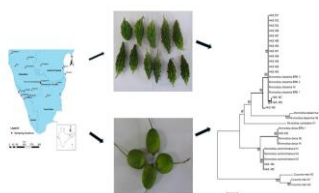
Santhosh Kumar J.U.^{1, 2}, Krishna V¹, Uma Shaanker R^{2,3} & Ravikanth G³

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²School of Ecology and Conservation, Department of Crop Physiology, University of Agricultural Sciences, GKVK, Bangalore-560065, India

³Ashoka Trust for Research in Ecology and the Environment, Royal Enclave, Srirampura, Jakkur Post, Bangalore-560064, India

Medicinal plants and their products, since time immemorial, have been used in virtually all cultures as a source of medicine. In India, a number of plant species are used as medicine, and in recent years, the trade in medicinal plants has increased several fold. However, with increasing demand for, and burgeoning trade in, raw herbal products, there has been concern over the safety and the efficacy of the herbal products. In recent years, a number of studies have highlighted the rampant adulteration and species admixtures in raw herbal trade. Here we evaluate the extent of adulteration in the raw herbal trade of *Momordica charantia*, commonly used in the treatment of Type-2 diabetes in south India. Eighteen markets samples representing the raw herbal products of *Momordica*, commonly called as “*karela*” in India, were purchased from local markets. The authenticity of the herbal samples was assessed by evaluating them against the DNA barcode developed for the biological reference standard of *Momordica charantia*. Our results indicate that the market samples sold were most authentic with only three of the eighteen samples containing species other than *M.charantia*. We discuss the implications of the study in the larger context of the concern of adulterations in the raw herbal trade.



This work was supported by Department of Biotechnology, Government of India (Grant number: No.BT/IN/ ISTP-EOI/2011). Authors also acknowledge National Bureau of Plant Genetic Resources (NBPGR), Regional Station, Thrissur, Kerala for providing the plant material for this study. We thank Dr. R. Ganesan, ATREE, Bangalore and Dr. Srikanth Gunaga, Forestry College, Sirsi for the taxonomic identification of the plant samples.



Michael Repka, Director Of The PII Center For Pharmaceutical Technology, University of Mississippi

Dr. Michael A. Repka
Chair of Pharmaceutics and Drug Delivery,
Director of the Pii Center for Pharmaceutical Technology,
Professor of Pharmaceutics and Drug Delivery

Education:

- Ph.D. University of Texas
- D.D.S. University of Texas
- B.S.Ph. University of Texas

Appointment(s):

- Chair of Pharmaceutics and Drug Delivery
- Professor of Pharmaceutics and Drug Delivery
- Director of the Pii Center for Pharmaceutical Technology
- Research Professor in the Research Institute of Pharmaceutical Sciences

Interests:

His research interests include “trans” systems, including transmucosal, trans-nail and transdermal drug delivery systems. Many of these systems are directed toward the delivery of poorly soluble drugs via hot-melt extrusion techniques. Polymeric drug delivery design and stabilization of conventional and novel drug delivery systems for natural product compounds such as THC, is a continued focus of research.



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Critical Issues in the Development of Tablets and Capsules



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The Next Chapter in the Analysis of Pesticide Residues in Cannabis Using GC/Q-TOF Instrumentation

Philip L. Wylie,¹ Mei Wang,² Mahmoud A. ElSohly^{2,3,4} Ikhlas Khan² Chandrani Gon³ and Mohamed Radwan³

¹Agilent Technologies, Wilmington DE; ²National Center for Natural Products Research,³Department of Pharmaceutics and Drug Delivery, School of Pharmacy, University of Mississippi, ⁴ElSohly Laboratory Inc.

Previously, we reported on the screening for pesticide residues in confiscated cannabis samples using a high resolution accurate mass GC/Q-TOF instrument. The method used a “Find by Fragments” algorithm in combination with a Pesticide Personal Compound Database and Library (PCDL). The software could screen for more than 850 pesticides in the PCDL by extracting out characteristic accurate mass ions for each compound at its locked retention time. In sixteen different samples, an average of almost six pesticides and related contaminants were found by this method. More recently, we have developed a quantitative method for more than 90 pesticides, most of which are halogenated. A major problem with analyzing pesticide residues in cannabis is that extracts contain very high levels of terpenes and cannabinoids which interfere with the pesticides. Halogenated fragments have a large negative mass defect which results in less interference from indigenous compounds. The new quantitative method has been applied to extracts of confiscated cannabis. The plan now is to try using a next generation GC/Q-TOF which has much higher resolving power, better sensitivity and the ability to use low energy ionization to increase the relative abundance of high mass ions. MS/MS will be tried in the high energy (70 eV) and low energy (12 – 15 eV) modes to determine if the added selectivity will allow more compounds to be quantified.



Giorgis Isaac, Principal Scientist, Waters

Giorgis Isaac is a Principal Scientist in the Pharmaceutical Life Sciences at Waters Corporation, Milford, MA. He has over 10 years of experience in the area of metabolomics and lipidomics liquid chromatography-mass spectrometry method development and various data handling informatics tools. He graduated from Asmara University, Eritrea in 1997 with a B.S. in Chemistry. Dr. Isaac continued with his graduate studies at Uppsala University, Uppsala, Sweden (2000-2005), where he worked with Professors Jonas Bergquist and Karen Markides on the development of a wide range of analytical method development for lipid analysis in complex samples. In 2005, Dr. Isaac received his Ph.D. from Uppsala University in Analytical Chemistry. He conducted postdoctoral research in biological mass spectrometry under Professor Ruth Welti at Kansas Lipidomics Research Center, Kansas State University in Manhattan, KS. Prior to joining Waters Corporation in 2010 he was a senior postdoctoral research scientist at the Pacific Northwest National Laboratory (PNNL) Richland, WA (2008-2010) where the focus of his research was mainly to establish a metabolomics and lipidomics platform. He has authored over 25 publications and 4 patents. He has presented poster and oral presentations in various national and international scientific meetings. A major analytical challenge in natural product is the complexity of the samples. Dr. Isaac current research is focusing on novel analytical and informatics method development to solve these analytical challenges in natural product analyses.



Authentication of Botanicals and Herbal Products Using UPLC/Ion Mobility QTOF-MS and a Metabolomics Approach

Giorgis Isaac¹, Avula, B.², Wang, YH², Jimmy Yuk¹, Bae, JY.², Wang, M², Rob Plumb¹, Khan, IK.²

¹Waters Corporation, 34 Maple Street, Milford, MA 01757, USA; ²National Centre for Natural Products Research, School of Pharmacy, University of Mississippi, MS 38677, USA

Metabolomics can be used to provide an unbiased, comprehensive qualitative and quantitative overview of the metabolites present in botanicals and dietary supplements. Compared to conventional analyses which are focused on a limited set of compounds, metabolomics approaches, together with novel data processing tools, enable a more holistic comparison of samples. *Fadogia agrestis* also known as black aphrodisiac is an erect small shrub indigenous to Africa. The aqueous stem extract containing saponins, flavonoids, etc has been used in traditional medicine as an aphrodisiac. The metabolite profiles of authentic *Fadogia* and *Fadogia* commercial products were investigated. The samples were randomized and injected three times with a set of QC pooled sample runs in both positive and negative ion mode. Details of data file format and a list of expected adducts are entered to facilitate the handling of data import followed by automatic retention time alignment. Metabolomics experiments involve large amount of sample runs that may result in a shift in retention time. The UPLC/IM-QToF-MS data was first aligned to correct any retention time drift between analytical runs. After retention time alignment, automatic peak detection, normalization, deconvolution, compound quantitation, identification and statistical analysis were performed. Principal component analysis (PCA) was performed and different groups were separated on the basis of the PCA analysis, reflecting authentic *Fadogia* and corresponding commercial products. Significantly changing metabolite markers that differentiate between authentic *Fadogia* and commercial products were identified that can be used as a target markers for *Fadogia* authentication. The identification of the marker metabolites was based on exact mass precursor ion, theoretical isotopic distribution, retention time and high energy fragment ion information. To improve the confidence in the compound identification, theoretical fragmentation of a candidate compounds was performed and then matched to the resulting '*in silico*' fragmentation against the measured fragments for a compound. The potential of ion mobility for the separation of isomers and chromatographically co-eluting compounds will also be investigated.



Maged Sharaf, Chair Advisory Board & Director, CAMAG Scientific Inc.

Maged Sharaf, Ph.D., M.Sc., B. Pharm. is Chief Science Officer at the American Herbal Products Association (AHPA) where his duties include helping to set quality standards for the botanical products industry and providing guidance and advice to AHPA member companies, related organizations, government agencies, scientific publications, and the popular press.

Before joining the American Herbal Products Association, Dr. Sharaf spent 15 years with the United States Pharmacopeial Convention (USP) assuming several responsibilities including: director, Foods, Dietary Supplements and Herbal Medicines; principal scientific liaison and senior scientific liaison (botanicals), Standards Development; manager analytical services and scientist, Verification Programs; coordinator, Quality Control Laboratory; and project leader, Research and Development Laboratory.

During his tenure at USP, he directed and coordinated the activities of a cross-functional team leading to the launch of the Herbal Medicines Compendium, a resource of public standards for herbal ingredients used in traditional and herbal medicines. He co-developed the Dietary Supplements Compendium, a resource of public standards and guidelines for the dietary supplement industry. He developed botanical standards for inclusion in the United States Pharmacopeia-National Formulary (USP-NF). He participated in building the Dietary Supplement Verification Program, as a public health program, and the Dietary Ingredient Verification Program as a support program for the dietary supplement industry. Dr. Sharaf collaborated with experts from around the world representing governments, academia, pharmacopeias, research institutes, industry, and industry/trade associations.

Before USP, Dr. Sharaf taught undergraduate and graduate courses in pharmacognosy, and pharmaceutical sciences. He has preceding experience conducting bioanalytical assay development and validation, and human bioequivalence studies in support of the pharmaceutical industry; quality control testing of finished dosage forms; dosage forms manufacturing; and retail pharmacy.

Dr. Sharaf earned his Ph.D. in pharmacognosy from the School of Pharmacy, University of Pittsburgh; a master of sciences in pharmacognosy from Al-Azhar University, Egypt; and a bachelor in pharmacy and pharmaceutical sciences from Cairo University, Egypt.

Dr. Sharaf co-authored several scientific publications, is an invited speaker, and a reviewer for a number of scientific journals. He is a member of the Egyptian Association of Pharmacists, American Society of Pharmacognosy (ASP), ASP Constitution and By-Laws Committee, Society for Medicinal Plant and Natural Product Research (GA), American Chemical Society, AOAC International, and Washington Chromatography Discussion Group. He is a council member of the Specialty Committee of Traditional Chinese Medicines—Pharmaceutical Analysis, World Federation of Chinese Medicine Societies; advisory board member, National Institute of Standards and Technology (NIST) Dietary Supplement Quality Assurance Program (DSQAP); scientific advisor, American Herbal Pharmacopeia (AHP); member, USP Nomenclature and Labeling Expert Committee; advisory panel member, AOAC International Stakeholder Panel for Dietary Supplements; and a founding, advisory board member, chair Method Review Committee of the International Association for the Advancement of High Performance Thin Layer Chromatography.



The International HPTLC Association

Sharaf, M

CAMAG Scientific Inc., Wilmington, NC, USA

The International Association for the Advancement of High Performance Thin Layer Chromatography (HPTLC Association) is a non-profit organization that promotes the use of HPTLC in plant analysis and other analytical fields. This presentation will review the goals of the Association, its structure, roles, and on-going projects, including the production of the International Atlas of HPTLC Methods for Identification of Herbal Drugs as a recognized reference tool for quality control.



**Ultra High Performance Liquid Chromatography—High Resolution Mass Spectrometry
Guided Characterization of New Fusaricidins From *Paenibacillus* sp. MS 2379**

Shi Qiu¹, Bharathi Avula¹, Steven Guan², Mei Wang¹, Jian-Ping Zhao¹, Ikhlas A. Khan¹, Maud Hinchee², Xing-Cong Li¹

¹*National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, School of Pharmacy, The University of Mississippi, University, Mississippi 38677, USA;*

²*Agricen Sciences, 801 Hwy 377 S, Pilot Point, Texas 76258, USA.*

Paenibacillus sp. MS2379 is a highly efficient microbial strain producing fusaricidins, a class of cyclic lipodepsipeptides, that have demonstrated strong antifungal activities against a broad array of fungal pathogens. This study presents an integrated approach that combines UHPLC-HRESIMS and NMR techniques to analyze the fusaricidins in column fractions derived from an n-butanol extract of MS2379. As a result, a total of 48 fusaricidins were identified, with fusaricidins A and B being the major compounds accounting for 27 and 26%, respectively, of the total fusaricidins. In addition, 28 new minor fusaricidins (each with a content $\leq 2.5\%$ of the total fusaricidins) were characterized through careful analysis of the HRESIMS fragmentation patterns. The structural characterization of the new fusaricidins by HRESIMS was validated by follow-up isolation and NMR spectroscopic analysis of representative compounds. This study has shown that UHPLC-HRESIMS is a powerful tool for structure elucidation of cyclic lipodepsipeptides, and the structural diversity of the identified fusaricidins makes this microbial strain unique as a potential biocontrol agent for the treatment of fungal diseases in agricultural crops.

This work is supported by Agricen Sciences and the USDA Agricultural Research Service Specific Cooperative Agreement No 58-6408-2-0009.



Good Medicinal Plants Practices (GMPP) -Assuring Safety, Efficacy, and Quality of Botanical Products – From Field to Firm

Mohammad Kamil

Zayed Complex for Herbal Research & Traditional Medicine – DHL&ME – Department Of Health- Abu Dhabi, UAE

The challenges are innumerable and enormous, making the global botanical market unsafe. The presentation seeks to enlighten physicians, pharmacists, consumers, researchers and stakeholders in botanical medicine on the need to establish quality parameters in totality i.e. from the birth of the plant until it is dispensed to the patients either in crude form or in form of the finished products, along with highlight on major causes of inconsistency in botanical drugs.

To start with good agricultural practices (GAP), selection of medicinal plants, documentation, seeds and propagation materials, cultivation -which require intensive care and management with details of site selection, ecological environment, soil, irrigation and drainage, plant maintenance & protection, harvest and personnel. Good field collection practices (GFCP) includes technical planning, permission & collection permit, selection of medicinal plants for collection, collecting techniques & procedures and storage. Necessity of identification and severity causes due to taxonomic misidentification, substitution and adulteration and much emphasis on chemical standardization and its advantages. General format for standardization from preliminary examination, microbial contamination, assay, physico- chemical constants, fingerprinting, marker compounds, inter and intra species variation, extract validation in laboratory (GLP), current good manufacturing practices (CGMP), specification of finished botanical products, designing of stability studies, batch to batch reproducibility, adverse interaction, pharmacovigilance, inadvertent substitution and intentional adulteration with specific examples of prescription drugs, the imperceptible use of pharmaceutical analogues and constraints in quality control of botanical products as good marketing practice market (GMP).

This poster is based on complete steps involved in good medicinal plant practices (GMPP) along with modern perspectives of high throughput technology, suggesting random amplified polymorphic DNA finger printing and hyphenated NMR techniques as future of the botanical drugs.

Thanks are due to Department of Health, with special reference to Director-HLME Division- DOH, Under Secretary-DOH and Chairman -Department Of Health-Abu Dhabi-UAE for providing facilities and giving their kind permission to attend this Conference and present this poster.



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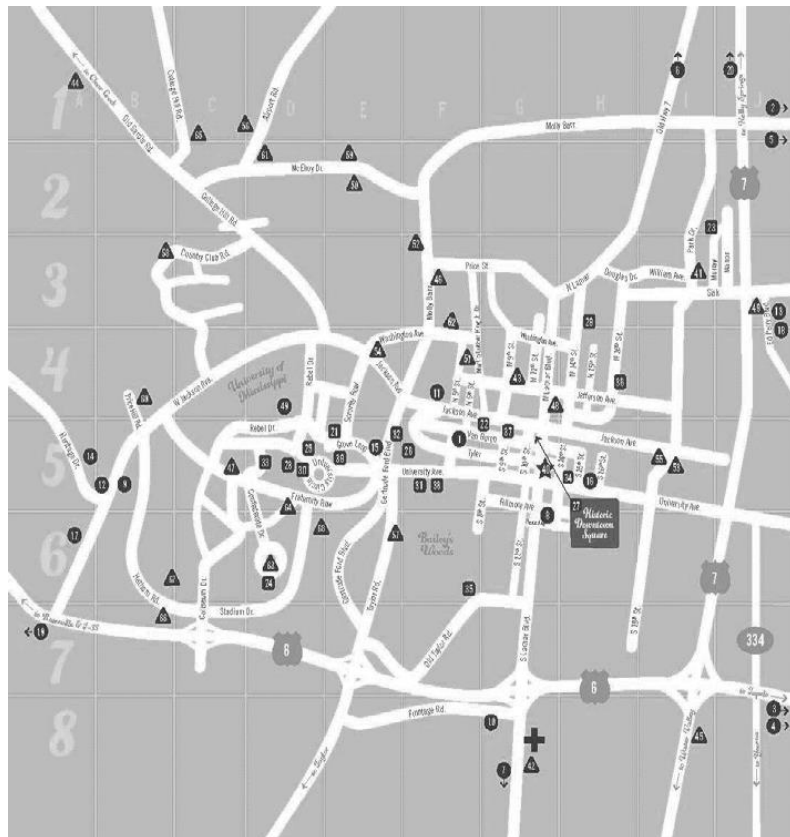
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 Hampton Inn, Ed Perry Blvd: 662-234-5565
 Marriott TownSuites, Ed Perry Blvd: 662-238-3522
 Hampton Inn, Jackson Avenue: 662-232-2442
 Holiday Inn Express: 662-236-2500

Shuttles - Mr. Audie Branch: 662-801-7890 or 662-236-1818

ICSB conference organizer 662-915-1090



Lodging

BED & BREAKFAST INNS

- 1 THE 512 (662) 234-4043
512 Van Buren Avenue (F5)
- 2 BLUE CREEK CABIN
(662) 238-2897
535 Hwy 30 E (U1)
- 3 THE BURROWS
(662) 236-3913 140 County
Road 287 (off Hwy 6 E) (U8)
- 4 CASTLE HILL RESORT
(662) 234-3735
20 County Road 413
(off Highway 6 East) (U8)
- 5 EMPTY NEST GUEST HOUSE
(662) 301-9369
81 County Road 231 (U1)
- 6 OAK HILL STABLES
(662) 381-0041 670 City Dr.
10 E. 10th St. (U1)
- 7 RAVINE (662) 234-4555
55 OR 321 (G8)
- 8 THE 2 OLD & BREAKFAST
(713) 927-1295
1405 Pierce Ave. (G8)

HOTELS & HOTELS

- 9 COMFORT INN
(662) 234-6000 1308
Jackson Avenue West (B5)
- 10 UNIVERSITY INN
(662) 234-9500
1101 Frontage Road (G8)
- 11 COURTYARD MARriott
catering soon (F4)
- 12 HAMPTON INN-WEST
(662) 232-2442
110 Heritage Drive (B5)
- 13 HAMPTON INN EAST
CONFERENCE CENTER
(662) 234-6565
103 Le Perry Blvd. (U1)
- 14 HOLIDAY INN EXPRESS
(662) 236-2500
1-800-HOLIDAY
112 Heritage Drive (B5)

Facilities

AREA CAMPGROUNDS

- 19 JOHN KYLE STATE PARK
(662) 487-1345
Hunting, fishing, hiking and
boating in nearby Sandis-
Reservoir and Holly Springs
National Forest (A7)
- 20 WALL DONEY STATE PARK
(662) 292-4211
Cabin, camping, fishing
and picnicking (U1)

Attractions

- 21 Barnard Observatory /
Center for the Study of
Southern Culture (C5)
- 22 Burns-Bailey Church (G5)
- 23 Cedar Oaks (D5)
- 24 Confederate Monument &
Cemetery (D6)
- 25 Fulton Chapel (D6)
- 26 Gertrude C. Ford Performing
Arts Center (F5)
- 27 Historic downtown Square (G5)
- 28 J.D. Williams Library (D5)
- 29 L.Q.C. Lamar House (H3)
- 30 Lycaeus/Civil Rights
Monument (E5)
- 31 Memory House (F5)
- 32 Oxford Depot (E5)
- 33 Park-Yates Chapel (D5)
- 34 The Powerhouse Community
Arts Center (H5)
- 35 Roman Oak (H3)
- 36 Saint Peter's Cemetery (H4)
- 37 Saint Peter's Episcopal
Church (D5)

Visitors Center

Facilities

- 38 THE INN AT OLE MISS
(662) 234-2311
University of Mississippi (C5)
- 39 OLE MISS MOTEL
(662) 234-2424
1517 University Avenue (H5)
- 40 SUPER 8 (662) 234-7013
2201 Jackson Avenue West (A6)
- 41 TOWNSHIP SUITES
MARriott (U3)
catering soon
- 42 University Museum /
Watkins Young House (F5)
- 43 Veterans Hall (E5)
- 44 Ament Park (U3)
- 45 English Memorial Hospital-North
Mississippi (G8)
- 46 Eukelade Reading Institute at
Iron Place (G4)
- 47 FNC Park (A1)
- 48 Grand Oaks Golf Course (H8)
- 49 Oxford Activity Center
John Leslie Tennis Courts (F3)
- 50 John M. Palmer Mitchell
Stadium Tennis Courts (C5)
- 51 Lafayette County Chancery
Building (G4)
- 52 Oxford Conference Center (D3)
- 53 Oxford Electric Department (E2)
- 54 Oxford Middle School (F4)
- 55 Oxford Police Department (F3)
- 56 Oxford State Park (D5)
- 57 Oxford-Lafayette County
Chamber of Commerce /
Economic Development
Foundation / Business Attraction
Program (E4)
- 58 Oxford-Lafayette County
Public Library (D5)
- 59 Oxford-University Airport (C1)
- 60 Oxford-University Stadium &
Swamp Field (E6)
- 61 Patricia C. Lamar Park (D3)
- 62 Post Office (E2)
- 63 Price Hill Park (B4)
- 64 Saxon / Cotton Complex (D2)
- 65 Stone Park & Recreation (F4)
- 66 Tootie's Coliseum (D4)
- 67 Turner Center (D5)
- 68 University Golf Course (C1)
- 69 University Soccer Fields (D1)
- 70 University Softball Fields (B6)
- 71 Vought-Henrieville
Stadium (D4)