22nd Annual OXFORD ICSB

April 15th - 18th 2024

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 controland adverse event reporting (AER) for botanical dietary supplements (BDS) and natural products
- Regulatory aspects with perspectives from government, manufacturers and trade associations

Conference Agenda

- Daily Schedule
- Speaker Bios
- Speaker Abstracts

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April 15, 2024

Dear Friends,

On behalf of the Organizing Committee, I would like to invite you to participate at April 14th -18th, 2024 for the 22nd International Conference on the Science of Botanicals (ICSB) being held jointly with the 7th World Congress of Medicinal Aromatic Plants (WOCMAP) to be held in beautiful Oxford, MS. The ICSB is organized by the National Center for Natural Products Research (NCNPR), University of Mississippi, and an FDA Center of Excellence.

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

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

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

Sincerely,

Ikhlas Khan

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

Day 1

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

Opening Session-OCC Auditorium

9:00-10:30 am

Noel Wilkins, Provost, *University of Mississippi* -Welcome On Behalf Of The University Of Mississippi

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

WOCMAP-Introductory Remarks

Cara Welch, 30 Years of Science-Based Regulation for Dietary Supplements

10:30-10:50 am Break

Session 1	**30 Years of DSHEA** Chair: Joe Betz, *Emeritus National Institute of Health*	OCC Auditorium			
10:35-11:00	**Mark Blumenthal, *American Botanical Council,*** HerbalGram at 40 Years: A Brief History of Issues and Milestones in the Evolution of the Modern Herb Movement				
11:00-11:25	**Bill Giebler, *Nutrition Business Journal* ,** The U.S. Herbs & Botanicals market. The DSHEA years through a market-sizing lens				
11:25-11:50	**Loren Israelsen , *UNPA,*** Botanical Education In The U.S. In The Post-DSHEA Era (1994-2024)				
11:50-12:00	**Conference Photography**-Meet At OCC Side Patio Across From Cedar Room Dining Hall				
12:00-1:00	Lunch	OCC Cedar Room	12:00-1:00	Lunch	
Session 2a	**Harnessing African's Herbal Wisdom: A Global Health Perspective** Michael Heinrich, *University of London*	OCC Auditorium	**Session 2b**	**Nurturing Quality Of Botanicals** Chair: Steven Dentali, *Dentali Botanical Sciences*	OCC Magnolia
1:00-1:30	**Ben-Erik Van Wyk, *University of Johannesburg,*** The True History Of Aloes And Beyond		1:00-1:15	**James Harnley, *United States Department of Agriculture,*** One-Class Modeling For The Authentication Of *Actaea racemosa* And Evaluation Of The Variation Between Botanical Reference Materials	
1:30-2:00	**David Katerere, *Tshwane University of Technology,*** African & Carribean Herbal Pharmacopieae-Curating Data For Product Development		1:15-1:30	**Maria Monagas, *United States Pharmacopeia,*** Understanding Plant To Extract Ratios Of Botanical Extracts And Their Implications In Product Labeling	
2:00-2:30	**Alvaro Viljoen, *Tshwane University of Technology,*** The Medicinal And Aromatic Flora Of South Africa – The Opportunity, Progress, And Challenges		1:30-1:45	**Vincent P Sica, *Proctor & Gamble,*** Characterization Of Ashwagandha Using A Multi-Detector Approach	
			1:45-2:00	**Brett Smith, *Young Living,*** Challenges Of Building Specifications For Essential Oils: And Industry Persepective	
			2:00-2:15	**Sara Handy, *Food and Drug Administration,*** Whole Genome Skimming To Gels: Development Of PCR Primers Targeting Toxic Plants In Support Of Food Safety	
			2:15-2:30	**Rahul Pawar, *Food and Drug Administration,*** A Survey Of Melatonin In Dietary Supplement Products Sold In The US	
2:30-3:00	Break		2:30-3:00	Break	
Session 3a	**Hiding In Plain Sight: Transparency In Botanical Supply Chains** Chair: Jason Mulligan, *Eurofins*	OCC Auditorium	**Session 3b**	**Unveiling The Power Of Botanicals** Chair: Shabana Khan, *University of Mississippi*	OCC Magnolia
3:00-3:30	**Cristina Amarillas, *Eurofins,*** Plenary Session: Trends Of Testing Botanicals At Third Party Labs		3:00-3:15	**Nicole Stevens, *DoTERRA,*** Evaluation Of A Lavender-Based Natural Product System For Sleep Support	
3:30-4:00	**John Travis, *NSF,*** Adulteration - Why Does It Still Proliferate?		3:15-3:30	**Rachel Mata, *University of Mexico,*** Zopilote: A Selected Species for The Treatment Of Type 2 Diabetes Mellitus In Mexico	
4:00-4:30	**Katarzyna Banaszewski, *Now Foods,*** Preventing Ingredient Adulteration To Maintain Botanical Integrity		3:30-3:45	**Mark Hamann, *Medical University of South Carolina,*** A Combination Of Clinical Studies With Chemical-Biochemical Informatics And Modeling To Arrive At The Active Pharmaceutical Ingredients Found In Botanical Supplements Using Frankincense As A Model	
			3:45-4:00	**Kashif Shamim, *University of Mississippi,*** Immulina Enhances Immune Resilience Against Influenza In Mouse Models	
			4:00-4:15	**Smita Mishra, *University of Delhi,*** Enrichment Of Glycyrrhiza glabra Root Extract For Phytopharmaceutical Ingredient Development As An Anti-Diabetic Drug Candidate	
Session 4	**2nd Annual JD McChesney Seminar** Chair: JD McChesney, *Cloaked Therapeutics, LLC-*	OCC Auditorium			
4:30-5:30	**Steve Duke, *University of Mississippi,*** Natural Producrts In Food And Agriculture				

6:00-8:00 **Reception/Mixer -Award Presentation: Outstanding Contribution In Natural Product (The Lyric 1006 Van Buren Ave., Oxford, MS 38655)**

Day 2

Session 5: The Nutrition Continuum And Whole Person Health-OCC Auditorium

Session Chair: Ikhlas Khan, *University of Mississippi*

8:00-8:30 am

Helene Langevin-*National Center for Complementary and Integrative Health* , The Nutrition Continuum And Whole Person Health

Session 6: Update And Future Perspectives From The FDA-OCC Auditorium

Session Chair: Gregory Noonan, Food and Drug Administration

8:30-10:00 am

Steven Musser, *Food and Drug Administration* , Research Gaps Limiting The Use Of New Alternative Methods (NAMs) In CFSAN's Regulatory Mission

Betsy Jean Yakes, *Food and Drug Administration,* What's Old Is New Again And Other Changes To Ingredients – Insights From The FDA

Troy Hubbard, *Food and Drug Administration,* Introduction To The Premarket Review Of Human Food Ingredients In The United States And Concepts In The Safety Assessment Of Novel Plant-Derived Ingredients

10:00-10:30 am Break

Session 7a	**IND: When And WhyThey Matter**	OCC Auditorium	**Sessioni 7b**	**Afro-Caribbean Healing Plants**	OCC Magnolia
	Chair: Gailen Marshall, *University of Mississippi Medical Center*			Chair: Ben-Erik Van Wyk, *University of Johannesburg*	
10:30-10:50	**Gailen Marshall, *University of Mississippi Medical Center,*** TBN		10:30-10:50	**Zella Palmer, *Dillard University,*** Afro-Caribbean Influences on the American South	
10:50-11:15	**Cassandra Taylor, *Food and Drug Administration,*** FDA Investigational New Drug (IND) Applications		10:50-11:10	**Anthony Richards, *Freelance,*** From Slave Foods To Superfoods Chapter 2	
11:15-11:40	**Nadina Jose, *Rutgers University,*** Navigating the IND Process to Get your Clinical Trial Started: Know the Regulations!		11:10-11:30	**Sonia Peters, *BERP,*** Revisiting The Dependendence On Indigenous Plant Resources To Inform Interventions For The SARS-COV-2 Pandemic	
11:40-12:00	**Question & Answer Session**		11:30-11:50	**Thera Edwards, *University of West Indies,*** African Plants In Jamaican Farms And Gardens	
			11:50-12:05	**Panel Discussion**	
12:00-1:00	Lunch	OCC Cedar Room	12:00-1:00	Lunch	OCC Cedar Room
Session 8a	**Uncovering Ingredients In Dietary Supplements**	OCC Auditorium	**Session 8b**	**Natural Products Sustainability And Bioeconomy**	OCC Magnolia
	Chair: Brian Schaneberg, *Illinois Tech Institute for Food Safety and Health*			Chair: Umesh Patil, *Dr. Harisingh Gour Vishwavidyalaya*	
1:00-1:25	**Shannon Aldrich, *Food and Drug Administration,*** FDA/ORA Health Fraud Updates		1:00-1:30	**Thomas Efferth, *University of Mainz*** , Cold-Water Extraction Of Nerium oleander Leaves Inhibits Cancer: From Bench To Bedside	
1:25-1:50	**Andrea Lindsey, *The Consortium for Health and Military Performance,*** Uncovering Dietary Supplement Ingredients: Education For Informed Use		1:30-2:00	**Michael Heinrich, *University of London*** , Herbal Medicines: We Care About Sustainability, But What Do We Need To Do To Get It Right.	
1:50-2:15	**Victor Navarro, *Jefferson Health*** , The Clinical Implications of Unlabeled Ingredients in Dietary Supplements		2:00-2:30	**Gaia Scalabrino, *Trinity College Dublin,*** Natural Products Ireland: From Bioactives To The Bioeconomy-A Systems-Based Approach	
2:15-2:30	**Question & Answer Session**				
2:30-2:50	Break		2:30-2:50	Break	
Session 9	**Botanical Dosage Forms: Disintegration and Dissolution Challenges**	OCC Auditorium			
	Chair: Adam Kuszak, *National Institute of Health*				
2:50-3:15	**Bill Gurley, *University of Mississippi,*** Dosage Form Performance Assessment Of Commercially-Available Soft Gel Capsules Containing Essential Oils				
3:15-3:40	**Natalia Davydova, *United States Pharmacopeia,*** USP Resources for Performance Testing Of Bothanical Dieteary Supplement Dosage Forms				
3:40-3:50	**Adam Kuszak, National Institute of Health,** New Natural Product Certified Reference Material Resources Supported By The NIH Office Of Dietary Supplements				
Session 10	**Essential Oils: Global Trades And Obstacles In Substantiating Claims**	OCC Auditorium			
	Chair: John Cavallo, *Citromax*				
3:50-5:20	**Fatih Demirci, *Anadolu University,*** *In-vitro* & *in-silico* enzyme inhibitions by essential oils **Russ Osguthrope, *DoTERRA,*** Current Obstacles Relating To Substantiating Essential Oil Dietary Supplement Claims And Proposed Solutions **Gyorgyi Horvath, *University of Pecs,*** Biological Activity Of Essential Oils – Focus On Antibiotic Resistance				
5:30-8:00	*POSTER SESSION*	OCC Auditorium	5:30-8:00	*POSTER SESSION*	
	Chair: Amar Chittiboyina, *University Of Mississippi*			Chair: Amar Chittiboyina, *University Of Mississippi*	
6:00-8:00		**Dinner-OCC Cedar Room**			

Day 3

Session 11a	**Cannabis: Current Status And Future Outlook**	OCC Auditorium	**Session 11b**	**Latest News On The Global Frankincense Scene**	OCC Magnolia
	Chair: Larry Walker, *Emeritus University of Mississippi*			Chair: Denzil Phillips, *Association of African Medicinal Plants Standards (AAMPS) and Global Frankincense Alliance (GFA)*	
8:30-8:40	**Cassandra Taylor, *Food and Drug Administration,*** Opening Remarks		8:30-8:50	**Anjanette De Carlo, *University of Vermont* and Denzil Phillips, *Association of African Medicinal Plants Standards (AAMPS) and Global Frankincense Alliance (GFA),*** Conservation Status Of Frankincense With Special Reference To Recent CITES Review And Recommendations	
8:40-9:05	**Patrick Cournoyer, *Food and Drug Administration,*** A New Way Forward For Cannabidiol (CBD) And Other Hemp Products		8:50-9:10	**Abdul Latif Khan, *University of Houston,*** Frankincense Tree Genomics And Resin Synthesis Pathway	
9:05-9:30	**Tahmina Khan, *Food Standards Agency,*** A provisional ADI for CBD – The UK assessment experience		9:10-9:30	**Stephen Johnson, *FairSource Botanicals,*** Leveraging Technology To Improve Governance And Impact In Frankincense Value Chains	
9:30-10:00	**Marilyn Huestis, *Thomas Jefferson University,*** Short & Long-Term Consequences Of Cannabis Intake & Differences Between Occasional & Chronic Frequent Cannabis Use		9:30-9:50	**Thomas Brendler, *Plantaphile,*** The State Of Indian Frankincense – An Update	
			9:50-10:05	**Panel Discussion**	
		10:00-10:30 am Break			
Session 12a	**Korean Ginseng: Safety, Efficacy And Neuroprotective Insights**	OCC Auditorium	**Session 12b**	**Navigating NDI Notifications**	OCC Magnolia
	Chair: Seikwan Oh, *Ewha Womans University*			Chair: Gregory Noonan, *Food and Drug Administration*	
10:30-11:00	**Laurie Dolan, *GRAS Associates,*** Safety In Use Of Korean Red Ginseng Extract As A Dietary Supplement And Food Ingredient: A Review Of Pre-Clinical, Clinical, And Traditional Use		10:30-11:00	**Shontell Wright, *Food and Drug Administration* ,** New Dietary Ingredient Notifications: A Key Step Prior to Launching a New Dietary Supplement in the United States	
11:00-11:30	**Yuan Shiun Chang, *China Medical University* ,** Antifatigue, Memory Enhancing and Blood Circulation Effects of Korean Red Ginseng		11:00-11:30	**Rebecca Adams, *NSF,*** Setting The Standard: Expert Insights On Best Practices And Safety Considerations For New Dietary Ingredient (NDI) Notifications	
11:30-12:00	**Seung-yeol Nah, *Konkuk University,*** Gintonin, Korean ginseng-Derived LPA Receptor Ligand, Alleviates Memory Dysfunctions via Non-Amyloidogenic Pathway and Blood-Brain Barrier Protections in Alzheimer's Disease Animal Model		11:30-12:00	**Question & Answer Session**	
12:00-1:00	Lunch	OCC Cedar Room	12:10-1:00	Lunch	OCC Cedar Room
Session 13a	**MoCRA: The Intersection Of Science And New Cosmetic Regulations**	OCC Auditorium	**Session 13b**	**Sustainable Crop Qualtiy Assurance Amid Climate Change**	OCC Magnolia
	Chair: Rick Kingston, *Safety Call*			Chair: Alvaro Viljoen, *Tshwane University of Technology*	
1:00-1:30	**Rick Kingston, *Safety Call,*** Impact Of MoCRA On Monitoring Botanical Safety		1:00-1:15	**MavisHong-Yu Yik, *University of Hong Kong,*** HerBChain, A Blockchain-Based Inforamtive Platform For Quality Assurance And Enhancing The Market Share Of Herbal Products	
1:30-2:00	**Jannavi Srinivasan, *Food and Drug Administration,*** Session E Overview of the U.S. Cosmetics Regulatory Framework		1:15-1:30	**Deshanie Rai, *OmniActive,*** Coming Full Circle On Sustainability -A Case Study Of The Alpinia galanga And Tagetes erecta Botanical Extracts	
2:00-2:30	**Brandi Reinbold, *National Science Foundation,*** MoCRA And The New Cosmetics GMPs		1:30-1:45	**Constance M Maxwell, *New Mexico Water Reseources Research Institute,*** Future Crops For An Increasinly Arid New Mexico: A Crop Selection Protocol To Support Farmer Resilience To Climate Challenges With High Economic And Culturally Valuable Herb, Medicinal And Aromatic Crops	
			1:45-2:00	**Ahmad Al Rawahi, *University of Nizwa,*** Frankincense: Bridging The Gap Between Research And Industry	
3:30-5:00	***ICSB Yard Games & Competition***				
6:00-8:00	**Bowling And Southern Fish & Chicken (Premier Lanes, 204 Commonwealth Blvd., Oxford, MS)**				

Day 4

Session 14	**The Science Behind Traditional Medicine** Chair: Michael Smith, *ISURA*	OCC Auditorium
8:30-9:00	**Bhushan Patwardhan, *Savitribai Phule Pune University,*** An Overview Of Ayush Research In India	
9:00-9:30	**Geetha Krishnan, *World Health Organization,*** The Gujarat Declaration Principles And Overview Of The WHO-GTMC's Evidence Workstream	
9:30-10:00	**Dennis Chang, *Western Sydney University* ,** Development Of A Novel, Standardised Herbal Formula For The Treatment Of Vascular Dementia	

10:00-10:30 am Break

Session 15a	**Advancing Botanicals Safety: New Approaches, Herb-Drug Interactions, And In Vitro vs. In Vivo Toxicological Insights** Chair: Amy Roe, Proctor & Gamble	OCC Auditorium	**Session 15b**	**The Importance Of Reference Standards** Chair: Thomas Brendler, *Univrsity of Johannesburg*	OCC Magnolia
10:30-11:00	**Cynthia Rider, *National Institute of Environmental Health Science,*** The Botanical Safety Consortium: Collaborative Effort to Improve Botanical Safety Methods		10:30-10:50	**Thomas Brendler, *Univrsity of Johannesburg,*** What Guides Natural Product Commercialization – Past And Present	
11:00-11:15	**Islam Husain, *University of Mississippi,*** Screening Of Medicinal Herbs To Predict The Potential Perpetrators Of Herb-Drug Interaction		10:50-11:10	**Kirsten Tripplett and Melissa Daoust, *Traditional Medicinals, Inc* ,** Before The Monograph: Developming Novel Identity Methods For Botanical Ingredients	
11:15-11:30	**Young Hee Choi, *Dongguk Univeristy, Seoul,*** Multifaced Factors To Cause Conflictitng Outcomes In Drug-Herb Interactions Mainly Focusing On Reverse Pharmacokinetics		11:10-11:30	**Cuiying Ma, *United States Pharmacopeia,*** Water Determination For Plant Materials By Titrimetric Method	
11:30-11:45	**Angela Calderon, *Auburn University,*** Evaluation Of Botanical Extracts For Cytochrome P450 Inhibition Mediated Drug Interaction		11:30-11:50	**TBN**	
11:45-12:00	**Siva Vanapalli, *NemaLife Inc.,*** AI-Assisted Organisim-On-Chip Platform For Evaulating The Quality Of Bothanical Herbs And For Bioactive Discovery				
12:00-1:00	Lunch	OCC Cedar Room			
Session 16	**Mushrooms: Ensuring Authenticity And Quality** Chair: Stefan Gafner, *American Botanical Council* & Sanem Hosbas Coskun, *National Institute of Health*	OCC Auditorium			
1:00-2:30	**Chris Hobbs, *University of Massachusetts,*** The Re-discovery of Fungi **James Kababick, *Flora Research,*** Authentication Of Commercial Mushroom Products **Natascha Techen, *University of Mississippi,*** Genetic Identification Of (Edible) Mushroom Species **Arun Krishnamurthy, *Purity IQ,*** Beyond Appearance: NMR Metabolomics For Mushroom Qulaity Assurance & Authenticity **Julie Daoust, *M2 Ingredients,*** Metabolite Profiling of Functional Fungi Strains Of *Hericium erinaceua* & *Cordyceps militaris* : Using Phenotypes, Untargeted Metabolomic By Mass Spectrometry And Cell-Based Assays				
2:30-3:30	**ICMAP-**General Assembly				
6:30 PM	**Closing Ceremony & Banquet (OCC Cedar Room)**				

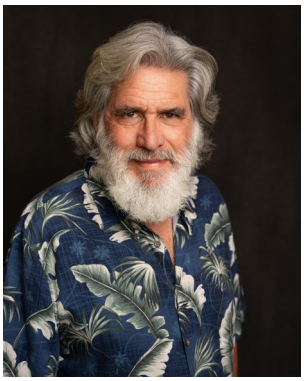
KEYNOTE SPEAKER

Cara Welch

Food and Drug Administration

Cara Welch**,** Ph.D., is the Director of the Office of Dietary Supplement Programs in FDA's Center for Food Safety and Applied Nutrition. Dr. Welch has been with FDA since 2014 in different roles working on regulatory, compliance, and scientific matters for the agency's regulation of dietary supplements. She also worked in the Office of the Commissioner as the Acting Special Assistant to the Deputy Commissioner for Policy, Legislation, and International Affairs providing expertise on agency level food policy issues. Prior to joining FDA, Dr. Welch was the Senior Vice President of Scientific and Regulatory Affairs at the Natural Products Association. Welch earned her Ph.D. in Medicinal Chemistry from Rutgers University working with traditional medicinal African plants.

Notes



Mark Blumenthal

American Botanical Council

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

HerbalGram at 40 Years: A Brief History of Issues and Milestones in the Evolution of the Modern Herb Movement

Blumenthal, Mark

American Botanical Council

Bill Giebler

Nutrition Business Journal

Award-winning author and journalist and seasoned natural products industry veteran—with experience in dietary supplement retail, healthy lifestyle mail order, and organic textiles product development—Bill Giebler manages Informa's Nutrition Business Journal (NBJ).

Since 1996, NBJ has offered business intelligence and thought leadership to all levels of the nutrition industry. At the core of this is the market-sizing data that shows the what, the where, and the why of the dietary supplement industry. That is, the ingredients (vitamins, herbs/botanicals, sports nutrition, specialty ingredients and minerals), the channels in which they are sold (natural foods stores, vitamin shops, mass market retailers, e-commerce, MLMs, and the practitioner channel), and the health conditions for which consumers are purchasing them.

This data is the backbone of the several reports published each year, including the perennial Supplement Business Report, Condition-Specific Report and the Global Supplement Business Report as well as more targeted reports focusing on specific ingredients, conditions or purchasing cohorts. Additionally, NBJ publishes 11 annual journal issues probing into key industry themes, including science and innovation, branding and marketing, sustainability, transparency, regulatory concerns and the impact of fraudulent practices.

NBJ's parent company, Informa, operates the industry's largest trade shows, including Vitafoods, SupplySide and Natural Products Expo West.

The U.S. Herbs & Botanicals market. The DSHEA years through a market-sizing lens

Giebler, Bill

Nutrition Business Journal

Loren Israelsen

UNPA

Mr. 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.

Botanical Education In The U.S. In The Post-DSHEA Era (1994-2024)

Botanical education in the United States has an interesting history. Initially, organizations like the U.S. Pharmacopoeia, naturopaths and the eclectic physicians of the time were primary sources of botanical knowledge. In time, a new aspirational genre of literature, such as Back to Eden and The School of Natural Healing, exhorted the public to return to herbs as medicines, often with a spritual or religious aspiration. A dark period was the publication of the Flexner Report in 1910 which sought to organize medicine and exclude the natural healting arts. World War II triggered a national effort to develop new types of drugs to meet the needs of warfare and in turn commercialization of such discoveries. A dramatic drop in pharmacognosy as a field of study at university's ensued. Attention shifted to synthetic chemistry and " wonder drug "pharmaceuticals. The passage of DSHEA reinvigorated public interest in botanicals with a great need for re-education of both healthcare professionals, consumers, and policy makers. This lecture will examine the growth of academic and popular botanical education since the passage of DSHEA, with examples taken from conferences, teaching programs, along with new nonprofit and trade organizations providing high botanical education.

Ben-Erik Van Wyk

University of Johannesburg

Ben-Erik holds the SARChI National Research Chair in Indigenous Plant Use at the University of Johannesburg. He is a plant taxonomist with a research interest in ethnobotany and economic botany. He has authored more than 380 scientific papers, 20 books (including ca. 50 editions and translations), 30 taxonomic revisions, and more than 100 new species and other taxa. Awards include the SAAB Gold Medal in 2015 and the M.T. Steyn Award in 2020. He has supervised 32 MSc and 22 PhD students (10 are now professors) and was re-ected annually as Chairman of the Indigenous Plant Use Forum since 1996.

The True History Of Aloes And Beyond

B.-E. Van Wyk

Department of Botany and Plant Biotechnology, University of Johannesburg, P.O. Box 524, Auckland Park 2006, Johannesburg, South Africa.

The recorded history of aloes dates back thousands of years, with early recordings in the Papyrus Ebers (ca. 1550 B.C.) and in Dioscorides's Herbal (1st cent. A.D.). Aloe has been used as a two-in-one medicine, not only by early explorers but also as a material of strategic military importance, with the yellow juice effective against the stomach problems of an army on the march and the white juice (gel) used to treat the wounds of battle. Aloe vera is the correct name for the "true aloe", as the specific epithet "vera" indicates. The origins of the plant are shrouded in mystery, but the species (probably a cultigen) is thought to be endemic to the Hajar Mountains of Northern Oman, from where it was dispersed to many parts of the Old World (and later via Portugal and Spain to the New World). It became so firmly established in the New World that many people are under the impression that Barbados aloes or Curaçao aloes are native to the Caribbean. There are many uncertainties and inaccuracies associated with the famous Aloe vera. This includes its history, correct name, traditional uses, efficacy, and aspects of modern-day commercial marketing.

David Katerere

Tshwane University of Technology

Prof David Katerere is the Research Platform Chair of Pharmaceutical and Biotech Advancement in Africa (PBA2) at Tshwane University of Technology. He is co-director of the recently established CSIR / TUT Cannabis Research Centre. He is the co-editor of the African Herbal Pharmacopiea (AfHP).

Prof Katerere holds a PhD in Pharmaceutical Science from the University of Strathclyde, Scotland. He has worked in pharmaceutical and biotech practice and research in the past 25 years in 4 countries on 3 continents. He has several inventions to his name including the nutraceutical, Niselo and CovidConnect App for use in clinical trials and post-recovery and KovaNix hand and surface sanitizer. He has published over 50 journal articles and is co-editor of three books: Ethnoveterinary Botanical Medicines (T&F) (2010), Systems Analysis Approach for Complex Global Challenges (Springer) (2018) and Traditional and Indigenous Knowledge for the Modern Era (T&F) (2019).

He is a member of advisory committees of SAHPRA and the Global Health Supply Chain Consortium, co-founded by faculty at University of Michigan and University of Southern California. Prof Katerere teaches and researches across the pharmaceutical and biotech value chain including product development from medicinal plants (for food, nutraceuticals and medicines) and clinical testing, substandard and falsified medicines / vaccines and medicine governance.

African & Carribean Herbal Pharmacopieae-Curating Data For Product Development

David R. Katerere

This presentation aims to provide a comprehensive examination of the Africa Herbal Pharmacopoeia (AHP) and the Caribbean Herbal Pharmacopoeia (CHP), highlighting their respective similarities and differences in the realm of traditional herbal medicine and product development. Both pharmacopoeias are important initiatives in curating indigenous knowledge related to medicinal plants. They are valuable resources for researchers, healthcare practitioners, and industry.

This presentation will outline the methodological and logistical approaches employed in putting together monographs and the challenges faced. Furthermore, the comparative analysis will explore the regional nuances that shape the content of each pharmacopoeia, considering factors such as local traditions, ecological variations, and historical influences. This will be illustrated by way of case studies on a couple of monographs from each pharmacopiea.

The over-arching role of pharmacopiea is to create standards which can be used by industry for quality control, product development and sustainable trade. In addition, the pharmacopiea initiative should also serve as a platform to advocate for clinical testing and standardization of herbal medicinal products from the two regions. These elements have hitherto been neglected and without such initiatives we may lose important ecological and cultural knowledge associate with these genetic resources.

Alvaro Viljeon

Tshwane University of Technology

Born in 1969, Pretoria South Africa. Completed a BSc, BSc Hons. (cum laude) and MSc (cum laude) in Botany at Stellenbosch University (SA). 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 ninety 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 >300 peer reviewed papers (h index 52) mostly on the phytochemical exploration and pharmacological 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), Phytochemistry (Elsevier) and is the Editor-in-Chief of Journal of Ethnopharmacology (Elsevier) since 2017. In October 2013 Alvaro was awarded the National Research Chair in Phytomedicine a position which he holds concurrently as Director of the SAMRC Herbal Drugs Research Unit in South Africa.

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The Medicinal And Aromatic Flora Of South Africa – The Opportunity, Progress, And Challenges

AM Viljoen [a,b]

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South Africa is considered to be one of the most biodiverse areas in the world which includes an impressive number of medicinal and aromatic plants. This unique botanical heritage and the indigenous knowledge systems of various ethnic groups creates a perfect research opportunity for pharmacognosy-based studies. While there are significant opportunities in medicinal plant research in South Africa, there are also challenges such as “biopiracy”, unsustainable harvesting practices, and the need for capacity building in research and development. Addressing these challenges requires a multidisciplinary approach involving stakeholders from government, academia, industry, and local communities. The pharmacognosy research landscape in South Africa will be discussed and examples from our own research group presented to illustrate the importance of evidence-based ethnopharmacological studies. Our contribution to documenting the safety, efficacy and quality of indigenous medicinal and aromatic plants will be discussed.

Collaboration between different sectors and a commitment to sustainable practices are essential for harnessing the full potential of medicinal plants in South Africa

One-class modeling for the authentication of Actaea racemosa and evaluation of the variation between botanical reference materials

James Harnly

One-class modeling based on soft independent modeling of class analogy (SIMCA) is a simple but powerful method for comparing the chemical composition of botanical materials using non-targeted chromatograms (GC, LC) or spectra (IR, MS, NIR, NMR). The methodology is available on any commercial chemometric platform. Authentication is based solely on the characteristics of the botanical material of interest. Detection of adulteration is determined for each variable and requires no identification of adulterants. Some highly characterized botanical reference materials (BRMs) may account for species, cultivar, and year and location of harvest while more generic BRMs may have minimal characterization. All of these factors can result in variability in the chemical composition that may lead to statistically significant differences when applying one-class modeling. Using flow injection mass spectrometry (FIMS), principal component analysis (PCA), and factorial multivariate analysis of variance (factorial mANOVA), statistically significant (95% confidence limit) differences in chemical composition were found between 4 sources of A. racemosa BRMs and between Actaea species. Interestingly, the variability of 6% of the mass variables were found to be quantitatively conserved (variability of <10%) and reduced the compositional differences between the 4 sources of root BRMs but reduced discrimination between species. Weighting of the variables based on their ability to discriminate between species increased differences between the 4 sources of BRMs. Frequency distribution plots provided the best means for understanding the impact of these variables on cross-validation, sensitivity, and specificity. Sensitivity ranged from 94% to 97% and specificity ranged from 21% to 89%.

Notes

Understanding Plant To Extract Ratios Of Botanical Extracts And Their Implications In Product Labeling

Maria Monagas, Thomas Brendler, Josef Brinckmann, Steven Dentali, Stefan Gafner, Gabriel Giancaspro, Holly Johnson, James Kababick, Cuiying Ma, Hellen Oketch-Rabah, Pilar Pais, Nandu Sarma, and Robin Marles

Dietary supplement current good manufacturing practice (cGMP) in the U.S. requires the establishment of quality parameters for each component used in the manufacture of a dietary supplement to ensure that specifications for the identity, purity, strength, composition, and limits on contaminants are met using scientifically valid methods of analysis. However, specifications for botanical extracts (including fungal and algal extracts) routinely include additional data that are not amenable to verification through analytical methods. Such descriptive information may include Plant to Extract ratios, which are ratios of the quantity of botanical article used in the manufacture of the extract to the quantity of extract obtained. Plant to Extract ratios can be misleading when their meaning is not clearly understood. Plant to Extract ratios do not completely describe botanical extracts because other important factors influence the make-up of final extracts, such as the quality of the starting raw material (as defined by pharmacopeial standards), extraction solvent(s) used, duration and temperature of extraction, and percentage and type of excipients present. Other important qualitative descriptions may include constituent "fingerprinting." In addition, Plant to Extract ratios are often misused as a measure of extract strength for dosage calculations. This oral presentation covers the effort of the USP Botanical Dietary Supplements and Herbal Medicine Expert Committee to clarify the meaning of Plant to Extract ratios that resulted in the Frontiers publication "Understanding plant to extract ratios in botanical extracts", Front Pharmacol. 2022; 13: 981978 (https://doi.org/10.3389/fphar.2022.981978). Examples of common misconceptions will be provided, and special emphasis will be given to the proper use of Plant to Extract ratios in describing and labeling botanical extract ingredients and finished products.

NOTES

Characterization Of Ashwagandha Using A Multi-Detector Approach

Sica VP, Baker TR

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

Botanicals are complex mixtures that present unique analytical challenges. A multi-detector chromatographic approach can provide accurate, constituent-based data to ensure proper identification and quantification of botanicals. These data are often used to help drive in silico safety assessments to identify suspected toxicants and assess the potential for deleterious effects using structure activity relationships.

To showcase this approach, ashwagandha extracts were characterized to determine authenticity and to guide the necessary toxicological studies. To ensure the full constituency of the extracts are evaluated, a multi-detector system (UHPLC-PDA-CAD-HRMS) was employed and subjected to a comprehensive chemical constituent identification (CCID) process. All of the constituents above a threshold of toxicological concern (TTC) were quantified and identified. Identification was performed using HRMS and comparing fragmentation data to standards, literature, and/or online databases. These identifications were used to provide data for an in silico safety assessment. These data guide or obviate the need for classical in vitro and in vivo safety studies.

NOTES

Challenges Of Building Specifications For Essential Oils: And Industry Persepective

Brett L. Smith[1], Christopher R. Bowerbank[1], Richard E. Carlson[1]

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The rise in essential oil popularity is creating unprecedented demand worldwide. With the increased demand, the worldwide supply chain is challenged with maintaining consistent quality standards. Some essential oil producers may be motivated to use new and innovative methods to alter their products to meet quality standards and extend their current oil supplies. Climate change is also affecting growing season conditions, leading to changes in essential oil composition compared to past harvests. These factors create challenges for industry in establishing updated quality and commerce specifications beyond traditional ISO, AFNOR, and pharmacopoeia standards for essential oils.

To meet these supply chain challenges, Young Living Essential Oils has established relevant processes and testing procedures to establish current essential oil specifications which incorporate these worldwide economic and agricultural challenges. To address potential adulteration, modern analytical techniques including chiral gas chromatography (CGC) and gas chromatography-isotope ratio mass spectrometry (GC-IRMS) are increasingly used to verify that authentic essential oils are free from dilution or substitution with a similar essential oils or synthetic components.

Some keys to a robust essential oil supply chain include direct partnerships and transparent discussions around product specifications with growers. Inherent is the need to directly understand the environmental conditions under which crops are grown, the potential impact on crop harvests, essential oil yield, and the potential impact on worldwide supply. The importance of building impactful relationships directly with growers will be discussed.

With resulting natural variation of crops due to current environmental factors, the utilization of essential oil standards as guidelines rather than strict specifications will also be discussed.

NOTES

Whole Genome Skimming To Gels: Development Of PCR Primers Targeting Toxic Plants In Support Of Food Safety

Sara M. Handy, Elizabeth Sage Hunter, Sydnee Fo, Robert Literman, Weili Xiong, and Jennifer Wolny

Safeguarding consumer well-being and maintaining public health necessitates ensuring that Food and Drug Administration (FDA)-regulated products do not contain toxic ingredients or contaminants. This can be particularly challenging when dealing with complex mixtures of botanical ingredients, where there is a need to either confirm the identity of declared botanical ingredients or determine if any undeclared botanical ingredients are present. Developing DNA based methods for toxic plant species is beneficial to help effectively and efficiently monitor FDA-regulated products. Digitalis, known for its colorfulness and medicinal properties, possesses toxic compounds which, even in minute quantities, can cause adverse human health effects. Recent research conducted by Hunter, Literman, and Handy (Foods, 2021), leveraged advanced data analyses and single nucleotide polymorphisms (SNPs) to identify toxic Digitalis species. The present study aims to capitalize on the SNP library established in their work to develop a rapid PCR assay to detect Digitalis species. Ten pairs of PCR primers, designed for this project from our previous data, were tested against 60 vouchered specimens. The two best primer sets were used in food matrix assays that included botanically complex teas and spices. Spiked samples, various plant tissues, limit of detection, and comparison to toxin abundance by chemical methods were also examined. This study enhances the range of DNA-based identification tools available to FDA, thereby contributing to the agency's efforts in promoting consumer safety.

NOTES

A Survey Of Melatonin In Dietary Supplement Products Sold In The US

Pawar, RS, Coppin JP, Khanna S, Parker CH

In the United States, melatonin products are widely available to consumers as dietary supplements. During the past few decades, melatonin products have gained increased popularity primarily as a sleep aid, with a variety of product forms available for different age groups of consumers. Recent reports have highlighted a rise in melatonin ingestion among children reported to poison control centers across the U.S. The increased use of melatonin-containing dietary supplements and reported deviation from labeled quantities has emphasized the need for additional research to better understand products in the marketplace.

The objective of this work was to measure the melatonin content in products sold as dietary supplements and targeted towards children, evaluate if the analytical method is accurate across different product forms and to determine if product forms have an impact on melatonin stability. From a list of 200 products identified through searches on internet and dietary supplement databases, 110 products were randomly selected for the study. Melatonin concentration and percent label claim was evaluated to inform safety assessments and investigate potential factors for underreported concentrations, including product stability and matrix influences. Sample preparation was optimized for analyte extraction from diverse product types such as gummies, liquids, and tablets using a Quick, Easy, Cheap, Effective, Rugged, and Safe (QuEChERS) procedure with identification by liquid chromatography-tandem mass spectrometry (LC-MS/MS). The targeted method was validated for the qualitative determination of serotonin and quantification of melatonin, N1-acetyl-N2-formyl-5-methoxykynuramine (AFMK), and N1-acetyl-5-methoxykynuramine (AMK) in dietary supplements labeled to contain melatonin and applied to product analysis. Although the first step in this study was the quantification of melatonin and evaluation of label claim, initial results on product stability will also be discussed using AFMK and AMK as markers of melatonin stability.

NOTES

Cristina Amarillas

Eurofins

Cris Amarillas, Ph.D., is the Chief Science Officer, Botanicals at Eurofins Food & Feed. She serves as the scientific botanical resource, providing technical direction across food chemistry testing and quality ensuring continued ISO 17025 compliance. She actively participates in developing methods, trouble shooting and mentoring scientists.

Before joining Eurofins, Dr. Amarillas spent a year consulting for dietary supplements, drugs/OTC, cosmetics, and food brands and vendors. Prior to that, she spent 12 years with Traditional Medicinals in Quality and R&D. She oversaw daily testing and disposition of components and finished products, while providing technical and herbal direction. She led and participated in stages of product development from formulation through commercialization. She established the supplier quality team. She worked closely with regulatory, marketing and procurement.

Dr. Amarillas holds her Ph.D. in Chemistry from Stanford University. She is a clinical herbalist, completing two certificate programs at the California School of Herbal Studies (CSHS) in Northern California.

Cris brings her passion about herbalism, botanical chemistry, regulatory frameworks, and industry applications to all aspects of her professional life. She continues to teach at CSHS.

Plenary Session: Trends Of Testing Botanicals At Third Party Labs

Cristina Amarillas

Eurofins

John Travis

NSF

Adulteration - Why Does It Still Proliferate?

Adulteration of dietary supplements continues to plague the industry, but why? There are many factors which impact why and how the finished product in that home delivered package or on that retail store shelf become adulterated. Some are unintentional and attributed to inadequate specifications. Many times, the adulteration is intentional and designed to catch the victim unawares. This presentation will describe the many ways in which the craft of adulteration is plied by its perpetrators.

Katarzyna Banaszewski

Now Foods

Katie Banaszewski, Senior Director of Quality at NOW Foods, strongly believes great things are never done by one person, but by a team of people. Driven by curiosity and her passion for science, she joined NOW in 2013 with a plan to transform the analytical capabilities of their labs from just being one of the industry's best, to being the most capable in-house testing lab, by far. During her tenure at NOW, she has led the development and implementation of a routine pesticide residue monitoring program, among other achievements. She plays an integral role in continually expanding the company's analytical capabilities. Katie focuses on recent issues within the dietary supplement industry and ensures NOW remains the industry leader in holding high-quality standards.

Preventing Ingredient Adulteration To Maintain Botanical Integrity

Katarzyna Banaszewski
Sr. Director of Quality, NOW Health Group

The growing popularity of botanical products combined with the challenges of the supply chain to meet the ingredient demand has created opportunities for dishonest companies to take advantage of their clients for financial gain. Suppliers and manufacturers must comply with cGMPs (current Good Manufacturing Practices), specifically when it comes to the basic requirements of properly identifying crude botanicals in whole, cut, or powdered form, as well as botanical extracts and essential oils. Despite this regulatory requirement, a large portion of botanical ingredients and products sold in the marketplace are adulterated. Popular ingredients in high demand are intentionally substituted, diluted, or "fortified" with lower-cost substitutions. While most of the time laboratory assays can detect adulterants, some adulteration techniques are very sophisticated so the ingredient can mimic the physical properties or chemical composition of the genuine botanical and deceive the analytical methods used for botanical authentication. Furthermore, when a supplier faces a material rejection due to adulteration, the material is often sent back to the supplier and sold to another customer, with potentially lower quality standards or ability to detect the adulterant. Despite continuous efforts of the natural product industry, there are still ongoing challenges with analytical methods allowing laboratories to reveal mischief, and there is a need for guidance regarding the disposition of material that is adulterated or irreparably defective.

Evaluation Of A Lavender-Based Natural Product System For Sleep Support

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Introduction

Sleep is an important foundation of health, yet the U.S. Centers for Disease Control (CDC) notes that about 30% of adults to not get the recommended minimum of 7 hours' sleep per night. Prescription treatments may help, but they carry risks such as side-effects, dependency, and medication interaction. Natural botanical extracts are a therapeutic possibility for improving sleep quality, but additional research is needed on their efficacy and safety. A system of natural products based on lavender was developed and tested in a human clinical study to evaluate effect on sleep, blood and safety markers, and gene expression modulation after six weeks of use.

Materials and Methods

A single-blind, progressive study was carried out in 42 healthy participants, males and females, ages 35-50. Following baseline sample collection, three lavender-based products (an essential oil blend for diffusion, a solid stick for topical application, and a supplement for internal consumption) were added sequentially and participants were monitored for efficacy and safety. Participants wore fitness trackers and filled out weekly surveys detailing their experience. Sample collection was repeated at the end of six weeks.

Results

Fitness tracker data showed that the amount of sleep for participants using the product system was not significantly increased (about 10 additional minutes). However, subjective surveys suggested that the quality of sleep and the perception of wellbeing improved when participants were using the lavender-based products. Gene expression analysis revealed 94 genes that were significantly up- or down-regulated as participants used the product system. Many were related to cellular processes, and several had potentially direct ties to circadian rhythms and sleep pathways (ZMIZ2, LRP5, and DNMT3B). Epigenetic clocks, including PC Horvath 2, PC Hannum, PC PhenoAge, PC GrimAge, OMICmAge, and systems clocks, showed that using the product system decreased age acceleration values significantly. Differential expression was noted between study participants whose sleep patterns were regular versus participants who got similar amounts of sleep but had inconsistent patterns. The most common adverse events reported using the products were headache, digestive upset, and vivid dreaming. No serious adverse events were reported.

Conclusion

In this pilot study, a collection of lavender-based products showed promise in improving sleep quality and outcomes for healthy participants. Overall, the products appeared to be well tolerated. Additional research is needed to understand safety and efficacy in larger populations, over longer periods of time, and when used in combination with other medications. It will also be important to understand the effects these products may have in consumers with sleep disorders or other diseases.

NOTES

Zopilote: A Selected Species for The Treatment Of Type 2 Diabetes Mellitus In Mexico

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A decoction of the seeds of "zopilote (Swietenia humilis Zuccarini, Meliaceae) is a popular herbal remedy for treating type II diabetes in Mexico. The traditional preparation (SHD) was not toxic when tested with the Lorke method, but SHD (31.6, 100, and 316 mg/kg) showed noted hypoglycemic when tested in healthy and hyperglycemic [NA (50mg)-STZ (150 mg/kg)] ICR mice Furthermore, during an oral glucose tolerance test, the decoction also significantly reduced the postprandial peak suggesting an augmentation in glucose utilization. The antihyperglycemic, hypoglycemic, and hypolipidemic effects of SHD in Sprage-Dawley rats (230 g) with metabolic syndrome (MS) induced by fructose were also assessed. The control group (C1; n = 6-8) received regular rodent chow and water. The fructose groups (FIMS1-FIMS3; n= 6-8) were fed a regular diet and 10 % fructose drinking water for 12 weeks. Since week 13, groups FIMS2 and FIMS3 were treated daily with SHD (100 and 316 mg/kg) for a week; the treatments provoked a significant hypoglycemic effect and reduced serum triglycerides without significant changes in fasting insulin levels or body weight.

Interestingly, the hepatic glycogen content increased, and the abdominal fat decreased compared to rats fed only with fructose. Altogether, these results suggested that the decoction has an insulin-sensitizing mechanism since it provoked a significant reduction in abdominal fat, serum triglycerides, the postprandial peak during an oral glucose tolerance test, and augmentation of glycogen content, without changes in fasting insulin levels. The active principles turned out to be the limonoids of the plant, which also displayed hypoglycemic and antihyperglycemic effects and increased insulin actions in mice. The mode of action of the main limonoid, 2-hydroxy-destigloyl-6-deoxyswietenine acetate, was due to a partial blockade of sensitive K+-ATP channels, a serotonergic modulation on 5-HT2 receptors, insulin secretion, inhibition of hepatic glucose phosphatase, and stimulation of muscle glucose uptake.

Acknowledgements:

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NOTES

A Combination Of Clinical Studies With Chemical-Biochemical Informatics And Modeling To Arrive At The Active Pharmaceutical Ingredients Found In Botanical Supplements Using Frankincense As A Model

Nancy Klauber-DeMore[1] and Mark T. Hamann[2]

Frankincense and the Boswellic acids has been shown to suppress tumor proliferation in vitro with a strong clinical trial safety profile in patients with inflammatory diseases. We performed a Phase Ia window of opportunity trial of Boswellia serrata (B. serrata) in patients with breast cancer to evaluate its biologic activity and safety. Patients with invasive breast cancer were treated pre-operatively with B. serrata (2400 mg/day PO) until the night before surgery for a median of 11 days (SD 6 days; range: 5–23 days). Paraffin-embedded sections from pretreatment diagnostic core biopsies and post-treatment surgical excisions were evaluated using a tunnel assay and immunohistochemistry staining with Ki-67 antibodies. A non-intervention retrospective control arm consisting of core and surgical tissue specimens from untreated patients was used to compare patients treated with B. serrata. The change in proliferation and apoptosis between diagnostic core specimens and surgical specimens was compared between the control and treatment groups using a two-tailed paired t-test. Twenty-two patients were enrolled, of which 20 received treatment, and 18 had sufficient tissue for IHC. There was an increase in percent change in proliferation from core biopsy to surgical excision in the control group (n = 18) of 54.6 ± 21.4%. In the B. serrata-treated group there was a reduction in proliferation between core biopsy and excision (n = 18) of 13.8 ± 11.7%. This difference was statistically significant between the control and B. serrata-treated groups (p = 0.008). There was no difference in change in apoptosis. There were no serious adverse events related to the drug. Thus Boswellia serrata inhibited breast cancer proliferation and was well-tolerated in a Phase Ia window of opportunity trial. An in vitro study of the extract and purified molecules failed to yield a single API thus we completed a global assessment using molecular modeling approaches of all the published structures as

NOTES

Immulina Enhances Immune Resilience Against Influenza In Mouse Models

Shamim K, Mir TM, Zhang J, Khan SI, Tripathi SK, Khan IA, Marshall GD, Ashfaq MK, Pugh ND

Influenza remains a persistent global health concern. The University of Mississippi Botanical Dietary Supplements Research Center is focused on investigating the use of Immulina, an oral supplement derived from Limnospira (formally Arthrospira), as an immune-based antiviral resilience promotor against influenza. Immulina concentrates the level of immunomodulatory activity due to Braun-type lipoproteins.

The objective of this study was to generate preclinical data on Immulina's efficacy in a rodent model of experimental influenza infection utilizing 3 distinct treatment regimens: prophylaxis, prodromal, and therapeutic. The prophylactic model involved administering Immulina only for the 2 weeks before viral infection, while the prodromal model entailed administering Immulina starting on the same day as infection (prior to the emergence of viral illness symptoms). In contrast, the therapeutic model involved feeding Immulina starting 3 days post-viral infection (at the onset of symptoms). Immulina (25, 50 and 100 mg/kg body weight) was orally administered to both genders of mice.

Compared to the infected control mice, animals fed Immulina exhibited statistically significant resilience against viral illness in the prophylactic and prodromal models (improved clinical scores, reduced body weight loss, decreased lung/body weight ratio and lower lung viral load). The effects are likely mediated through the host immune system since the level of various cytokines (IL-6 and IFN-gamma) were significantly increased in lung tissue. Substantially less / minimal effect was observed in the therapeutic model.

The results of this study indicate that Immulina was most effective at enhancing immune antiviral resilience if administered before or soon after initial infection but may not be effective if given after the onset of symptoms. The results will help to optimally design future clinical trials.

NOTES

Enrichment Of Glycyrrhiza glabra Root Extract For Phytopharmaceutical Ingredient Development As An Anti-Diabetic Drug Candidate

Smita Mishra[1,2], Ritu Tiwari[1], Varsha Mehra[2]

[1] Indian Pharmacopoeia Commission, Ministry of Health & Family Welfare, Government of India; [2] Department of Biomedical Sciences, Shaheed Rajguru College of Applied Sciences for Women, University of Delhi, Delhi; Presenting author: Dr. Smita Mishra, Indian Pharmacopoeia Commission, Ministry of Health & Family Welfare, Government of India, Ghaziabad – 201002

Background: Herbal drugs are gaining popularity in the present scenario due to the major concerns arising with the synthetic drugs. However, their acceptability in the pharmaceutical industries and medical field is still questionable because of the lack of sufficient scientific evidences. To tackle this problem, CDSCO has defined a separate class of drugs, known as Phytopharmaceutical Ingredients (PPI), which governs purified fractions of medicinal plant part with minimum four bioactive compounds attributing pharmacological and therapeutic activities.

Objective: Indian Pharmacopoeia Commission has conducted a research study on Glycyrrhiza glabra roots, to prepare its PPI monograph to address diabetes.

Materials and Methods: In-vitro and in-silico antidiabetic activity of the plant extract was conducted along with phytochemical profiling via biochemical tests. Extract enrichment was done by using phytoconstituents elution and purification by chromatographic methods. Detection and quantification of four bioactive markers viz., liquiritin, glycyrrhizin, formononetin, and glabridin was done by various high throughput methodologies viz., HPTLC, HPLC, FTIR, and NMR.

Results: We have successfully enriched the total content in the extract by 12.87% w/w, assayed by HPLC. The enriched extract consisted liquiritin and glycyrrhizin in highest content, i.e., 5.95% and 4.33% w/w respectively, followed by glabridin and formononetin by 2.25% and 0.34% w/w respectively. The prepared extract showed excellent inhibitory effect on α-amylase enzyme and in-silico study showed liquiritin and glycyrrhizin being potent anti-diabetic compounds.

Conclusion: This study is a scaffold for upcoming PPI monograph designing and IP-PPIRS development of Glycyrrhiza glabra in Indian Pharmacopoeia 2024 (IP-2024).

NOTES

Steven Duke

University of Mississippi

Stephen Duke received his Ph.D. in botany and biochemistry from Duke University in 1975, after which he joined the Agricultural Reseach Service (ARS) of the United States Department of Agriculture (USDA). He was Director of the Southern Weed Science Laboratory of ARS from 1987 unitl 1996 and was Research Leader of the ARS Natural Products Utilization Research Unit in Oxford, Mississippi from 1996-2020. After retirement from USDA, he became a Principal Scientist at the National Center for Natural Products Research of the School of Pharmacy, Univ. Mississippi. He is best known for his research on herbicide and natural phytotoxin modes of action and natural products for pest management. He is also an authority on herbicide-resistant crops and weeds and allelopathy (the chemical ecology of plant/plant interactions). He has published over 500 peer-reviewed papers that have resulted in a Web of Science h-index of 72. He has written or edited twelve books. His past elected scientific society offices include President of the Weed Science Society of America, the International Allelopathy Society (IAS), and the International Weed Science Society, as well as Chair of the Agrochemical Division of the American Chemical Society (ACS). His many awards include Fellow of ACS and of the American Association for the Advancement of Science, the Molisch Award (IAS), honorary doctorate from the University of the Basque Country (Bilbao, Spain), and inductee into the USDA, ARS Hall of Fame. He has been Editor-in-Chief of the Society of Chemical Industry journal Pest Management Science for more than 12 years. He continues to conduct research on both natural and synthetic compounds as pesticides with emphasis on discovery of compounds with new molecular targets.

Natural Producrts In Food And Agriculture

Stephen O. Duke

National Center for Natural Products Research, School of Pharmacy, University of Mississippi

Before the National Center for Natural Products Research (NCNPR) existed, I was Director of a USDA weed management lab. Two of my interests were natural products as herbicides and the chemical ecology of weed/crop interactions (allelopathy). Dr. James McChesney and I had several conversations about his vision for the NCNPR on the University of Mississippi campus. I was very interested in becoming a part of this, as his plan was to have a USDA lab that would study natural products for use in food and agriculture as part of the center. The USDA Agricultural Research Service established the Natural Product Utilization Research Unit (NPURU) as part of the NCNPR in 1996, when I arrived here. Most NPURU research has dealt with the use of natural products for pest management, but some of the most successful work has been on nutraceuticals. The late Agnes Rimando published extensively on the health benefits of pterostilbene, generating several patents. Her work, much of it with Univ. of Miss. colleagues, showed beneficial effects of pterostilbene as an antioxidant, antiaging, anti-cholesterol, anticancer, and antidiabetic compound. 2-Methylisoborneol from cyanobacteria bioaccumulates in the flesh of aquaculture-produced fish. Collaborative work of NCNPR and NPURU led to the patenting of a selective cyanobactericide that selectively kills cyanobacteria without harming beneficial green algae. This product worked well in field trials in eliminating MIB of harvested fish. Several patents have been obtained for novel natural-product-based fungicides, herbicides, insecticides, and insect repellents. This work led to the discovery of much-needed new molecular target sites of pesticides and determination of one that was unknown for many years. Long-range research is being conducted to produce crops that produce their own herbicides. Current cooperation extends to novel natural product-based pesticides that are being patented for consideration by the pest management industry.

Helene Langevin

National Center for Complementary and Integrative Health (NCCIH)

Helene M. Langevin, M.D., is director of the National Center for Complementary and Integrative Health (NCCIH) at the National Institutes of Health (NIH).

As NCCIH director, Dr. Langevin oversees the U.S. Federal government's lead agency for research on the fundamental science, usefulness, and safety of complementary and integrative health approaches and their roles in improving health and health care.

Prior to coming to NIH in 2018, Dr. Langevin was the Director of the Osher Center for Integrative Medicine, jointly based at Brigham and Women's Hospital and Harvard Medical School, Boston, and professor-in-residence of medicine at Harvard Medical School from 2012 to 2018. She also previously served as professor of neurological sciences at the University of Vermont Larner College of Medicine, Burlington, Vermont.

Over her career, Dr. Langevin's research interests have centered around the role of connective tissue in chronic musculoskeletal pain and the mechanisms of acupuncture, manual, and movement-based therapies. Her more recent work has focused on the effects of stretching on inflammation resolution mechanisms within connective tissue. She is a fellow of the American College of Physicians.

Dr. Langevin received an M.D. degree from McGill University, Montreal. She completed a postdoctoral research fellowship in neurochemistry at the MRC Neurochemical Pharmacology Unit in Cambridge, England, and a residency in internal medicine and fellowship in endocrinology and metabolism at The Johns Hopkins Hospital in Baltimore, Maryland.

The Nutrition Continuum And Whole Person Health

Helene Langevin

National Center for Complementary and Integrative Health

Research on nutrition tends to be fragmented, such that topics including botanicals, “food as medicine”, nutrition-related behaviors, food access and regenerative agriculture are generally studied separately despite being deeply interrelated. This lecture will discuss the “nutrition continuum” in the context of whole person health, and why an integrated approach to nutrition can help connect across the biological, behavioral, social and environmental domains.

Steven Musser

Food and Drug Administration

Dr. Musser is the Deputy Center Director for Scientific Operations at the U.S. Food and Drug Administration's (FDA) Center for Food Safety and Applied Nutrition (CFSAN). In addition to managing the Center's scientific operations, he oversees the Center's activities in cosmetics safety, color certification, pre-market review of food additives, food contact notifications and foods derived from bioengineered plants. For the last decade, he has directed the Center's research in precedent setting areas of food and cosmetic safety research, which include food allergens, chemical contaminants, dietary supplement safety, toxicology and the application of whole genome sequencing to food safety issues.

Dr. Musser received his B.S. degree in Biology from Millersville University and his Ph.D. in Medicinal Chemistry from the University of Maryland-Baltimore. He then completed a post-doctoral research fellowship at the National Institutes of Health, National Cancer Institute.

Research Gaps Limiting The Use Of New Alternative Methods (NAMs) In CFSAN's Regulatory Mission

Steven M. Musser, Ph.D.

Deputy Director for Scientific Operations, Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration

While animal studies remain the gold standard for evaluating the toxicity and overall safety of chemicals in foods, there is a global emphasis on reducing the use of animals for toxicity testing. As a result, new approach methodologies (NAMs) are experiencing significant growth due to their potential to more quickly and effectively predict or screen for toxicity, eliminating the need for animal testing. These techniques span a broad range of approaches including in silico, individual in vitro tests and micro-physiological systems that mimic multiple organ systems. The research work in NAMs is providing increasing evidence these systems can more rapidly and reliably screen large numbers of chemicals, identify important biomarkers of toxicity, characterize pathways, and more accurately represent human toxicity. However, there are still significant gaps preventing widespread adoption of NAMs. Examples include costs, ADME, intra and interlaboratory reproducibility, mixture analysis and quantitative relevance. Understanding and addressing these research gaps are key elements to advancing the widespread use of NAMS to protect human health.

Betsy Jean Yakes

Food and Drug Administration

Dr. Betsy Jean Yakes is the Chief of the Identity and Status Branch (ISB) in the Division of Research and Evaluation, Office of Dietary Supplement Programs at FDA's Center for Food Safety and Applied Nutrition (ODSP/CFSAN/FDA). In this role, she is responsible for leading and providing oversight to subject matter experts in ISB who evaluate dietary ingredients/supplements, including in new dietary ingredient notification reviews. She coordinates the technical evaluation of regulatory and scientific issues regarding dietary ingredients and other ingredients in dietary supplements. Additionally, she and her team respond to inquiries from other FDA components and provide expert support for ingredient analysis, policy, and action as appropriate._x000D_
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Prior to being in ODSP, Betsy spent over 15 years (2007 – 2022) in the Division of Analytical Chemistry in the Office of Regulatory Science (ORS/CFSAN/FDA). As a Research Chemist and principal investigator for research on portable devices and biosensors, she developed accurate biosensor detection for toxins and pathogens as well as spectroscopy methods for improved authentication and adulteration evaluation for foods, dietary supplements, food contact materials, and cosmetics. She has authored over 45 publications and obtained 2 patents in both novel (e.g., toxin and biomarker detection) and applied (e.g., portable detection techniques) advancements that furthered the mission of the Agency and garnered international impact. She has served as the FDA Chair of the Portable Devices Technical Advisory Group for foods, the ORS/CFSAN coordinator for an FY18 Congressional special appropriation to study seafood decomposition, the FDA Liaison to the international U.S. Pharmacopeia (USP) Skim Milk Powder Advisory Group, and the Chair of the Forensics and Security Section at SciX. Her favorite awards are her "24" Award at the Gordon Research Conference on Lasers in Medicine and Biology (2018) which was given to the best presentation and the one that "saved the session" and the American Chemical Society, CSW Local Section Outreach Volunteer of the Year (2018). Additionally, while in ORS, she is proud to have been the primary mentor for 5 undergraduate interns, 1 graduate student, and 1 post-doctoral fellow, as well as co-mentor for numerous others, who have gone on to become leaders in their own areas. Previous to joining FDA, she obtained her Emergency Medical Technician license from Madison Area Technical College in 1999, earned a B.A. with a Chemistry major and Mathematics minor from Luther College in 2002, and achieved a Ph.D. in Analytical Chemistry at Iowa State University in 2007 with a dissertation focused on advanced detection and separation methods.

What's Old Is New Again And Other Changes To Ingredients – Insights From The FDA

Betsy Jean Yakes

Food and Drug Administration

The determination of what makes a dietary ingredient "new" which may then require a New Dietary Ingredient (NDI) Notification has received much attention. Indeed, the 2016 Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Draft Guidance for Industry contains clarifications on the meaning of new dietary ingredients and recommendations on submission information to help industry comply with 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) which requires the manufacturer or distributor of an NDI to submit a new dietary ingredient notification (NDIN) to FDA at least 75 days before introducing the product into interstate commerce. Despite the guidance, the definitions and nuances in the recommendations can be complicated. For example, what changes in the manufacturing process would impact a dietary ingredient and result in an NDI? How does a change in source material effect the ingredient status? What changes in physical properties are likely to result in a new ingredient? What chemical alterations would change the ingredient enough to make an NDI? Additionally, what impact do changes to conditions of use have on an ingredient's status? In many cases, the answers to these questions would be qualified with "it depends" which can cause confusion. This presentation will highlight what makes a dietary ingredient "new", give insights into when dietary ingredients become new forms that may require an NDIN, and supply recommendations for seeking further support on these topics.

Troy Hubbard

Food and Drug Administration

I completed my Ph.D at The Pennsylvania State University in 2017, in the lab of Dr. Gary Perdew, where I studied the aryl hydrocarbon receptor (AHR), which is a ligand-activated transcription factor that participates in an array of physiological functions, such as xenobiotic metabolism, immune regulation, epithelial barrier function, and intestinal homeostasis. My thesis research focused upon how evolutionary selection has adapted the human AHR to produce a biological sensor that is distinctive in its responsiveness to environmental toxins and endogenous signals.

Following my graduate work, I was an Intramural Research Training Award (IRTA) Fellow in the Toxicology Branch of the Division of the National Toxicology Program (DNTP) at the National Institute of Environmental Health Sciences (2017-2020). As a study scientist, I worked in cross-functional teams to evaluate the potential toxicity and carcinogenicity of chemical agents nominated to the NTP testing program, such as pharmaceuticals, food chemicals, botanicals, and environmental contaminants. My responsibilities include design and implementation of toxicity studies and communicating study results by preparation of NTP technical reports and writing of manuscripts for publication. My primary research interests included in vivo toxicity, hepatotoxicity, mixtures, and reproductive and developmental toxicology.

I am currently a toxicologist at the Food and Drug Administration, Center for Food Safety and Nutrition, Office of Food Additive Safety, where I serve as review scientist evaluating the safety of food additives and ingredients (food additive petitions, color additive petitions, and generally recognized as safe (GRAS) notifications). Additionally, I serve as a toxicology subject matter expert to support the review of food derived from new plant varieties (Plant Biotechnology Consultation Program) and CFSAN Coordinated Outbreak Response and Evaluation (CORE) network to support efforts to find, stop, and prevent foodborne illness outbreaks and provide subject matter expertise related to food ingredient safety.

Introduction To The Premarket Review Of Human Food Ingredients In The United States And Concepts In The Safety Assessment Of Novel Plant-Derived Ingredients

Troy Hubbard

U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition (CFSAN), College Park, MD, USA

Premarket regulation of ingredients added to food is a key pillar ensuring the safety of food as it allows the opportunity to address potential safety concerns prior to consumer exposure. In the United States, food and color additives are substances that are intentionally added to food and are subject to pre-market approval by the Food and Drug Administration (FDA) and require a listing in the Code of Federal Regulations, unless the intended use of the substance is generally recognized as safe (GRAS), among qualified experts. GRAS is not an inherent property of a substance, as is often misunderstood; rather, it relies on the substance's proposed use and use level, the manufacturing process, dietary exposure, and other relevant safety data and information. Currently, the U.S. FDA manages a notification program, in which a manufacturer may inform FDA of its conclusion and basis that the use of a substance is GRAS. Notably, the safety standard is the same for food and color additives and GRAS substances—reasonable certainty of no harm. FDA's general approach to the safety assessment of food ingredients with consideration for novel plant-derived ingredients will be discussed. FDA routinely engages in outreach to help food safety professionals and manufacturers understand U.S. food ingredient regulations, the GRAS provision, and welcomes consultations with the Agency throughout the process to support the safe and legal marketing of ingredients added to human foods.

Gailen Marshall

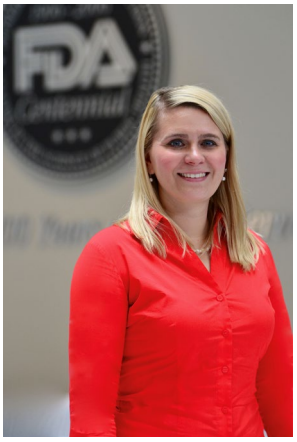
University of Mississippi Medical Center

Gailen D. Marshall, Jr. MD PhD is the R Faser Triplett Sr MD Chair of Allergy and Immunology, Professor of Medicine, Pediatrics , Pathology and Population Health Science, Executive Director of the Mississippi Clinical Research and Trials Center, Medical Director of the UMMC Clinical Research Support Program, Vice Chair for Research in the Department of Medicine, Director of the Division Clinical Immunology and Chief, Laboratory of Behavioral Immunology Research at the University of Mississippi Medical Center in Jackson. He received both his PhD in Immunology and MD from the University of Texas Medical Branch in Galveston, did internal medicine training at the University of Iowa and completed his internal medicine residency, chief residency and Allergy-Immunology fellowship at the University of Tennessee at Memphis. He spent the first 15 years of his career at the University of Texas Health Sciences Center at Houston and came to UMMC in 2004. He is an active clinician, educator and research investigator and currently serves as President of the American College of Allergy, Asthma and Immunology.

TBN

Gailen Marshall

University of Mississippi Medical Center



Cassandra Taylor

Food and Drug Administration

Cassandra Taylor, Ph.D. is a Public Health Advisor at U.S. Food and Drug Administration (FDA) within the Center for Drug Evaluation and Research's (CDER) Office of the Center Director and leads CDER's cannabis science and research portfolio. She serves as a cannabis subject matter expert (SME) for CDER and across FDA, concentrating on the botanical and quality aspects of cannabis. She received her B.S. in Chemistry from St. Francis University (2005), and her Ph.D. in Analytical Chemistry from the University of Maryland (2014). Dr. Taylor has evaluated over 150 botanical drug submissions across CDER's clinical divisions, with a focus on reviewing cannabis submissions and was the technical lead on the draft and finalized FDA guidance for industry titled "Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research." She leads and coordinates many cannabis initiatives within CDER and FDA. Dr. Taylor is an active SME in the FDA cross-agency cannabis working group, Cannabis Product Committee (CPC) and has published multiple cannabis manuscripts. She collaborates with colleagues across FDA to help close substantial knowledge gaps about the science, safety, and quality of cannabis and cannabis-derived products.

Investigational New Drug (IND) Applications

Cassandra Taylor, Ph.D.

Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA.

During a new drug's early preclinical development, the sponsor's primary goal is to determine if the product is reasonably safe for initial use in humans, and if the compound exhibits pharmacological activity that justifies commercial development. When a product is identified as a viable candidate for further development, the sponsor then focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies.

FDA's role in the development of a new drug begins when the drug's sponsor (usually the manufacturer or potential marketer), having screened the new molecule for pharmacological activity and acute toxicity potential in animals, wants to test its diagnostic or therapeutic potential in humans. At that point, the molecule changes in legal status under the Federal Food, Drug, and Cosmetic Act and becomes a new drug subject to specific requirements of the drug regulatory system.

In this presentation, the audience will learn about the three IND types (Investigator IND , Emergency IND, and Treatment IND), the two IND categories (Research and Commercial), and information that an application must contain (Animal Pharmacology and Toxicology Studies, Manufacturing Information, and Clinical Protocols and Investigator Information). The general process for IND submission will be presented along with resources to assist researchers wishing to submit an IND.

Nadina Jose

Rutgers University

Dr. Nadina Jose is an educator and clinical research professional committed towards the development and teaching of courses geared towards professionalizing the role of clinical research professionals at Rutgers University's School of Health Professions, Masters in Clinical Research Management program in the Department of Health Informatics. She assumed a variety of roles in the pharmaceutical, biotech, and clinical research management industry for more than 35 years. Dr. Jose continues to be a subject matter expert and consultant for various biopharma and technology companies for medical affairs, site management, clinical operations, quality management, strategy development and overall clinical research management. She is actively involved in assisting regulatory agencies like the Philippine FDA as a Scientific Advisory Committee Member and faculty for training and continuing education of agency reviewers and inspectors. She was a former task force member of the Duke-National University Singapore Center for Regulatory Excellence initiative which set forth the process of providing training focused on the standardization of regulatory affairs for ASEAN countries.

She worked with programs that saw the successful delivery of blockbuster products to market such as Viagra, Seroquel, Zyprexia, Lupron, Biaxin, Adderall, Risperidone, Ciprofloxacin to name a few, along with landmark devices like Uroflow, ESWL and studies that validated PSA as a biomarker for Prostate Cancer. Dr. Jose continues to be actively involved with various industry organizations, is a regular contributor to industry publications and is a frequent speaker and lecturer at global conferences and workshops.

Navigating the IND Process to Get your Clinical Trial Started: Know the Regulations!

Nadina Jose

Rutgers University

Zella Palmer

Dillard University

Zella Palmer, is an author, professor, filmmaker, curator, scholar and the Chair and Director of the Dillard University Ray Charles Program in African-American Material Culture in New Orleans, Louisiana. Palmer is committed to documenting and preserving the legacy African American, Creole, Indigenous and LatinX culinary history. As the Chair of the Dillard University Ray Charles Program, Palmer filmed and produced the Story of New Orleans Creole Cooking: The Black Hand in the Pot documentary. In 2020, under Palmer's leadership, Dillard University launched a Food Studies Minor, 1 of 2 accredited academic Food Studies programs at a (HBCU) Historically Black College & University.

Palmer's latest publications, Recipes and Remembrances of Fair Dillard: 1869-2019 (University of Louisiana at Lafayette Press) and Ed Mitchell's Barbeque (Harper Collins, June 2023) shares some of her rich research. Palmer was a guest or keynote speaker for NYU, Nicholls State University, Maryville University, University of Gastronomic Sciences (Turin, Italy) Essence Festival and for the 2022 American Community Gardening Association Conference.

Palmer's research and articles appeared in the Louisiana Endowment for the Humanities 64 Parishes, Essence and For the Culture magazines. Palmer received the 2018 'Cultural Bearer Award' from the Mardi Gras Indian Hall of Fame, 2020 New Orleans Magazine 'People To Watch' and 2022 Dine Diaspora Black Women in Food 'Trailblazer' Honoree. Palmer hosts Culture & Flavor podcast on Heritage Radio Network.

Afro-Caribbean influences on U.S food and nutrition habits

Zella Palmer

This presentation presents the profound and enduring influence of Afro-Caribbean culture on the food and agriculture of the American South. Beginning with the transatlantic slave trade, which brought African and Afro-Caribbean peoples to the region. Starting with the evolution of culinary practices, agricultural techniques, crop varieties, plant medicine and spirituality. It highlights the ways in which enslaved Africans and their descendants preserved, adapted, and transformed their foodways, enriching Southern cuisine and agriculture with diverse flavors, ingredients, and agricultural practices. Through a combination of historical research and analysis of contemporary food systems, this research sheds light on the enduring legacy of Afro-Caribbean influences particularly from Haiti, Cuba, Puerto Rico, Panama and the Bahamas on the food and agriculture of the American South. In addition, political movements and uprisings that were directly influenced from revolutionary movements from the 19th to 20th century that impacted food and agriculture in the American South.

Anthony Richards

Freelance

From Slave Foods To Superfoods

Anthony Richards

Freelance

Sonia Peters

BERP

I am a Natural Product Chemist with a significant interest in Ethnobotany and Ethnomedicine. I am a graduate of the University of the West Indies where I gained my BSc. and Ph.D. qualifications. Socialisation within this layered interest profile led me to establish the non-profit organization, the Biocultural Education and Research Programme to promote the conservation of the plant resources, at a national and regional level, and also the embedded traditional knowledge, utilising platforms of education and research. To this end, the inaugural edition of our biennial symposium, Plants and Planting for the Future, was staged in 2019 and brought together scientists from across the Caribbean and the United Staes to share their professional activities within the areas of drug discovery, agriculture and ethnobotany. We have experienced successful editions in 2021 and 2023. We also reach out to the general public and youth to enhance awareness using varied modalities including workshops, documentaries, publications and garden development.

We are especially proud of the collaboration with Andromeda Botanic Gardens that led to the establishment of an Ethnobotanical Garden celebrating the plants found useful during the period of slavery on the island. The garden will hold approximately 60 plants found useful for varied applications including wound healing, digestive issues, skin disorders and upper respiratory tract irritation from colds and flu. Research is being conducted on the validation of some of these applications with a focus on the modern chronic health issues including the impact of the COVID 19 corona virus. In 2023 I was successful in the submission of a plant based formulation for the regulation of diabetes and won first place in the Phytoinnovation Challenge. This product is being developed into a nutraceutical in collaboration with the Life Sciences unit of the Barbados Industial and Development Corporation Export Barbados.

Revisiting The Dependendence On Indigenous Plant Resources To Inform Interventions For The SARS-COV-2 Pandemic

Sonia Peter, Ph.D., Executive Director, Biocultural Education and Research Programme,

59 Meadowvale, St. James, Barbados; biosciencebdos@gmail.com

Over the period of the Atlantic Slave Trade, it is documented that approximately 12.5 million men, women and children were forcibly transported from Africa, with an estimated 80 - 90 % landing in the Americas. Barbados was the most easterly of the islands targeted in the Caribbean archipelago and became a key site of the economic activity associated with the use of forced labour for sugar cane production. The Caribbean received a population of West Africans, whose traditions continue to permeate our culture. The horrific Middle Passage saw the ancestors arriving in a poor state of health which was further exacerbated by the inhumane working and living conditions. West African biocultural traditions would have been vital for the resilience of the enslaved population in Barbados during the 16th to early 19th centuries. Historians report that a 'Slave Medicine' emerged based on the knowledge of healing plants and traditional practice. Common illnesses, due to lack of proper nutrition and harsh working conditions, included skin lesions, convulsions, beriberi, pellagra, and kwashiorkor. Of the 60 plants featured in the Slave Medicine Pharmacopoeia, wound healing plants belonged to families including Euphorbiaceae (Croton flavens), Asteraceae (Chromolaena odorata), Lamiaceae (Ocimum campechianum) and Peperomiaceae (Peperomia magniliifolia). These families are also important, medicinally, in Ghana. Natural products from these plants, including flavonoids, are implicated in the anti-inflammatory response that promotes healing. In the modern application of the traditional knowledge that has been passed on through time, plants used to promote healing as vulneraries are now used for respiratory symptoms of colds and flu. Preliminary screening of selected plants belonging to the Lamiaceae family, involving structural elucidation and computer modelling of compounds, demonstrated the potential of flavonoids for hindering the SARS-COV-2 virus based on functional group interactions. This is a narrative on how our history speaks to us in the future.

Key words: Traditional knowledge, African heritage, wound healing, anti-inflammatory response, flavonoids, SARS-COV-2

Thera Edwards

University of West Indies

Dr. Thera Edwards is Lecturer and Map Curator in the Department of Geography and Geology at The University of the West Indies, Mona Campus in Jamaica. Her early training was in botany and environmental sciences leading to the award of a B.Sc. Environmental Sciences (Botany Major) in 1993 and M.Sc. Environmental Management in 1999 from The University of the West Indies (UWI), Mona Campus and University of London respectively. She received a Ph.D. in Landscape History in 2013 from The UWI, Mona.

Her interdisciplinary research includes landscape change and history, climate change responses, vegetation ecology, archaeology and geomorphology. Archival manuscripts, historical maps, aerial photographs, satellite imagery and Geographical Information Systems (GIS) are key components of her research and analyses. In the past 23 years, her work has covered environmental management and sustainable development, with particular emphasis on biodiversity, forestry, watersheds, agriculture and protected areas management. Since 2020, as a member of the Caribbean Food for Climate Justice Research Group she has embarked on more focused research investigating traditional food production systems, food culture, crop histories and their nexus with climate resilience.

Thera has written and co-authored technical reports and papers for several development agencies as well as for presentation at conferences and symposia. In 2016, she co-edited the volume “Global Change and the Caribbean: Adaptation and Resilience” along with David Barker, Duncan McGregor, and Kevon Rhiney.

African Plants In Jamaican Farms And Gardens

Thera Edwards Ph.D.

Plants of all growth forms and regeneration strategies were introduced to Jamaica by European slavers and by Enslaved Africans. Some species such as Tamarind used to purify drinking water on ships arrived through purposes of practicality while others that such as yam and plantain were transported as food supplies on the ships or by the Enslaved Africans as tubers for planting in their countries of destination. Tuber crops proved to be invaluable in hurricane prone islands such as Jamaica as the underground tuber was left undamaged by the high winds of the storms. Other crops such as Plantain while not as resistant to storms were brought as they were mainstays of the traditional African diet. Still other plants such as Bissy (Kola Nut) were brought for their medicinal properties Through the Enslaved Africans and the Slave Traders a diverse food and medicinal plantscape emerged on plantations in subsistence plots dubbed Negro Grounds. In looking at these plants of African origin on farms, in kitchen gardens or in food forests one cannot help but note their near complete absence in the formal Jamaican Botanical Gardens at Bath, Castleton and Hope Gardens in comparison to plants from Asia and the Pacific. This paper looks at these plants through the lens of the concept of Botanical Gardens as repositories and places of study of introduced and exotic plants. It argues that Negro grounds and the subsequent kitchen gardens of the free peasantry and contemporary small farmers became refugia of plant stock and gene pools of plants from the mother countries that these displaced Enslaved Africans saw as critical for their cultural continuity and survival.

Shannon Aldrich

Food and Drug Administration

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

FDA/ORA Health Fraud Updates

Shannon Adrich

Food and Drug Administration

Andrea Lindsey

The Consortium for Health and Military Performance

Andrea Lindsey serves as Director of Operation Supplement Safety (OPSS) and Senior Nutrition Scientist with the Consortium for Health and Military Performance (CHAMP), Uniformed Services University. She received her Master of Science degree in Nutrition from University of Maryland, College Park. Andrea is a nutrition information specialist with extensive experience in the field of dietary supplements, and she has considerable knowledge and understanding regarding the content, safety, labeling, and marketing of these products.

At CHAMP, most of her work encompasses the topic of dietary supplements and their ingredients, which involves reviewing, evaluating, and interpreting the scientific literature; writing; and directing the program. Ms. Lindsey also regularly educates Service Members, healthcare providers, military family members, and leaders about dietary supplements. She also manages a team of nutritionists for CHAMP, overseeing all of the nutrition content. She works closely with Federal partners and other health professionals in and outside the military to exchange relevant and pertinent information about nutrition and dietary supplements.

Ms. Lindsey currently maintains membership in the American Public Health Association, American Society for Nutrition, and the Collegiate & Professional Sports Dietitians Association.

Uncovering Dietary Supplement Ingredients: Education For Informed Use

Andrea T. Lindsey[1,2], Cindy Crawford[1,2], Patricia A. Deuster[1]

[1]Consortium for Health and Military Performance, Department of Military and Emergency Medicine, F. Edward Hebert School of Medicine, Uniformed Services University, Bethesda, MD; [2]Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. Bethesda, MD

Dietary supplement (DS) consumption occurs for various reasons- to improve performance, to lose weight, or for overall health. In general, the public perceives the DS industry as trustworthy. However, some claims can be deceiving, and the use of some DS can result in adverse events. Consumers often get their information from social media or other outlets fraught with misinformation, rather than consulting a healthcare provider or relying upon evidence-based resources.

Operation Supplement Safety (OPSS) is the Department of Defense's (DoD) go-to program for DS. All Services come to OPSS for DS education. OPSS maintains the DoD Prohibited Dietary Supplement Ingredients List, provides education, performs outreach, and hosts social media campaigns. OPSS's website includes evidence-based articles, videos, and more. Priorities for content are based on input and feedback from the Services, inquiries through Ask-the-Expert (ATE) (~ 130/mo), through working with other federal departments, professional and academic institutions, and by tracking marketplace trends. The OPSS Team uncovers many ingredients, some of which can be a concern for Service Members. In collaboration with University of Mississippi, OPSS engages in rigorous product testing and analyses of DS, with the goal of raising awareness for informed use and public health.

OPSS's comprehensive ingredient database (OPSSID) is used to track substances that appear on labels of DS products and associated information (e.g., whether they are prohibited by DoD and safety information). The DS market is ever-changing; claims are now emerging for more holistic solutions with products containing multiple combinations of botanical ingredients and purported 'natural stimulants.' Many label claims are not just for losing weight (for example) but also to enhance energy and performance- all packed into one pill. This presentation will demonstrate how OPSS navigates the ever-changing DS landscape for the mission of informed use.

Victor Navarro

Jefferson Health

Dr. 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 obtained fellowship training in Gastroenterology, Hepatology, and Hepatobiliary Endoscopy at Yale University. 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.

In 2002, Dr. Navarro assumed a 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. 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. In 2016, Dr. Navarro became the founding medical chair of the Department of Digestive Disease and Transplantation for the Einstein Healthcare Network; in this position, he oversees Divisions of Hepatology, Gastroenterology, Transplant and Hepatobiliary Surgery.

As a mentor, Dr. Navarro has been directly responsible for the scholarly and clinical training of many young and mid-career health professionals and academicians. Dr. Navarro's chief sources of research funding are the National Institutes of Health as an investigator for the U.S. Drug Induced Liver Injury Network (DILIN), and the Patient Centered Outcomes Research Institute for his study of Palliative Care in Patients with End Stage Liver Disease.

The Clinical Implications of Unlabeled Ingredients in Dietary Supplements

Thomas Efferth

University of Mainz

University of Mainz, Chair, Dept. of Pharmaceutical Biology
1990, PhD thesis, German Cancer Research Center, Heidelberg, Germany;
2005 Group leader, German Cancer Research Center, Heidelberg, Germany;
2007, Associate (apl.) Professor, University of Heidelberg, Germany;
2009, Full professor and Head of Department of Pharmaceutical Biology, Johannes Gutenberg University, Mainz, Germany;
2021, Director, Institute of Pharmaceutical and Biomedical Sciences, Johannes Gutenberg University, Mainz, Germany;
2023, Ordinary Member, Academia Europaea (London);
800+ papers in PubMed-listed journals;
H-index: 107;
60,000 citations;
9 awards;
5 honorary professorships and a professional professorship at the Harvard Medical School, Boston, USA).

Cold-Water Extraction Of Nerium oleander Leaves Inhibits Cancer: From Bench To Bedside

Luay J. Rashan[1], Nadire Özenver[2,3], Joelle C. Boulos[2], Mona Dawood[2,4], Wynand P. Roos[5], Katrin Franke[6], Ioannis Papasotiriou[7], Ludger A. Wessjohann[6], Heinz-Herbert Fiebig[4], and Thomas Efferth[2]*

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Nerium oleander is a well-known medicinal plant used in the Mediterranean region and traditional Indian medicine (Ayurveda) against a variety of diseases, including cancer.

We investigated a cold-water extract of N. oleander leaves for their anticancer activities in vitro and in vivo. The cytotoxicity testing in the Oncotest panel of tumor cell lines and concomitant COMPARE analysis showed a high degree of similarity to mitosis-inhibiting compounds. We verified this hypothesis by treating tumor cells transfected with a tubulin-GFP fusion cDNA construct and confocal microscopy as well as a biochemical tubulin polymerization assay. N. oleander showed a similar inhibition of tubulin depolymerization as the control drug paclitaxel.

Furthermore, the N. oleander extract inhibited the growth of human mammary cancer xenograft MAXF 401 alone (test/Control value 24%) in nude mice. In combination with paclitaxel, it effected a strong synergism in combination with paclitaxel resulting in complete remissions.

A clinical phase I trial with breast or colon cancer patients showed tolerable side effects (fever, vomiting, nausea, diarrhea, fatigue). A subsequent clinical phase II trial with 300+ patients revealed tumor control rates (complete and partial remissions plus stabilizations) in a range of 8-70% in 18 different tumor types.

Reference:

Rashan LJ, Özenver N, Boulos JC, Dawood M, Roos WP, Franke K, Papasotiriou I, Wessjohann LA, Fiebig HH, Efferth T. Molecules. 2023;28(4):1871.

Michael Heinrich

University of London

Michael Heinrich is a Professor of Ethnopharmacology and Medicinal Plant Research (Pharmacognosy) at the UCL School of Pharmacy (from 1999 – 2011School of Pharmacy – Univ London) and was until 2017 the head of the research cluster 'Biodiversity and Medicines' at the UCL School of Pharmacy. From 2017 until 2023 he served as the joint chair of UCL's Research Ethics Committee (with Dr. L. Ang, Institute of Education, UCL). Since 22024 he has been a Yushan Fellow at China Medical University, Taichung, Taiwan,

For many years the group's (currently fice PhD students and one postdoc) research has been based on a transdisciplinary and translational perspective integrating approaches from the natural and social sciences with an overall aim of tackling the fast changing global health needs focusing on the use of plant derived products as 'medicinal plants', 'health foods' or nutraceuticals, botanicals and the like. After initial research on traditional medicine most notably in México, I developed a strong research focus on anti-inflammatory agents. My group was one of the first to identify NF-kappaB inhibitors based on medicinal plants and their metabolites incl. ones used for brain inflammation. More recently my group's research has centered on value chains of herbal medicines in a globalized context (incl. their impacts on livelihood and quality of products), sustainable sourcing and on strategies for improving the outcome of drug development based on medicinal plants . Since 2000 he has developed diverse research collaborations in China, Thailand and other Asian countries focusing on the pharmacological effects and quality of herbal medicines. In both cases the use of plant metabolomics proved to be a very successful tool for analysing the complexity of these products.

Herbal Medicines: We Care About Sustainability, But What Do We Need To Do To Get It Right.

Heinrich M [1,2], Jalil B[1] & Mykhailenko O[1,3]

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Herbal medicine users often argue that using such medicines is sustainable and not detrimental to the environment. However, what is the empirical basis for this? We need to consider two fundamental areas: the impact the field has on the environment and the challenges it faces due to the dramatic environmental and climate changes (Applequist et al., 2020). In times of evidence-based practice, such claims will remain weak unless practitioners and researchers have a clear understanding of such impact. Currently, the challenges the field faces are at best addressed generically. The environmental impact we have has not been addressed in detail. Here we argue that we need a paradigm change responding to the challenges (and opportunities) posed by the Anthropocene. Famously, in 1962 Thomas S. Kuhn argued for paradigms shifts (a 'scientific revolution') in response to "anomalies". While his ideas were driven primarily by scientific 'progress', the current environmental crisis points to how policy and daily human activity impact on practice and research.

In this presentation, we use a series of case studies highlighting emerging research questions and problems to assess how our approaches need to change. We need to shift the paradigm to understanding sourcing, the impact of climate change, as well as the environment and how this translates into new policies/requirements. The addition of Rhodiola rosea L. to Cites Appendix II is one now widely discussed example. Other examples include the shift of cultivation, e.g. for Crocus sativus L. and Lavandula angustifolia Mill., but also the obvious cases of overexploitation posing a species at risk of extinction (mainly based on multiple uses, and not only for medical purposes) but also for the challenges of 'wild' crafting of widely used species (Schindler et al., 2022).

This presentation raises more questions than it can offer answers. It is part of an ongoing debate about changing priorities in research/practice for all of us.

Gaia Scalabrino

Trinity College Dublin

As a life science professional with a Ph.D. in Natural Products Organic Chemistry and postgraduate qualifications in business, project management and regulations, Dr Gaia Scalabrino held several strategic and operations roles across functions in the private and public sectors. Currently, Gaia works as the Executive Director of the NatPro Centre for Natural Products Research based at the School of Pharmacy and Pharmaceutical Sciences in Trinity College Dublin (TCD), Ireland. She grew the Centre from inception to deliver sustainable bio-based solutions derived from nature to benefit health and to support transition to a bioeconomy in Ireland. She is also an Advisory Board Member of the Society for Medicinal Plant and Natural Product Research. Previously, Dr Scalabrino worked in drug development as Vice President of Operations and Quality at Trino Therapeutics Ltd, driving the start-up from an academic project to a first-in-class new chemical entity derived from nature in clinical trials. In addition, she advised SMEs based in EU and US to support their business growth and product development portfolio in the role of Operations and Pharmaceutical Consultant at HiTech Health Ltd. Gaia was raised in a multi-cultural environment, living in Italy and Kenya, embracing diversity, curiosity and change, and currently lives in Ireland.

Natural Products Ireland: From Bioactives To The Bioeconomy-A Systems-Based Approach

Gaia A. Scalabrino[1] and Helen Sheridan[1]

[1] NatPro Centre, Trinity Centre for Natural Products Research, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Dublin, Ireland

Natural Products (NP) are on the rise across the world, driven by economic, environmental, health and societal needs. An increasing focus has been placed on the role of boglands within climate change as peatlands store 1/3 of the world's soil carbon and provide water storage. With our project 'Unlocking Nature's Pharmacy' we aim to increase public awareness and drive Ireland towards a bioeconomy where Natural Product Science (NPS) plays a key role.

At the NatPro Centre, the Trinity Centre for Natural Products Research, we use systems-based approaches (SBA), for example looking at the bogs of Ireland, to identify innovative bio-based solutions to support health and enable change on a scientific, social and governmental level. Using multidisciplinary research ranging from ethnopharmacology to systems pharmacology, we present scientific knowledge linked to the cultural, therapeutic and commercial potential of native species growing on boglands. We have identified key functional bioactives from over 70 plant species, the majority being angiosperms, bryophytes and lichens. We have investigated these species using chemical analysis, metabolomic profiling and genomic studies, as well as in vitro, in vivo and ex vivo models. To date circa 10 leads have progressed to advanced screening, with two species being considered for potential commercialisation.

The project is embedded in NatPro sustainability approaches, green practices and quality systems, which complement laboratory practices. NatPro acts as a beacon for education, government and industry engagement, integrating innovative approaches, scientific knowledge and regulation to inform policy and to build capacity among NP stakeholders, including businesses, communities and students, to support the Irish transition to a bioeconomy. We use NPS to drive transformative practices to address urgent needs. Here we present a systemic view from bogs to Irish bioeconomy: potted history, current status and future prospects.

Bill Gurley

University of Mississippi

Professor and Principal Scientist, National Center for Natural Products Research (NCNPR), School of Pharmacy, University of Mississippi; Chair of the University of Mississippi Institutional Animal Care and Use Committee. Prior to joining the NCNPR in 2019, Gurley was 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. Gurley has been conducting basic and clinical research on various aspects of dietary supplement efficacy and safety for almost 30 years. His research on Ephedra-containing dietary supplements was used by the FDA to remove those problematic products from the U.S. market in 2004. He was the first investigator to systematically evaluate the herb-drug interaction potential of popular dietary supplements and to assess their clinical relevance. Accordingly, his research team was the first to document the serious clinical repercussions of herb-drug interactions involving St. John's wort. Gurley's research interests include pharmacokinetics, mechanisms of herb-drug interactions, toxicity of multiple-component herbal dietary supplements, phytochemical modulation of human drug metabolizing enzymes/transport proteins, and human phytochemical disposition, all of which have been the subject of more than 200 peer-reviewed scientific publications. He is a member of the United States Pharmacopoeia's Expert Panel on Dietary Supplements, an advisor to the American Botanical Council, and a co-editor of the American Herbal Products Association's Botanical Safety Handbook. He sits on the editorial boards for the journals Clinical Pharmacology & Therapeutics, Phytomedicine, HerbalGram, and Clinical Therapeutics. Gurley received a B.S. in Chemistry from Tennessee Technological University and a B.S. in Pharmacy and Ph.D. in Pharmaceutics from the University of Tennessee Health Science Center.

Dosage Form Performance Assessment Of Commercially-Available Soft Gel Capsules Containing Essential Oils

Gurley BJ, Gurley CM, Khan IA, Ikhlas S,

Soft gel formulations have become a mainstay for many types of botanical dietary supplements, especially essential oils. However, many manufacturers overlook that essential oils often contain aldehydes, which can cross-link gelatin polymers and impede disruption in gastric/intestinal fluids. Such interactions may, in turn, affect product efficacy. This study examined the disruption profiles of various essential oil-containing soft gels from different manufacturers (prior to label-recommended expiration dates) in biorelevant gastric and/or intestinal fluids, mimicking a fasted state. It included both animal- and vegetable-based gels as well as enteric-coated products with the latter tested in simulated intestinal fluid. According to USP guidelines (Chapters <1094> and <2040>), if a soft gel doesn't disintegrate within 15-30 minutes, specific digestive enzymes are to be added: pepsin for animal-based, non-enteric coated gels; papain for animal-based, enteric coated; and alpha-amylase for vegetable-based, non-enteric coated. Disruption tests (n=6 per run) were conducted per with an Agilent 708-DS dissolution system, Type 2 (paddle apparatus), using spiral wire sinkers, for 4 hours or until all capsules disrupted. Of the 50 products tested to date, 25% failed to meet USP disruption criteria. Where products failed, a second lot was tested, and a third if results varied, indicating potential manufacturing issues. Products formulated with multiple essential oils failed most consistently, though some with single oils also failed (e.g., cinnamon, copaiba, oregano, peppermint). Our findings reveal that many essential oil-containing soft gels don't disrupt in a timely fashion, pointing to possible quality control issues, aldehyde-gelling agent interactions, or both.

Natalia Davydova

United States Pharmacopeia

Natalia Davydova, Ph.D. is a Principal Scientist at the Dietary Supplements and Herbal Medicines Department at USP. She has over twenty years of experience in development and validation of analytical methods for analysis of drugs and vitamins in solutions, formulations, and biological fluids. She has extensive experience with drug pharmacokinetics, quality assurance of medicines, and post-marketing surveillance.

Dr. Davydova joined USP in 2001, working first for the Reference Standards Laboratory as Chemist III-IV, then at the USP International Technical Alliances Program (ITAP) as Program Manager, and, starting from June 2008, at the Dietary Supplements and Herbal Medicines Department as the scientific liaison with the responsibility of development of dietary supplement ingredients and dosage forms monographs and standards related to performance tests (Disintegration and Dissolution) for dietary supplements.

Before joining USP, Dr. Davydova worked for 3.5 years at the Bioanalytical Laboratory at Department of Pharmacology of Georgetown University, Washington DC, where she was responsible for development and validation of analytical methods for analysis of drugs in formulations and biological fluids. Prior to her career at Georgetown University, Dr. Davydova worked as a post-doctoral research associate at the Department of Medicine of University of Florida, Gainesville, FL on vitamins stability and drugs pharmacokinetics and metabolism.

USP Resources for Performance Testing Of Bothanical Dieteary Supplement Dosage Forms

Davydova N.[1]

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Botanical dietary supplements continue to gain popularity in the market. It is important that manufacturers of botanical supplements produce high quality products that can deliver the intended nutritional benefits indicated on the product label.

The absorption of botanical ingredients from dietary supplement oral dosage forms, such as tablets, capsules, and chewable gels (gummies), depends on the ability of the dosage forms to release the botanical dietary ingredients. Disintegration and dissolution tests are quality control tools used to assess performance characteristics of dietary supplement finished dosage forms. These tests are useful during dietary supplement product development for identifying critical manufacturing attributes such as the impact of ingredient properties and the impact of the manufacturing process on finished product performance. After the finished dosage form is released for marketing, disintegration and dissolution tests may be useful to detect manufacturing process issues, such as over compression and over drying, that would affect the release characteristics of the final dosage forms. These tests are not intended to be used as a demonstration or as a surrogate for in vivo absorption, bioavailability, or effectiveness, unless an in vitro–in vivo correlation (IVIVC) has been established.

This presentation provides information on U.S. Pharmacopeial resources on disintegration and dissolution tests as quality control tools to assess performance characteristics of botanical dietary supplement finished dosage forms.

Fatih Demirci

Anadolu University

He received his degree from the Faculty of Pharmacy of Anadolu University, in 1992. In the year 1995, he obtained his MSc degree with his work on the "Synthesis of Phosphatidylcholine Analogues" from the School of Chemical Sciences of the University of East Anglia, Norwich in UK. During his PhD, he has worked both at HEJ Research Institute of Chemistry, in Pakistan and at the Department of Pharmacognosy at the Faculty of Pharmacy, University of Mississippi,Oxford, respectively. His PhD project: "Microbial Transformation of Bioactive Monoterpenes" was finished in 2000 at Anadolu University. He got his Faculty position the year after, and was appointed as staff and Assist. Prof. in the Department of Pharmacognosy at the Faculty of Pharmacy, Anadolu University, Eskisehir, Turkiye. In 2002, he moved as post-doctoral scientific co-worker to the University of Regensburg, Department of Pharmaceutical Biology, Germany, where he worked on bioassays, herbal medicinal products besides teaching, until the end of 2003. In 2005, he was appointed as full time staff as Associate Professor in the Department of Pharmacognosy, Eskisehir, and in 2010 he was appointed as Professor. He served over a decade in administration in the Graduate School of Health Sciences, and was also the founding Dean of the Faculty of Health Sciences of Anadolu University. He also worked also as a visiting Professor in the Eastern Mediterranean University, N.Cyprus.

He has more than 180 international peer reviewed research publications, 20 PCT applications, 25 book Chapters, is editor of several text books and works in the editorial boards of various Natural Product journals. He has worked on more than 50 national -international industry/research projects including postgraduate MSc and PhD studies. Badebio Biotech Ltd. is the spin-off technopark company founded in 2009 with Prof. Baser. He is still working as a full faculty member in the Faculty of Pharmacy.

In-vitro & in-silico enzyme inhibitions by essential oils

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Essential oils have been utilized for many centuries in different ways, such as in aromatherapy. In the present work interaction of various enzymes associated with pathologies as potential targets will be elaborated for possible future natural products-based drug development both from in vitro and in silico point of view. Choline esterase such as AChE and BuChE, lipoxygenase (5-LOX), cyclooxygenase (COX-1 and COX-2), matrix metallo-proteinases (MMP), angiotensin-converting enzyme 2 (ACE2), neuraminidase (NA) and transmembrane serine transferase (TMPRSS2) examples will be discussed. In-vitro micro spectrophotometric absorbance/fluorescent based assays were on hands experimented, in addition the oils were evaluated by current in-silico methods for the discovery of mode of action of the selected essential oil constituents as well. The current work will explore how enzyme assays can influence the future potential of essential oils as therapeutics.

Acknowledgments

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Russ Osguthrope

DoTERRA

Dr. Russell J. Osguthorpe serves as the Chief Medical Officer of doTERRA International and is responsible for Clinical Research, Quality, Product Safety and Prime Meridian Healthcare. His work focuses on how science, clinical research and technology can improve health and wellness and to prove out the value of doTERRA Essential Oils in Healthcare settings. Quality of essential oils and Consistency in chemistry are required for clinical research, and he works with his teams to ensure both. He and his team of dedicated scientists and providers are focused on prevention as a service and work to provide tools that will help families and individuals improve their metabolic health and wellness. Dr. Osguthorpe received his medical degree from McGill University School of Medicine. He is a Board-Certified Pediatrician and Infectious Diseases Specialist trained at Denver Children's Hospital, University of Colorado School of Medicine and St. Louis Children's Hospital, Washington University School of. Medicine.

Current Obstacles Relating To Substantiating Essential Oil Dietary Supplement Claims And Proposed Solutions

Russell J. Osguthorpe MD, CMO doTERRA, Assoc. Professor Pediatrics University of Utah

Essential Oils (EO) have been extensively studied for decades but progress has been limited due to problems of adulteration and a combination of a lack of industry wide quality metrics and regulatory enforcement. Chemometric analysis of EO has been shown to be an effective tool at defining quality standards for EO and allows for structure function claims and disease efficacy claims to be evaluated and then subsequently reproduced by others. Industry wide acceptance of quality standards of EO have profound influence on both safety and efficacy testing. The standard set by DSHEA and enforced by the FDA requires that dietary supplements require competent and reliable scientific evidence to support claims. Structure Function Claims allowed by DSHEA are inherently different from disease claims and the scientific methods used to evaluate dietary supplements should be carefully considered to ensure compliance. Epigenetic modification of gene expression by dietary supplements is both economical and claims generated from these analyses are compliant with dietary supplement law.

Gyorgyi Horvath

University of Pecs

She was born in 1976 in Kaposvár city, Hungary. She completed her high school studies in Kaposvár, and then she was admitted to the biology major of the University of Pécs (UP) (Hungary), where she obtained her diploma in 1999. Between 1999-2002, she was a PhD student at UP, in the Doctoral School of Biology. Between 2002 and 2006, she worked as a scientific assistant at the Department of Pharmacognosy of UP, while successfully defending her PhD dissertation in 2005. Between 2006-2012, she was assistant professor, then in 2012 she completed her habilitation on the field of Pharmaceutical Sciences at UP. From 2012 she is associate professor at the Department of Pharmacognosy, Faculty of Pharmacy, UP. Now she is also the head of this Department. Between 2016 and 2023 she was vice-dean for science and student welfare. She has been involved in teaching and research at the university for 25 years. She is course supervisor of several compulsory and elective courses, e.g. Pharmacognosy 1-2; Essential oils and Clinical Aromatherapy; Plant products in Pharmaceutical Practice; Medicinal Plant Biotechnology. She has a German basic level, an English intermediate level and an advanced-level language exam in medical English. Her scientific field of interest is the isolation, analytical, microbiological and pharmacological investigation of plant bioactive compounds, especially essential oils. She had some study trips with the aim of studying new techniques (e.g. in Austria, Poland, China). She received some professional awards, e.g. in 2015 young scientists award from the Pecs Committee of the Hungarian Academy of Sciences. She has several professional positions and memberships (e.g. president of the Talent Council of Senate Committee of University od Pecs; Member of Executive Board of the Confucius Institute for Traditional Chinese Medicine; President of Pecs Committee of the Hungarian Academy of Sciences, Division of Pharmacy; Member in the Permanent Committee of International Symposium on Essential Oils). The number of her publications in international or national journals: 75; Independent citations: 1572; Hirsch index: 24. Currently she is a Section editor of Routledge Resources Online: Essential Oils and Aromatic Plants Encyclopedia organized by Taylor and Francis.

Biological Activity Of Essential Oils – Focus On Antibiotic Resistance

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Abstract

The discovery of antibiotics was a revolutionary step in the treatment of infectious diseases. However, the microbiologists encountered resistant strains early. For instance, methicillin was approved in 1958, and the first methicillin-resistant strain was isolated in 1961 [1]. Today the resistant strains have spread all over the world mainly in hospitals where they are responsible for nosocomial/healthcare-associated infections (HAI). Antimicrobial resistance (AMR) contributes significantly to a general increase in morbidity and mortality and imposes heavy financial costs on health care systems worldwide. Essential oils (EOs) are very interesting "natural products" containing biological active secondary metabolites. The popularity of EOs is growing worldwide, and a lot of EOs are used for treating different diseases, via e.g. aromatherapy. Recently, the biological effects (e.g. anti-inflammatory, antimicrobial, enzyme inhibitory, psychological, anti-carcinogenic, etc.) of EOs have been widely researched [2]. Among them, the investigation of antimicrobial activity is outstanding because of AMR. It is well known that EOs have antimicrobial potential, which may enable their application in the fight against multidrug-resistant pathogens. However, the question is how this phenomenon of EOs can be utilized in a clinical atmosphere against different infections.

The lecture will focus on what trends are typical in the research of biological activity of EOs. The background of antibiotic resistance will be presented and what kind of mechanisms of antibiotic resistance can be influenced with EOs. The technical problems in laboratory experiments, which may cause wrong and questionable results about antimicrobial activity of EOs will be introduced. Furthermore, some preliminary results focusing on anti-biofilm activity and formulation of EOs from our research group will be shown.

Acknowledgement

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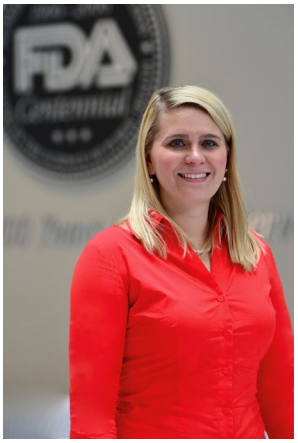


Cassandra Taylor

Food and Drug Administration

Cassandra Taylor, Ph.D. is a Public Health Advisor at U.S. Food and Drug Administration (FDA) within the Center for Drug Evaluation and Research's (CDER) Office of the Center Director and leads CDER's cannabis science and research portfolio. She serves as a cannabis subject matter expert (SME) for CDER and across FDA, concentrating on the botanical and quality aspects of cannabis. She received her B.S. in Chemistry from St. Francis University (2005), and her Ph.D. in Analytical Chemistry from the University of Maryland (2014). Dr. Taylor has evaluated over 150 botanical drug submissions across CDER's clinical divisions, with a focus on reviewing cannabis submissions and was the technical lead on the draft and finalized FDA guidance for industry titled "Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research." She leads and coordinates many cannabis initiatives within CDER and FDA. Dr. Taylor is an active SME in the FDA cross-agency cannabis working group, Cannabis Product Committee (CPC) and has published multiple cannabis manuscripts. She collaborates with colleagues across FDA to help close substantial knowledge gaps about the science, safety, and quality of cannabis and cannabis-derived products.

Cannabis Opening Remarks

Cassandra Taylor

Food and Drug Administration

Patrick Cournoyer

Food and Drug Administration

Patrick Cournoyer is a senior science advisor who leads the FDA's Cannabis Product Committee, managing and coordinating the Agency's cannabis-related activities. Before starting this position in 2022, he served as a regulatory scientist in the Office of Food Additive Safety (OFAS) in the FDA's Center for Food Safety and Applied Nutrition (CFSAN), advising on the regulation of cannabis-derived substances as food ingredients, including cannabidiol and hemp seed. In OFAS, Patrick also specialized in the food safety evaluation of new plant varieties, including those developed through genetic engineering and genome editing. Before joining the FDA in 2013, he completed his PhD at Yale University, where he investigated the cell and molecular biology of the plant immune system.

A New Way Forward For Cannabidiol (CBD) And Other Hemp Products

Patrick Cournoyer

The FDA announced that existing regulatory frameworks for foods and supplements are not appropriate for cannabidiol (CBD). Given the available evidence, it is not apparent how CBD products could meet safety standards for dietary supplements or food additives. A new regulatory pathway for CBD is needed that balances individuals' desire for access to CBD products with the regulatory oversight needed to manage risks.

Tahmina Khan

Food Standards Agency

I have a first class undergraduate degree from The University of Exeter in Biological and Medicinal Chemistry (with industrial experience) and a PhD in Biotechnology from The University of Manchester, UK. The research was sponsored by CooperVision;particular focus was in developing various cell lines, employing high content analysis techniques and fluorescence microscopy to understand the clinical signficance of ophthalmic dye uptake in cells in an in vitro model (https://doi.org/10.1016/j.biocel.2018.05.011).

Since graduating from The University of Manchester, my focus has been on developing a career in regulatory science in the UK Civil Service. I gained 2.5 years experience in regulating plant protection products within the chemistry and residues team for the Chemicals Regulation Divison, Health and Safety Executive before moving to the Food Standards Agency (FSA) in 2021.

I am currently a senior risk assessor at the FSA in the Food and Innovations Team, managing the program of work on bringing cannabidiol (CBD) into compliance under the UK novel food regulation and esuring its safety for the consumer.

A provisional ADI for CBD – The UK assessment experience

Tahmina Khan

Food Standards Agency

In the UK, cannabidiol (CBD) has entered the food sector as beverages, edible oils, food supplements and chewables and confectionary. The novel food status of CBD was confirmed in January 2019, and is why CBD food products require authorisation before they can be sold legally in Great Britain (GB). There are currently no authorised CBD extracts or isolates on the market in GB.

Having initially received over 1000 applications, the Food Standards Agency (FSA) now have a little under 100 applications with sufficient quality of data and information to allow the assessment of the safety of CBD consumption. Specifically, in assessing toxicological information provided by applicants, our independent scientific advisory committee have determined a provisional acceptable daily intake (ADI) of 0.15 mg/kg bw/day for pure forms of CBD. The FSA look to applying this ADI where appropriate and facilitate bringing the CBD market in GB into compliance.

Marilyn Huestis

Thomas Jefferson University

Professor Dr. Dr. (h.c.) Marilyn A. Huestis retired as a tenured senior investigator and Chief, Chemistry and Drug Metabolism Section, IRP, National Institute on Drug Abuse, National Institutes of Health in 2016 after 23 years of conducting controlled drug administration studies. She was an Adjunct Professor, University of Maryland School of Medicine, Baltimore, MD from 1999-2017. Currently, she is a Senior Science and Policy Advisor for PinneyAssociates, Professor at the Institute on Emerging Health Professions, Thomas Jefferson University, Philadelphia, PA, Adjunct Professor, University of New Mexico, College of Pharmacy, Honorary Professor, Barts & London School of Medicine & Dentistry, Queen Mary University of London, England on the Smart Approaches to Marijuana (SAM) Science Advisory Board, and President of Huestis & Smith Toxicology, LLC. Her research program focuses on the neurobiology and pharmacokinetics of cannabinoid agonists, kratom/mitragynine, psilocybin, effects of in utero drug exposure, oral fluid drug testing, driving under the influence of drugs, and identification and quantification of drugs by mass spectrometry. She published 568 peer-reviewed manuscripts and book chapters and hundreds of invited lectures and abstracts were presented at national and international meetings. Professor Huestis received a bachelor's degree in biochemistry from Mount Holyoke College, a master's degree in clinical chemistry from the University of New Mexico, and a doctoral degree in toxicology from the University of Maryland. Professor Huestis received a Doctor Honoris Causa from the Faculty of Medicine, University of Helsinki in Finland. Other important awards include the 2023 CMCR Pioneer in Medicinal Cannabis Research Award, 2023 Mechoulam Award from the International Cannabinoid Research Society, 2021 American Association for Clinical Chemistry (AACC) Outstanding Lifetime Achievement Award, 2021 National Safety Council Distinguished Service to Safety Award, 2021 American Academy of Forensic Sciences (AAFS) Alexander O. Gettler Award, 2018 National Safety Council's Borkenstein Award, 2017 Sir Kenneth Standard Distinguished Lecturer for the University of the West Indies, 2016 Victorian Institute of Forensic Medicine Orator, Melbourne, Australia, 2016 Marian W. Fischman Lectureship Award from the College on Problems of Drug Dependence, 2016 Saferstein Memorial Distinguished Lecturer at Northeastern University, 2015 Norman P. Kubasik AACC Lectureship Award, 2015 Distinguished Fellow from AAFS, 2010 The International Association of Forensic Toxicologists (TIAFT) Alan Curry Award, 2008 AACC Outstanding Contributions in a Selected Area of Research Award, 2007 International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) Irving Sunshine Award, 2005 AAFS Rolla N. Harger Award, and 1992 Irving Sunshine Award for Outstanding Research in Forensic Toxicology. The journal Clinical Chemistry featured her as an "Inspiring Mind". She currently serves on the World Anti-doping Agency's Prohibited List Committee, and the National Safety Council's Alcohol, Drugs and Impairment Division Executive Board. Professor Huestis served on the National Commission on Forensic Sciences. She is past president of the Society of Forensic Toxicologists, past Chair of the Toxicology Section of the American Academy of Forensic Sciences, and past president of The International Association of Forensic Toxicologists.

Short & Long-Term Consequences Of Cannabis Intake & Differences Between Occasional & Chronic Frequent Cannabis Use

Marilyn A. Huestis[1]

[1]Institute of Emerging Health Professions, Thomas Jefferson University, Philadelphia, PA 19107

As the medicalization and legalization of the United States continues to increase it is important to understand the short- and long-term consequences of cannabis use. The endogenous cannabinoid neurotransmitter system is critical for the appropriate functioning of survival functions including hunger, body temperature control, memory and reproduction. When individuals use cannabis, they hijack the normal functioning of the system that attempts to maintain homeostasis.

The most important short-term consequence of cannabis use is the morbidity and mortality of driving under the influence of cannabis. Also, legalization reduced the perception of risk of using cannabis that leads to higher adolescent and adult cannabis intake. Accidental intake by children increased emergency department visits, especially with the advent of edibles, frequently packaged to be attractive to children and adolescents. However, adults unfamiliar with the pharmacokinetics of oral cannabis and the time required to reach peak effects, may ingest multiple doses, become highly intoxicated and require emergency assistance as well. The lack of quality control of unregulated cannabis can result in serious harm, as occurred with the vaping crisis, when vitamin E acetate, harmless when taken orally or used topically, was seriously toxic when inhaled.

The developing brain is adversely affected by exposure to cannabis with long-term consequences. In utero exposure during maternal cannabis use can produce long-term effects on offspring. Many pregnant women do not believe that cannabis is harmful to the fetus. Two long-term follow-up studies of maternal cannabis use, one in middle-class Caucasian women and one in lower socioeconomic class African-American women, showed similar impairments in developmental outcomes.

There clearly are differences in the effects of occasional (less than daily) cannabis use and chronic frequent (daily) cannabis intake. Additional research is critically needed into the effects of long-term daily cannabis use, whether for medical purposes or recreational use.

Denzil Phillips

Association of African Medicinal Plants Standards (AAMPS) and Global Frankincense Alliance (GFA)

Lawrance Denzil Phillips has worked in the field of botanicals and natural products in Africa, Asia and the Caribbean for more than 35 years. Denzil co-founded High Value Horticulture plc in 1989 and launched Denzil Phillips International Ltd (DPIL) in 1998. DPIL has undertaken consultancy assignments with many of the world's leading natural product, beauty care and phyto-pharmaceutical companies. It also advised many African and Caribbean governments and international agencies such as World Bank, Commonwealth Secretariat and the European Commission (EU)

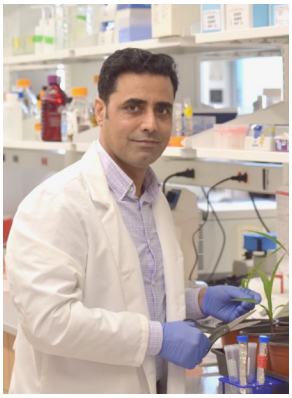
Denzil now lives in Barbados where he works on building bridges between Africa and the Caribbean in the field of high value crops. He was founder Director of the Association of African Medicinal Plants Standards (AAMPS) an organisation dedicated to promoting quality standards for African medicinal plants, founder Director of the Global Frankincense Alliance (GFA) and is an advisor to the Spa and Wellness Association of Africa (SWAA) and the Global Wellness Institute (GWI)

Denzil has worked in more than 55 countries many of them in Africa and the Caribeean. These include Barbados, Burkina Faso, Gambia, Grenada, Jamaica, Kenya Uganda and South Africa. He specialises in the conservation and sustainable sourcing of high value natural products many of which are indigenous plants. He also helped organise the first Medicinal Plants Business Forum for Commonwealth Africa in Kirstenbosch in 2000 and the World Congress on Medicinal and Aromatic Plants in Cape Town in 2008 (WOCMAP IV) Denzil has presented at more than 65 international botanical meetings during in his long career and is passionate about sharing his knowledge with young African and Caribbean researchers in the field of natural products(www.denzil.com)

Conservation Status Of Frankincense With Special Reference To Recent CITES Review And Recommendations

The Boswellia CITES Review

CITES (The Convention on International Trade in Endangered Species of Wild Fauna and Flora) is a near-universal treaty designed to control the negative impacts of trade on biodiversity. The Plants Committee of CITES is currently reviewing the status of the genus Boswellia (the frankincense trees) to determine if any or all of them meet the criteria for inclusion in the CITES Appendices, and what the potential outcomes would be. While CITES is a powerful tool for regulating trade, the decision whether to list or not is complicated by a variety of factors, including the lack of strong data on some species, institutional challenges in exporting states, cultural and humanitarian concerns, and the potential unintended consequences of reduced trade in some species. This talk will provide an update on the status of the CITES Boswellia review, identify key considerations for and against listing, and discuss potential pathways to sustainability for the global frankincense trade.



Abdul Latif Khan

University of Houston

Dr. Abdul Latif Khan is working as an Assistant Professor in the Biotechnology Program at the Cullen College of Engineering, University of Houston. His lab works on Plant climatic stress tolerance and the microbiome's function. The goal is to elucidate the plant-microbiome-stress interactions and strategies to improve stress signaling mechanisms in essential crops. His lab also works on the genomics and evolutionary history of orphan crops and medicinal plants that are highly important for conservation, ecology, and human benefits. He received an MS in Chemical Ecology from the University of Tsukuba, Japan, and a Ph.D. in Plant Physiology at the School of Applied Biosciences, Kyungpook National University, South Korea. Later, he worked as an Assistant Professor at the Natural & Medical Sciences Research Center, University of Nizwa-Oman.

Frankincense Tree Genomics And Resin Synthesis Pathway

Abdul Latif Khan[1], Ahmed Al-Harrasi[2]*, Jin-Peng Wang[3], Sajjad Asaf[2], Jean-Jack M. Riethoven[4], Tariq Shehzad[5,6], Chia-Sin Liew[4], Daniel P. Schachtman[4], Ahmed Al-Rawahi[2], Jeffrey L. Bennetzen[7], Xi-Yin Wang[3]*

[1]Department of Engineering Technology, Cullen College of Engineering, University of Houston, Sugar Land, TX, USA; [2]Natural and Medical Sciences Research Center, University of Nizwa, Nizwa, Sultanate of Oman; [3]School of Life Sciences, North China University of Science and Technology, Caofeidian Dist., Tangshan, Hebei, China; [4]The Nebraska Center for Biotechnology, University of Nebraska–Lincoln, Lincoln, NE, USA; [5]Plant Genome Mapping Lab, Center for Applied Genetic Technologies, University of Georgia, Athens, Georgia, USA; [6] Syngenta Crop Protection LLC, Bioinformatics and Genotyping, Research Triangle Park, NC, USA; [7] Department of Genetics, University of Georgia, Athens, GA, USA; [8] School of Applied Biosciences, Kyungpook National University, Daegu, South Korea

Historically, frankincense is one of the three gifts offered to Christ by the three Wise Men and is mentioned 22 times in the Bible. This iconic product, with a history dating back to the late 4th millennium B.C., was behind the flourishing trade between South Arabia and the rest of the world. Modern medicine has unraveled the medicinal secrets of frankincense, demonstrated by its discovery of superior anti-inflammatory, anti-cancer, and anti-depression properties. Despite the advances in its medicinal chemistry, its genomic and transcriptomic data remained unknown. How the trees respond to tapping and methods to improve the recovery process remain poorly understood. We reported the de novo assembled genome (667.8 Mb), comprised of 18,564 high-confidence protein-encoding genes. We elucidated key signaling network-related factors by performing de novo site-specific transcriptomic, phytohormonal, and gene expression analysis of the frankincense tree. Wounding immediately activates several cell developmental and regeneration processes, defense-induced terpenoids, and phytohormonal metabolism to heal damaged tissues in the epidermis. The current talk will explain these different physiological and molecular mechanisms of wound-induced tapping responses in frankincense.

Stephen Johnson

FairSource Botanicals

Stephen Johnson is a technical advisor on biodiversity, human rights, transparency, and risk management in botanical value chains. He is an interdisciplinary ecologist who works to leverage the commercial value of botanicals and forest products to deliver greater social and environmental benefits across the supply chain and to incentivize conservation and protection of biodiversity. He has been working on frankincense sustainability issues since 2016, has published more than a dozen peer-reviewed papers, book chapters, and technical reports, and conducted socio-ecological research on frankincense in Somaliland (Somalia), Puntland (Somalia), Ethiopia, Oman, Burkina Faso, and Ghana.

Leveraging Technology To Improve Governance And Impact In Frankincense Value Chains

Stephen Johnson

The global trade in medicinal and aromatic plants (MAPs) generates billions of dollars annually, with at least two thirds of MAP species harvested from the wild. Wild botanical value chains frequently face a variety of challenges, including a lack of transparency, unsustainable harvesting practices, and poor benefits to harvesters and their communities. Frankincense (Boswellia species) is a good example of this. Extensive research over the past two decades has revealed significant threats facing Boswellia species, including real or potential declines in multiple populations. Harvesting resin for commercial trade is a key threat in many species, highlighting the importance of ensuring sustainable harvesting practices in commercial value chains. However, like many wild botanicals, frankincense is difficult to monitor: the trees grow in remote locations, harvesting areas can be widely dispersed, and conflict issues make it difficult to conduct on-the-ground audits. The integration of mobile data collection and documentation tools has some potential to address these challenges, and is already being implemented in some frankincense value chains. Distributed documentation tools, such as CyberTracker, ArcGIS Collector, or custom-designed apps, provide opportunities for supply chain actors to collect data and document practices in real time, even in difficult-to-survey areas. Data security technologies like blockchain further help protect the data from tampering once collected. Together, these technologies can improve the transparency of supply chains and strengthen audits against third party certification standards, such as UEBT or FairWild. Combining these approaches can improve the governance of wild botanical value chains and provide opportunities to improve the social and environmental impacts of commercial trade.

Thomas Brendler

Plantaphile

Dr. Thomas Brendler is a scientist and consultant focusing on all aspects of herbal product development, registration and licensing. For the last 30 years, he has developed and managed projects for industry on the use of plants in medicine, food, and cosmetics. He has been involved in the preparation, management, and execution of various publicly funded research projects, e.g., for the Millennium Challenge Corporation, the Centre for Development of Enterprise, and the International Trade Centre. In 2005 he co-founded the Association of African Medicinal Plants Standards and served as a director until 2018. He has authored, co-authored, edited and contributed to more than 50 publications topics related to ethnobotany, ethnopharmacology, phytotherapy and natural product regulation, most notably Physician's Desk Reference for Herbal Medicines, Medicinal and Aromatic Plants of Indian Ocean Islands, A Practical Guide To Licensing Herbal Medicinal Products, African Herbal Pharmacopoeia, and the translation into English of the German Commission E monographs. Thomas is a member of the editorial boards of Phytotherapy Research, Journal of Ethnopharmacology, Frontiers in Pharmacology and a regular peer reviewer for a variety of scientific journals. He has been a member of the US Pharmacopoeia Botanical Dietary Supplements & Herbal Medicines Expert Committee since 2015 and serves on the boards of the International Society for Ethnopharmacology and the American Botanical Council. He has received his PhD in Botany from the University of Johannesburg, South Africa, and holds a position as Associated Researcher there. Dr. Brendler is currently affiliated with Traditional Medicinals, Inc., USA, as Principal Scientist R&D.

The State Of Indian Frankincense – An Update

Brendler, T & Cunningham, A.B.

In 2015, we conducted assessments of several plant species, including Boswellia spp., on fulfilling the Conf. 9.24 Criteria for inclusion in CITES Appendix II based on Art. IV 2(a) on behalf of the German Federal Agency for Nature Conservation (BfN). For Indian frankincense, despite its large geographic range, we found the most extensive sustainability concerns to be habitat loss through clearing of B. serrata woodlands for farming and poor recruitment of seedlings and young trees into the population due to grazing and browsing by livestock. At the time, the regional conservation status of B. serrata ranged from Least Concern (LC) all the way to Critically Endangered (CE). Findings from this assessment were revised with new data and published in 2018 , showing signs of population decline and overexploitation of this resource, leading to a shift of demand pressure to African frankincense species as well as species admixture, substitution, and adulteration. What was not considered in these earlier assessments was 40 years of commercial logging of B. serrata trees in Madhya Pradesh to produce ca. 20,000 tons pulp/year for paper production. The potential listing of B. serrata to CITESAppendix II raises complex questions. Including the fact that CITES App. II listing is unlikely to have an impact on the most important factors - all non-trade related, such as habitat loss and grazing - that affect B. serrata populations. These need to be dealt with at a national level in India, given the importance of this species in India and importing nations. Ten years on, listing of frankincense has been controversially discussed at several CITES meetings, resulting in an extensive report on Boswellia species in international trade, presented to CoP19 in Panama, 2022 . The decision was made to defer any CITES listing decision to CoP20 which is scheduled for 2025. We present a summary of new data.

Laurie Dolan

GRAS Associates

Dr. Laurie Dolan holds a Ph.D. in Pharmacology and Toxicology. She is a board-certified toxicologist (DABT) with over 30 years of experience in regulatory submissions and safety assessments. She is a Fellow of the American College of Nutrition (FACN) and past president of the Food Safety Specialty Section of the Society of Toxicology (SOT). Dr. Dolan previously served as a Senior Toxicologist in the Contaminant Assessment Branch at FDA's Center for Food Safety and Nutrition and is currently Senior Staff Toxicologist for GRAS Associates, a Nutrasource/SGS Company.

Safety In Use Of Korean Red Ginseng Extract As A Dietary Supplement And Food Ingredient: A Review Of Pre-Clinical, Clinical, And Traditional Use

Dolan, L.C.

P. ginseng has a long and rich history of use in Korea and northeastern China and is available in dietary supplement products in the United States (US). There are three major types of P. ginseng preparations: “fresh ginseng” is obtained from plants less than 4 years old and is consumed fresh; “white ginseng” is derived from older plants , and is prepared by peeling off the peripheral skin and then drying the root; and “red ginseng” is derived from older plants as well, and is prepared by steaming and drying the root, resulting in a reddish color, resistance to deterioration and changes to the phytochemical profile compared to other types of ginseng. To be used in food or dietary supplements in the US, a substance should be demonstrated safe at the proposed level of consumption. Because the steaming process of red ginseng root may alter the concentrations of substances in the root, the toxicological profile of red ginseng products may be different from fresh or white ginseng products. Further, the toxicological profile of a red ginseng root product may vary depending on method of preparation – an ethanolic or methanolic extract may cause different effects in the body than a water extract. Therefore, for example, if a red ginseng product that is extracted with water is desired for use in food or dietary supplements, the preponderance of safety information should be on the substance itself rather than a different type of red ginseng extract or a water extract of a white ginseng product. The purpose of this presentation is to discuss traditional use and results of studies that have been performed with Korean Red Ginseng Extract (a water extract) to support use of the ingredient in food and dietary supplements.

Yuan Shiun Chang

China Medical University

Dr. Chang is a Professor of Pharmacognosy at the Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, College of Chinese Medicine, China Medical University, Taichung, Taiwan. Dr. Chang received his Ph.D. degree in Pharmacognosy from University of Illinois at Chicago, U.S.A. in 1989 under the supervision of renowned late Professor Norman R. Farnsworth. Besides teaching, he had served as Head of Herbal Pharmacy of China Medical University Hospital for more than 10 years. He collaborated closely with TCM communities in Taiwan. He often organized workshops and smposia in TCM. He had engaged in the quality control studies of TCM herbs for many years. He is the PI of the projects for the compilation of the 2nd ,3rd and 4th editions of both Chinese and English version of Taiwan Herbal Pharmacopeia (THP) which was promulgated and published by Department of Health and Welfare from 2012 to 2022. He has also been invited since 2011 to join Hong Kong Chinese Materia Medica Standard Project, Department of Health, Hong Kong as PI from Taiwan. Professor Chang is nominated as USP HMC East Asia Expert Panel member (EP) (2015-2020; 2020-2025) and USP Botanical Dietary Supplements and Herbal Medicine Expert Committee (EC), (2020-2025). He is also an EDQM TCM Working Party Member, European Pharmacopeia (2017-2019; 2020-2022; 2023-2025). Professor Chang is also appointed as Honorary Professor of College of Chinese Medicine, Hong Kong Baptist University (2019-2023). Professor Chang received Yu-Chieh TCM Award from Ministry of Health and Welfare in 2021 for his contribution to the TCM communities. Professor Chang was also listed as top 2% world scientists in Stanford University ranking in 2021 on both lifelong and 2021. Professor Chang was elected as Board member of GP TCM RA (2023 - 2024). He was also invited as Associate Editor of Pharmaceutical Biology. Professor Chang had just received 2023 Professional Medal from Ministry of Health and Welfare, Taiwan. To date, he has published 160 scientific papers and 27 books in TCM related fields. Most of the books were government publications through government research funding.

Antifatigue, Memory Enhancing and Blood Circulation Effects of Korean Red Ginseng

Yuan Shiun Chang

Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, College of Chinese Medicine, China Medical University
Taichung, TAIWAN

Korean red ginseng (KRG) had been reported in many in vivo and clinical studies to exhibit various beneficial biological effects such as immunologic, antifatigue, antineoplastic, neuroprotective, hepatoprotective, antidiabetic, antistress, lowering blood pressure, memory enhancing, anti-inflammatory, antihyperlipidemic, improve blood circulation and antioxidative properties, etc.. In this study, we like to share the antifatigue, memory enhancing and blood circulation effects of KRG.

KRG had been used in Asian countries to enhance vital energy since ancient times. Many in vivo and clinical studies had demonstrated that Korean red ginseng exhibited anti-fatigue activities (Brekhman, 1960; Chang, 1989). Li Zhang et.al 2019 evaluated the safety and antifatigue effect of KRG through a randomized, double-blind, and placebo-controlled clinical trial and found that KRG has a potent antifatigue effect disprove the common conception of “fireness” related to KRG.

KRG had been reported to be helpful for brain related diseases such as Alzheimer’s disease (AD), memory deficits in both in vivo and clinical studies. Young rats with hippocampal lesions displayed significant deficits in the place learning tasks (PLT). Treatment with KRG significantly ameliorated place-navigation deficits in young rats with hippocampal lesions in the PLT. The results, suggest that KRG ameliorates learning and memory deficits through effects on the central nervous system, partly through effects on the hippocampal formation (Nishijo et. al. 2004).

KRG platelet aggregation by regulating the synthesis of prostacyclin (PGI2), which has an antagonistic mechanism toward platelet aggregation, as well as thromboxane A2 (TXA2) and serotonin, which promote platelet aggregation, thus suppressing the generation of thrombi and improving blood circulation (So et al., 2018). Administration of KRG to healthy subjects significantly inhibited ADP-induced and collagen-induced platelet aggregation. KRG has a potential to improve blood circulation through antiplatelet activity in human (Shin et al., 2007).

In summary, KRG beneficial effects to fatigue, memory deficit and blood circulation had been proved through in vivo and clinical trials.

Seung-yeol Nah

Konkuk University

Department of Physiology, College of Veterinary Medicine, Konkuk University,
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Education

1979 - 1983: B. Sc., KonKuk University, Dept. of Veterinary Medicine, Seoul, Korea.
1983 - 1985: M. Sc. of Veterinary Medicine, Dept. of Veterinary Medicine, KonKuk University, Seoul, Korea.
1987 - 1993: Ph. D., Dept. of Neurobiology The Weizmann Institute of Science, Rehovot, 76100, Israel.
Thesis: Opioid receptor signal transduction and desensitization

1995 - 2002.8: Associate Professor, College of Veterinary Medicine, Chonnam National University, Kwangju, Korea 500-757

2002.9 - 2012.8. Professor, Department of Physiology, College of Veterinary Medicine, Konkuk University, Seoul Korea 143-701.

2012.9 - 2014.8: Dean (□ □), College of Veterinary Medicine, Konkuk University,
Seoul Korea 143-701.

The President, Korean Ginseng Society (2019.1.1 – 2020.12.31)
The Vice President, Korean Ginseng society (2013. 1.1 –2018.12.31)
Secretary General of Korean ginseng society (2005.1. 1 - 2006.12. 31)
Chief editor of Journal of Ginseng Research (2007.1.1 - 2008.12. 31)
Editorial board member of Journal of Ginseng Research (2010.1.1 –current)
Committee Member of Korean Society of Veterinary Medicine.

Gintonin, Korean ginseng-Derived LPA Receptor Ligand, Alleviates Memory Dysfunctions via Non-Amyloidogenic Pathway and Blood-Brain Barrier Protections in Alzheimer's Disease Animal Model

Seung-Yeol Nah

Ginsentology Research Laboratory and Department of Physiology, College of Veterinary Medicine, Konkuk University, Seoul 143-701, Korea

Ginseng, the root of Panax ginseng C.A. Meyer, is one of the oldest herbal medicines with a variety of physiological and pharmacological effects. Ginseng contains saponins and non-saponin bioactive components. Gintonin is a new material isolated from Korean red ginseng as a non-saponin component. Gintonin is a kind of glycolipoproteins and its active ingredients are lysophosphatidic acids (LPAs). LPA is a ligand for GTP protein-coupled LPA receptor, which is crucial receptor for brain development and learning and memory in adults. First, I will introduce to you what is gintonin. Next, we will show you the effects of gintonin on anti-Alzheimer's disease (AD) in AD animal model mouse. We found that acute gintonin activates non-amyloidogenic pathway in neuronal cells. Long-term administration of gintonin via oral route not only inhibits both amyloid plaque accumulations and inflammations in cortex and hippocampus, but also alleviates memory dysfunctions. In addition to gintonin-mediated attenuation of amyloid plaque accumulation in brain, long-term administration of gintonin via oral route also protects blood-brain barrier (BBB) disruptions by restoring gap junction proteins such as Claudin-5, Occludin, PECAM-1 and ZO-1. In the present talk, I will provide a evidence that Korean red ginseng also contains G protein-coupled receptor ligand, gintonin, and gintonin is a novel component of ginseng for alleviations of AD symptoms via attenuation of amyloid plaque accumulation and BBB protection in AD animal model.

Shontell Wright

Food and Drug Administration

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

New Dietary Ingredient Notifications: A Key Step Prior to Launching a New Dietary Supplement in the United States

Wright S

U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Dietary Supplement Programs, 5001 Campus Drive, College Park, MD 20740 USA; shontell.wright@fda.hhs.gov

The Dietary Supplement Health and Education Act (DSHEA) of 1994, which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act), transformed FDA's authority to regulate both finished dietary supplement products and dietary ingredients. DSHEA established the definitions of a dietary supplement and dietary ingredient, defined new dietary ingredient (NDI) notification requirements, and included dietary supplements under the FD&C Act's "adulterated food" provisions.

Under section 413(a)(2) of the FD&C Act, the manufacturer or distributor of an NDI that has not been present in the food supply as an article used for food, or of a dietary supplement that contains the NDI, must submit a premarket safety notification to FDA at least 75 days before introducing the product into interstate commerce. If the required premarket notification is not submitted to FDA, section 413(a) of the FD&C Act provides that the dietary supplement containing the NDI is deemed to be adulterated under section 402(f) of the FD&C Act.

Each dietary supplement manufacturer or distributor is responsible for determining whether each dietary ingredient in each of its dietary supplements is an NDI and ensuring compliance with the NDI notification requirements, if applicable. Determining when an NDI notification is required for an NDI can be a confusing process for manufacturers and distributors unfamiliar with the laws and regulations governing dietary supplements. Therefore, this presentation will briefly discuss how FDA regulates dietary ingredients under DSHEA, when an NDI or dietary supplement containing an NDI are subject to the premarket notification requirement, and what information should be included in a premarket notification submission.

Rebecca Adams

NSF

Rebecca Adams is a Principal Research Toxicologist and has been a member of the NSF toxicology department since 2016. Prior to that, she spent 7 years in the scientific and regulatory consulting sector. Ms. Adams expertise centers upon the safety and regulatory evaluation of dietary supplement and functional food ingredients. She has recently published a paper on chemical-specific maximum allowable levels for pesticide residues in dietary supplements. She has also developed safety criteria for probiotics as well as a risk-based approach for endogenous thresholds for athletically banned substances in natural products. In addition, Ms. Adams has authored numerous chemical hazard and risk assessments for water contaminants and has also worked on safety support evaluations for green chemistry solutions. Her experience in multiple disciplines including chemical-specific risk assessment, exposure assessment, toxic tort litigation, and public health and safety give her an expert perspective on potential risk factors for a variety of chemicals.

Setting The Standard: Expert Insights On Best Practices And Safety Considerations For New Dietary Ingredient (NDI) Notifications

Rebecca Adams

NSF

Rick Kingston

Safety Call

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

Impact Of MoCRA On Monitoring Botanical Safety

Kingston RL1-3

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The Modernization of Cosmetics Regulation Act of 2022 (MoCRA) became effective December 29th, 2023. MoCRA is the most significant expansion of FDA's authority to regulate cosmetics since the Federal Food, Drug, and Cosmetic (FD&C) Act was enacted in 1938. MoCRA expands the FDA's rulemaking and enforcement authority over cosmetics and creates new compliance obligations for manufacturers. There are six key areas of the legislation including Facility Registration, Product & Ingredient Listing, Safety Substantiation, Cosmetics Labeling, and Adverse Event Reporting and Record Keeping. Each of these areas has significant implications for manufacturers and the ingredients commonly found in cosmetics. Given the ubiquitous presence of botanical and other naturally occurring substances found in cosmetics, these ingredients will certainly be scrutinized as well. Questions remain regarding how compliance will be assessed and enforced. As an example, manufacturers will be required to maintain records that substantiate the safety of the ingredients. Although the legislation requires that qualified experts evaluate ingredient safety substantiation, does that suggest a performance vs. prescriptive approach would be required? As for adverse event reporting, new definition for "Serious Adverse Event Reports (SAERs)" will be applied that substantially change the way adverse events will be coded and SAERs will be flagged as compared to other FDA regulated products including dietary supplement. If a botanical is found "unsafe" in cosmetics would that impact their use in dietary supplements? Lastly, fragrance and flavor safety are specifically called out in the legislation, especially as to their role in allegedly contributing to SAERs. Many of these MoCRA related questions may ultimately be addressed with the help of best practices development in conjunction with authoritative third parties. These and other questions will be discussed and addressed in the session.

Jannavi Srinivasan

Food and Drug Administration

Jannavi is the Director of the Division of Cosmetics, Office of Cosmetics and Colors (OCAC) in FDA/CFSAN. She provides scientific, technical and policy leadership on matters related to the chemical, toxicological, and microbiological safety of cosmetics raw materials, ingredients, and products. Prior to joining OCAC, she served as a chemistry, specifications and dietary exposure expert for new GRAS ingredients, foods from new plant varieties and food and color additives, in the Division of Food Ingredients in the Office of Food Additive Safety (OFAS) in FDA/CFSAN. She has been an invited expert and member of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) since 2011. She also served as the technical expert for the US FDA delegation at OECD's Task Force for the Safety of Novel Foods and Feeds, as an invited expert to EFSA's CEF Panel (Panel on Food Contact Materials, Enzymes and Flavorings), and as a member of the US delegation to Codex Committee on Food Additives (CCFA).

Session E Overview of the U.S. Cosmetics Regulatory Framework

Srinivasan, Jannavi R.

Cosmetic products in the U.S. has been regulated by the Food and Drug Administration (FDA) according to the Federal Food, Drug, and Cosmetic Act which has provided for FDA's regulation of cosmetics since 1938. The Modernization of Cosmetics Regulation Act (MoCRA), enacted in December of 2022, significantly expanded and reformed regulations overseeing cosmetics in the U.S. Included in MoCRA among other provisions, are facility registration and product listing, reporting of serious adverse events, and a requirement that FDA propose a rule for good manufacturing practices. This presentation will provide an overview of cosmetics regulations including the major provisions of MoCRA and examples of ongoing work that supports the mission of the FDA to protect public health.

Brandi Reinbold

National Science Foundation

Brandi Reinbold is the Senior Manager, Global Certification at NSF, where she leads technical department in program design and management for NSF's Health Sciences Certifications business unit, which services the dietary supplements, cosmetics and over-the-counter drug industries. NSF Health Sciences provides accredited, third-party GMP certifications, evaluated by facility audits, and finished product certifications consisting of product label review, testing, and production audits.

She has been with NSF for nine years and was previously the Group Lead, Quality and Compliance and a Senior Certification Project Manager, Dietary Supplements. Brandi previously worked in biologics manufacturing at Vericel Corporation, clinical laboratory science at Wayne State University and immunology at the American Red Cross. She graduated with a Bachelor of Science in Biology from Oakland University.

MoCRA And The New Cosmetics GMPs

Brandi Reinbold

The Modernization of Cosmetics Regulation Act (MoCRA) enacted by Congress December 29th, 2022, includes provisions for the FDA to publish proposed Good Manufacturing Practice (GMP) regulations by the end of 2024 and a final rule by the end of 2025. In this talk we will explore what the language of MoCRA tells us about what GMPs are likely to be promulgated with a focus on GMPs related to ingredient and finished product identity and purity.

MoCRA exempts small cosmetics manufacturers from GMP compliance requirements and directs FDA to "take it easy" on other not-quite-so-small manufacturers. Despite these exemptions, most cosmetics manufacturers are likely to find themselves subject to complying with these GMPs, as MoCRA is just part of a broader paradigm shift impacting this and other consumer product categories. Modern consumers are informed, and increasingly demand proven safe, pure, authentic products. This demand is reflected in the proliferation of state level ingredient bans, consumer litigation and a vast market for "clean" and "natural" products. For these and other reasons we will examine, noncompliance is a losing long-term strategy for cosmetics brands.

HerBChain, A Blockchain-Based Inforamtive Platform For Quality Assurance And Enhancing The Market Share Of Herbal Products

Mavis Hong-Yu Yik[1], Pang-Chui Shaw[1,2,3]

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Recently, the use of herbal products and dietary supplements as complementary and alternative medicine has been on the rise worldwide. Accurate herbal authentication is of paramount importance to the safety and best interest of consumers. However, tracing the origin of herbs is also a critical aspect of herbal safety systems. With the advancement of information technology, a blockchain-based information platform, HerBChain, was created by our team with an association in the industry. HerBChain is an information platform for recording the entire manufacturing and supply chain of herbal products by using blockchain technology in the herbal industry. Six important processes in the manufacturing and supply chain are covered, including plantation base, TCM processing factory, TCM manufacturer, testing laboratory, distributor and retailer.

The unique characteristic of Blockchain include: (1) independent site-server (decentralized network), (2) tamper-proof recording (distributive immutable ledger), (3) lock-stepped (chained), (4) dated statement (time stamped), and (5) highly encryption (asymmetric cryptography). Being distinct from a simple data recording system, data entered into the platform cannot be altered or deleted easily. With minimum possibility of human manipulation of recorded information, quality assurance and quality control of herbal products can be enhanced and the number of adulterated herbal material and products in the market can be reduced. This is a step towards the goal of 'Traceable Origin, Trackable Supply Chain, and Accountable Liability'. As a result, consumer confidence and the value of the industry can be enhanced.

Additionally, HerBChain has already been connected to anti-counterfeiting label, authentication company and e-trading platform, for enhancing the customer confidence and facilitating the marketing of the products.

NOTES

Coming Full Circle On Sustainability -A Case Study Of The Alpinia galanga And Tagetes erecta Botanical Extracts

Deshanie Rai, PhD, FACN. OmniActive Health Technologies, Bridgewater, NJ, USA

Plants and plant-derived compounds have been used since the dawn of time as traditional medicine around the world. This has helped fuel current day consumer interest in using botanicals as complementary medicine to help address several health benefit outcomes, for e.g., vision performance, joint health, and mental wellbeing. In addition to safety and efficacy, consumers are also keen to understand the quality, transparency and sustainability aspects of the botanical supply chain from seed to shelf. How botanical extracts are sourced, agricultural practices including the treatment of the farmers, how the extracts are processed, manufactured, and handled along the way, effects on the environment, and finally data to support its authenticity, are important not just for the regulatory authorities, but now more than ever, for the consumer.

Herein, we will dive into the details of the product lifecycle of two well-established botanical extracts to describe how we leverage sustainable agricultural and product formulation practices through the product development lifecycle. But the journey with bringing botanical extracts to the market always starts with the consumer. With respect to the latter, highlights of why and how we developed the Alpinia galanga (enXtraTM) and Tagetes erecta (Lutemax 2020TM) extracts by keeping the needs of consumer top of mind and developing a research agenda around their needs, will be described. To support the sustainable quality of these extracts, methods to ensure authenticity, identify active constituents and their standardization, understand mechanisms of action, preclinical evaluation of toxicity and finally, clinical studies of safety and efficacy, and their registration strategies will also be further expanded on. Connecting these dots is a critical aspect of ensuring a sustainable supply chain of botanical extracts, and a sustainable botanical industry.

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Future Crops For An Increasingly Arid New Mexico: A Crop Selection Protocol To Support Farmer Resilience To Climate Challenges With High Economic And Culturally Valuable Herb, Medicinal And Aromatic Crops

Maxwell, C. M.[1], I. Guzman[2], K. Lombard[2,3], J. Lillywhite[4], R. Heyduck[5], S. Salmasi[5], A. Fernald[1,6,7], A. Oyenuga[4], R. Islam[1,6], and S. Karki[1,6]

[1] New Mexico Water Resources Research Institute; [2] New Mexico State University, Department of Plant and Environmental Sciences; [3] New Mexico State University, Agricultural Science Center at Farmington; [4] New Mexico State University, Agricultural Economics & Agricultural Business; [5] New Mexico State University, Sustainable Agriculture Science Center at Alcalde; [6] New Mexico State University, Water Science and Management; [7] New Mexico State University, Department of Animal and Range Sciences

The future of farming in New Mexico will be shaped by water stress and competition for limited water resources, which has significantly increased from the general drying trend in the American Southwest over the last four decades. The State's market opportunities likely lie in high value crops that excel or tolerate water stress and are adapted to southwestern climates, such as herb, medicinal, and aromatic crops. New Mexico has a long history of traditional use of medicinal herbs by Native American and Hispanic cultures. Our team adapted a southwestern, arid crop selection protocol with an overall goal of New Mexico agricultural community viability to identify promising crops for paired field and water budget studies in three variable regions of New Mexico, and to synthesize and disseminate the research to farmers on a broader selection of potential crops. The protocol has four main ranking criteria: 1) Marketability and community economic well-being, 2) Agroecological functions, with highest priority on crop water consumption, 3) Agronomic regional suitability, and 4) Food sovereignty and community health. We synthesized research and farmer interviews and examined 131 medicinal and aromatic crops with cultural value for New Mexico users, including Chinese Medicinals. The ranking results for field trials revealed crops that can be utilized holistically on the farm and its environs: 17 field crops, 14 that also comprise perennial hedgerows, four that can be planted along traditional irrigation ditches diverted from rivers (common to southwestern US agriculture), and three on floodplains for community flood mitigation and recharge projects. Our planned future work is to conduct in-depth interviews with a goal to link buyers to farmers. Culturally valued and traditional medicinal and aromatic crops show promise to be key for the future viability for New Mexico farmers in the face of diminishing water availability and other challenges exacerbated by climate change.

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Frankincense: Bridging The Gap Between Research And Industry

Ahmed Al Rawahi[1], Ahmed Al-Harrasi[1]

[1]Natural and Medical Sciences Research Center, University of Nizwa, Nizwa P.O. BOX 33, PC 616, Oman

Frankincense, derived from the resin of Boswellia trees, has been the subject of extensive research, exploring its diverse applications from traditional medicine to modern industries. Investigating its chemical composition, pharmacological properties, and sustainable cultivation practices has paved the way for the integration of frankincense into pharmaceuticals, cosmetics, aromatherapy, food supplements, and other commercial sectors, exemplifying a journey from ancient remedies to contemporary industrial innovation.

In the pharmaceutical sector, frankincense exhibits promise for addressing inflammation and offers potential therapeutic benefits, forming a bridge between ancient and modern medicine. Within cosmetics, its anti-aging and skin-nourishing properties make it a sought-after ingredient, blending ancient wisdom with contemporary beauty standards. Beyond traditional use, ongoing studies explore frankincense's efficacy in supporting overall well-being, including immune system modulation and potential anticancer properties, highlighting its significance in modern healthcare. Aromatherapy utilizes its aromatic essence for stress relief, contributing to mental well-being. The rising trend of incorporating frankincense into food supplements underscores its nutritional value and potential health benefits, fostering a holistic approach to well-being.

This presentation highlights the potential opportunities for industry presented by frankincense. Examining its versatile applications across various fields, showcasing its potential in medicine, cosmetics, aromatherapy, and food supplement. The narrative explores how frankincense emerges as a promising resource with the potential to contribute significantly to various industrial sectors.

Bhushan Patwardhan

Savitribai Phule Pune University

• Distinguished Professor and a highly accomplished academician with over 40 years of experience in higher education, scientific research, and institutional governance. An elected Fellow of the National Academy of Sciences and the National Academy of Medical Sciences in India and the founder and Editor-in-Chief of the Journal of Ayurveda and Integrative Medicine published by Elsevier.

• Senior consultant to the World Health Organization, Geneva, and Co-chair of the WHO Expert Group for the Global Centre for Traditional Medicine. Chairman, Interdisciplinary R&D Task Force on Covid-19 of the Ministry of Ayush, Government of India, member of the Lancet Citizen's Commission for India and Adjunct Professor at Western Sydney University in Australia.

• Significant contributions to the field of evidence-based Ayurveda, particularly in Ayurvedic biology, ethnopharmacology, natural product drug development, and integrative approaches to improving public health systems. Introduced innovative concepts such as Therapeutic Adjuvants, AyuSoft™, AyuGenomics™, Systems Ayurveda, Reverse Pharmacology, and Network Pharmacology, which have gained widespread recognition.

• Recipient of many orations and awards including the Sardar Vallabh Bhai Patel Award, Sir Ram Nath Chopra Oration, Waldemar Haffkine Oration, Dr P.K. Devi Oration just to mention a few. With 175+ scientific publications, 8 Indian, 2 US Patents and 12,600 citations he is listed amongst the world's top 2% biomedical scientists.

• Previously held prestigious positions such as Director of the Interdisciplinary School of Health Sciences, Savitribai Phule Pune University, Academic Head of Manipal Education Group, Vice Chancellor of a deemed University in Pune, Director of the Institute of Ayurveda and Integrative Medicine, Bengaluru. Chairman, National Assessment and Accreditation Council and Vice Chairman, University Grants Commission, Government of India.

An Overview Of Ayush Research In India

Bhushan Patwardhan
Savitribai Phule Pune University

India carries a rich legacy of traditional medicine practices and Sowa Rigpa including Ayurveda, Unani, Siddha. The Ministry of Ayush has supported several initiatives involving national and international institutes of repute to support basic biology, preclinical and clinical research. The Ministry supported quality and safety studies and large-scale population-based surveys, observational studies, and randomized controlled clinical trials to scientifically validate Ayush medicines. Ayurvedic botanicals such as Ashwagandha, Guduchi, Pippali, Yashtimadhu, AYUSH 64, and Anu Taila have shown beneficial effects as prophylactic agents and as an add-on in the standard care for mild to moderate cases of Covid-19. Transdisciplinary research on Ayurvedic biology has provided newer insights into underlying mechanisms of action. The Ministry has published several guidelines, compendium and monographs of a few important botanicals such as Withania sominfera, and Tinospora cordifolia. This lecture will offer a few glimpses of transdisciplinary research on Ayurveda in India.

Geetha Krishnan

World Health Organization

World Health Organization, Unit Head, Evidence and Learning

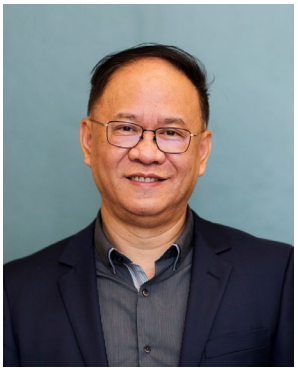
- Dr Geetha Krishnan Gopalakrishna Pillai heads the Evidence workstream of the newly established WHO's global traditional medicine centre, at Jamnagar, India.
- His work is aimed at supporting WHO's Member States to integrate traditional and complementary medicine, and indigenous health practices into national health systems, based on research-based evidence.
- He has rich experience of initiating and successfully concluding major projects on traditional medicine within WHO.
- He is an Ayurveda doctor with more than 25 years of experience. During this period, he has also conceived, established and headed the first integrative medicine department in a major multi-specialty hospital in India.
- He is researcher with diverse interests and has publications in areas of drug development, integrative medicine protocols and public health.

The Gujarat Declaration Principles And Overview Of The WHO-GTMC's Evidence Workstream

Geetha Krishnan GOPALAKRISHNA PILLAI

One hundred seventy Member States report the use of traditional medicine, and their priority request to WHO is for evidence and data to inform policies, standards, and regulatory frameworks for safe, cost-effective, and equitable use. Augmenting WHO's capacities to address the knowledge needs in Traditional, Complementary, and Integrative medicine is the main objective of WHO Global Traditional Medicine Centre (GTMC). It has a strategic focus on evidence and learning, data and analytics, sustainability and equity, and innovation and technology. GTMC is being established with the support of the Government of India and reflects the WHO Director-General's leadership vision that harnessing the potential of traditional medicine would be a game changer for health when founded on evidence, innovation, and sustainability.

The first WHO Global Traditional Medicine Summit, organized by the GTMC, was held on 17-18 August in Gandhinagar, Gujarat, India. The Summit highlighted the global need, interest, and commitment to assure evidence-based traditional, complementary, and integrative medicine for the millions of people using it worldwide, and the appreciation for WHO's leadership and transformative potential in this area of work. The Summit's five plenaries and six parallel sessions informed the Gujarat Declaration endorsed by participants. It sets out a vision and action agenda for WHO to provide global health leadership on traditional, complementary, and integrative medicine to improve health and wellbeing of the people and planet through universal health coverage, based on a primary health care approaches integrated into health systems. It envisages research-based evidence as the basis for such integration, while laying down biodiversity-protection, sustainability, human rights, equity, and ethics as its core principles. While advocating "to mobilize research funding commensurate with TCIM demand," the declaration points to the "appropriate use of existing and new research



Dennis Chang

Western Sydney University

Professor Dennis Chang is the Director of NICM Health Research Institute at Western Sydney University, Australia. He is recognised internationally as a leading researcher in pharmacology and clinical research of natural and traditional medicine. Professor Chang has successfully led a number of major multi-centre clinical trials to evaluate herbal medicine, yoga and tai chi for the treatment of vascular dementia, mild cognitive impairment, coronary heart disease, metabolic syndrome and type 2 diabetes. Professor Chang has conducted numerous laboratory-based studies to evaluate pharmacokinetic/bioavailability profiles and mechanisms of action of herbal medicine. His research has been widely published in high-quality international medical journals and attracted >A$7M funding support from various funding agencies, governments and industry. Professor Chang has also led the Institute's international engagement program, building and sustaining relationships and long-term partnerships with many prestigious universities, research organisations and pharmaceutical/complementary medicine industry around the world.

Development Of A Novel, Standardised Herbal Formula For The Treatment Of Vascular Dementia

Professor Dennis Chang, NICM Health Research Institute, Western Sydney University, NSW, Australia

Background: Vascular dementia (VaD) is a syndrome of cognitive and functional impairment caused by reduced blood flow to the brain. VaD is the second most common cause of dementia and no viable pharmaceutical options are currently available for the disease. Traditional Chinese medicine has a well-documented history of using herbal medicine for dementia-like disorders and could provide alternative interventions for VaD.

Methods: Three Chinese herbs including Ginkgo biloba, Panax ginseng and Crocus sativus were selected and combined in a formula, 'Sailuotong' (SLT). The optimal dose ratio, dosage regimen and mechanisms of action of the formula were determined in a series of preclinical studies using various pharmacokinetic and pharmacodynamic animal models. The acute and chronic toxicity of the formula was also determined. Two RCT trials were conducted to determine the efficacy and safety of SLT.

Results: Ten marker compounds were selected for batch-to-batch quality consistency of SLT. The pharmacological studies demonstrated significant improvements in learning and memory function, pathogenic biochemical parameters in blood and brain tissue, and antioxidant capacity. A great safety margin of SLT were demonstrated in animals and humans. A pilot RCT trial with 62 participants with possible VaD showed a significant improvement in cognitive function (ADAS-cog) after a 4-month treatment of SLT. The results of a phase 2 dose determination study of SLT (240 mg and 360 mg per day over 52 weeks) in 325 participants with probable VaD demonstrated that both low- and high-dose SLT treatments were associated with a significant improvement in VaD Assessment Scale–cognitive subscale scores compared to placebos.

Conclusion: SLT was well tolerated and may be useful in supporting cognitive function in VaD. Two phase 3 trials are currently being conducted to further assess the efficacy and safety of SLT.

The Botanical Safety Consortium: Collaborative Effort to Improve Botanical Safety Methods

Constance A Mitchell, Julie Krzykwa, Cynthia Rider, on behalf of the BSC Steering Committee

The use of botanical dietary supplements is increasing, making their safety a crucial issue for public health. This article discusses the role and goals of the Botanical Safety Consortium (BSC), a collaborative effort between the US FDA, the National Institute of Environmental Health Sciences, and the Health and Environmental Sciences Institute. Formed through a Memorandum of Understanding, the BSC aims to improve safety evaluation methods for botanicals. It operates as an international platform where experts from various sectors, including government, academia, industry, and non-profits, collaborate to advance and apply new approach methodologies (NAMs) for the safety assessment of botanical products.

The BSC's objectives include: 1) collaborating with global stakeholders to advance scientific safety methods; 2) determining the right level of chemical characterization for complex botanical mixtures; 3) finding practical, suitable NAMs for safety evaluation; 4) testing these methods against existing safety data on certain botanicals; 5) incorporating these methods into a systematic framework for assessing botanicals. Initially focusing on oral intake from dietary supplements, the BSC may broaden its scope in future work phases. This presentation will provide a detailed view of the BSC's structure, ambitions, and methodologies, with a focus on updating the audience on the past year’s work.

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Screening Of Medicinal Herbs To Predict The Potential Perpetrators Of Herb-Drug Interaction

Islam Husain, Bill J. Gurley, Amar G. Chittiboyina, Ikhlas A. Khan, Shabana I. Khan

Over time, the popularity and consumption of herbal medicine and its products like nutraceuticals, botanical drugs, and dietary supplements have increased immensely. Parallelly, several health issues associated with the overconsumption of these products have also been raised, which has attracted enormous attention. Herb-drug interaction (HDI) is a health issue caused by herbs or phytochemicals that modulate the homeostasis of drug-metabolizing enzymes (CYPs) and transporters, thus altering the pharmacokinetic of clinical drugs. To date, only a few medicinal herbs, such as Hypericum perforatum, Hydrastis canadensis, Glycyrrhiza glabra, and Camellia sinensis etc., were recognized as HDI perpetrators. However, many need to be yet identified.

As part of our continuous efforts towards studying the safety of medicinal plants, we screened the hydroethanolic extracts of a large collection of herbs for interaction with xeno-receptors (PXR and AhR), drug metabolizing enzymes (CYP 3A4 and 1A2), and transporters (P-gp). We found several plants displaying potent agonism with PXR and increased its activity to 4 to 7-fold at 60 µg/mL while others increased AhR activity up to 10 to 40-fold at 30 µg/mL. We also found the extracts of several plants that strongly inhibited CYP3A4 or CYP1A2 activity. Selected plants were studied further in more advanced assays involving gene expression and enzyme activity in hepatocytes. The HDI of some herbs like Bulbine natalensis, Zingiber officinale, Phyllanthus amarus, Garcinia gummi-gutta and Pausinystalia johimbe were studied in detail and some are underway. Further studies of selected candidates that could be future perpetrators of HDI are warranted.

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Multifaced Factors To Cause Conflictitng Outcomes In Drug-Herb Interactions Mainly Focusing On Reverse Pharmacokinetics

Young Hee Choi[1]

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Metabolic enzyme and/or transporter-mediated pharmacokinetic (PK) changes in a drug caused by concomitant herbal products have been a primary issue of herb and drug interactions (HDIs), because PK changes of a drug may result in the alternation of efficacy and toxicity. Studies on HDIs have been carried out by predictive in vitro and in vivo preclinical studies, and clinical trials. Nevertheless, the discrepancies between predictive data and the clinical significance on HDIs still exist, and different reports of HDIs add to rather than clarify the confusion regarding the use of herbal products and drug combinations. Here, the underlying mechanisms causing PK-based HDIs mainly focusing on the “reverse pharmacokinetics (e.g., systemic exposure and local tissue distributions)” are summarized. In addition, dose and treatment period effects as challenging issues in study designs and interpretations of HDI evaluation should be also considered. Several examples of HDIs are provided to describe these multifaced factors to be considered in the interpretation of HDIs.

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Evaluation Of Botanical Extracts For Cytochrome P450 Inhibition Mediated Drug Interaction

Zarna Raichura[1], Kabre Heck[1], Jaewoo Choi[2,3], Mikah Brandes[5], Cody Neff5, Claudia Maier[2,3,4], Amala Soumyanath[4,5], Robert Arnold[1], and Angela I Calderón[1].

[1]Department of Drug Discovery and Development, Harrison School of Pharmacy, Auburn University, AL 36849, USA, [2]Department of Chemistry and [3]Linus Pauling Institute, Oregon State University, Corvallis, OR 97331, [4]Botanicals Enhancing Neurological and Functional Resilience in Aging (BENFRA) Botanical Dietary Supplements Research Center and [5]Department of Neurology, Oregon Health and Science University, Portland, OR 97239.

There has been remarkable growth in consumption of botanical dietary supplements (BDS), making it important to understand the safety profile of BDS with respect to the pharmacokinetic properties for any potential of botanical-drug interactions. One such botanical interactions which has gained significant attention involves inhibition of cytochrome P450 (CYP450) enzymes by co-administered drugs. Our study involved examining two widely used botanicals, ashwagandha and açaí for any potential inhibition of CYP450. Four different ashwagandha extracts were tested, resulting in inhibition of CYP2B6 with IC50 < 100 µg/ml of extract and showed potential of time-dependent inhibition for CYP2C9 and CYP2D6 with an IC50 ~ 200 µg/ml of extract. In the case of açaí, seven different extracts were tested and only CYP2C9 was inhibited. The acidic methanol extract of açaí formulation showed an IC50 of 0.3 µg/ml of extract indicating potent inhibition of CYP2C9, while the methanol (IC50 ~ 91.75 µg/ml) & ethanol extracts of Mountain Rose açaí powder showed weak inhibitory effect with an IC50 < 100 µg/ml of extract for CYP2C9. The results reflect that both botanical extracts showed potential of CYP450 inhibition, suggesting that compounds in BDS can prolong the half-lives of medications leading to extended action or toxicity. Next step involves, testing subfractions of these extracts to identify the compounds responsible for the observed inhibition.

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AI-Assisted Organisim-On-Chip Platform For Evaulating The Quality Of Bothanical Herbs And For Bioactive Discovery

Siva A. Vanapalli[1,2], Supraja Rama Balaga[1], Taslim Anupom[1], Mohammed Adnan Qureshi[1], Mizanur Rahman[1], Amar G. Chittiboyina[3] and Ikhlas Khan[3]

[1]NemaLife Inc., Lubbock, TX; [2]Texas Tech University, Lubbock, TX; [3]National Center for Natural Products Research, University of Mississippi, MS

In this presentation, we discuss NemaLife's AI-assisted organism-on-chip platform for evaluating the safety and efficacy of bioactives. The high throughput platform integrates the invertebrate nematode model C. elegans, microfluidics, and visual AI. C. elegans is a celebrated model organism with conserved human biology that has been at the center of three Nobel-prize winning investigations. The microfluidic chips allow worm husbandry across life, and visual AI is used to extract phenotypic data from thousands of images collected during the experiment. The platform can be used to evaluate diverse bioactives ranging from phytochemicals to botanical herbs to pre/pro/postbiotics. The platform has been optimized for human-relevant safety (development and reproductive toxicology) as well as efficacy (stress resilience, gut health, cognitive health, muscle performance, weight management and longevity) end points. We present two case studies to highlight the power and significance of the platform. First, we comprehensively evaluate the quality of 16 Ashwagandha dietary supplements by mapping chemical, toxicity and efficacy profiles. The study covered a wide range of doses from 125 mg to 18000 mg, utilizing 10,000+ worm subjects. Second, we demonstrate a discovery pipeline, where bioactive compounds and their combinations are identified that confer multiple human-relevant health benefits. In summary, NemaLife's high throughput in vivo testing platform is compound-agnostic and aligns with the 2022 FDA Modernization Act 2.0 that supports new approach methodologies (NAMs) to reduce the reliance on mammals for assessment of safety and efficacy.

What Guides Natural Product Commercialization – Past And Present

Brendler, T.[1,2]

[1] Traditional Medicinals Inc., Rohnert Park, CA, United States; [2] Department of Botany and Plant Biotechnology, University of Johannesburg, Johannesburg, South Africa

Natural product commercialization is contingent to several factors, which if ignored or observed at the wrong time within the development life cycle, may cause serious impediment or result in outright failure. Study of product commercialization, specifically of botanical medicines, supplements and food products in key global markets over the last 150 years elucidated the evolution of these factors and created insights relevant to modern-day product developers. In simple terms, factors can be grouped into four clusters: the ingredients and their properties (covering the gamut from identity and ecological status via biochemistry, to toxicology, pharmacology, and clinical research), sustainable supply chains (e.g., cultivation vs. wild collection, scalability, traditional knowledge and access-benefit-sharing), regulations (governing bioprospecting, export, and regulatory categories and their stipulations in the target markets), and, last but not least, an understanding of the structure and dynamics of the target markets. It is noteworthy that some of these factors were of no relevance historically, their recent emergence and increasing relevance, however, has added significant onus on the product developer and has inadvertently created barriers to market access. This presentation further elucidates why addressing these factors in a timely fashion is paramount for successful commercialization.

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New Natural Product Certified Reference Material Resources Supported By The NIH Office Of Dietary Supplements

Zoe Ruan[1], Linda Smith[1], Sarah Ajaz[1], Uma Sreenivasan[1], Sabrina D. Giddings[2], Daniel G. Beach[2], Pearse McCarron[2], Stephen A. Wise3, Adam J. Kuszak[3]

[1] Cerilliant Corp/MilliporeSigma, Round Rock, TX, USA; [2] Biotoxin Metrology, National Research Council Canada, Halifax, NS, B3Z 3H1, Canada; [3] Office 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 promote and facilitate rigorous and reliable characterization of dietary supplement (DS) identity, composition, and purity, as well as assessments of authenticity and contamination of botanical and other natural product raw materials and finished products. AMRM goals are accomplished through development and validation of quantitative and qualitative methods, production of certified reference materials (CRMs), and support of dietary supplement focused laboratory quality assurance programs. Recent advances in DS analytical resources supported by AMRM include an expanded availability of CRM calibration solutions for key bioactive and marker phytochemical constituents of several popular botanical DS ingredients, and the development of two new cyanobacteria biomass CRMs to for the determination of cyanotoxins. The current portfolio of AMRM-supported CRM calibration solutions in partnership with MilliporeSigma includes mixture solutions of ginger gingerols and shogaols, ashwagandha withanolides and withanosides, kavalactones, echinacea phenolic compounds and isobutyl amides, and Silybum silybins, silychristin, and silydianin. AMRM partnered with NRC Canada to support the production of a cyanobacteria CRM with comprehensive non-targeted analyses and value assignments for the major classes of cyanotoxins (i.e., microcystins, nodularins, anatoxins, cylindrospermopsins, and saxitoxins) and a non-toxic Aphanizomenon sp. control CRM, which are anticipated to be available in 2024. These newly available resources should benefit natural product researchers and industry scientists, expanding the analytical resource toolkit to better support safety assessments or to improve our understanding of how the chemical composition of DS links to their effects their effects on health.

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Before The Monograph: Developming Novel Identity Methods For Botanical Ingredients

Daoust, M. [1] & Tripplett, K.[1]

[1]Traditional Medicinals, Inc., Sebastopol, CA

At Traditional Medicinals, Inc., pharmacopoeial monograph testing standards form the basis of most ingredient specification criteria to assure high-quality materials and cGMP regulatory compliance according to 21 CFR Part 111. For specific herbal ingredients/dietary supplements not yet included in national pharmacopeias, how does one approach the development of appropriate identification methods when authenticated reference materials and resources are not commercially available and/or difficult to obtain?

The authors investigate 3 herbal ingredients: Chinese blackberry or sweet leaf, wild apple, and butterfly pea flower, derived from leaves, fruits and flowers, respectively. Initial substantiation research revealed all three herbs to be lacking in both validated botanical identity methods and commercially available authenticated botanical reference materials (BRMs) for the plant parts of interest.

In response, we sought to implement a quality by design approach, developing orthogonal fit-for-purpose methods. We describe setting about compiling a reference collection, developing appropriate testing standards, including macro/microscopy and chromatographic methods, and our processes for establishing identity for these botanical taxa. We discuss potential consequences of method development based on relatively small study populations and, within these constraints, try to understand potential morphological and phytochemical variability ranges. In presenting our findings, we review questions and challenges encountered, including anticipation of possible adulterants and evaluation of potential downstream impacts on materials by processing and manufacturing methods, while highlighting the value of cooperative and transparent relationships with ingredient suppliers.

NOTES

Water Determination For Plant Materials By Titrimetric Method

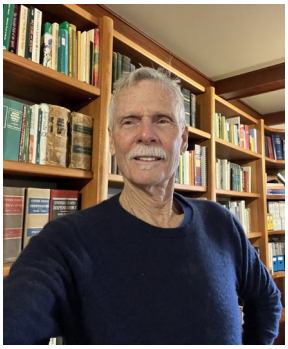
Cuiying Ma[1], Jesse Aplin[2], Nadine Lo[2], Nadejda Soukhova[2]

[1]Department of Dietary Supplements and Herbal Medicines, [2]Analytical Development Laboratory, U.S. Pharmacopeial Convention, 12601 Twinbrook Parkway. Rockville, MD, USA, 20852

Water determination for plant materials usually uses the Loss on Drying (LOD) methods. The Azeotropic-Toluene Distillation method is often used in pharmacopeial monographs to determine water content of plant materials containing volatile components. The Toluene Distillation method is complicated and time consuming plus toluene is a class 2 residual solvent; many laboratories prohibit use of large amounts of toluene and reject the use of this method. USP <921> Water Determination, Method I (Titrimetric), also known as Karl Fisher (KF) test, is recommended because titrimetric determination of water is an elemental reaction which depends on oxidation of sulfur dioxide by iodine in the presence of water. The method is simple, specific, and accurate.

Publications1-2 indicated that KF test correlate well with the azeotropic distillation method, with no significant differences between the results. Plant contains water in cells, which often causes difficulties for KF test when titrating the samples directly. When titrating the samples directly using methanol as the solvent, there is difficulty reaching the titration end point. Using methanol and formamide (1:1) as solvent to titrate samples directly is time consuming due to the delayed reaction and needs to change the KF solvent frequently due to more insoluble plant material. The USP laboratory therefore investigated and validated KF direct titration with external extraction as an alternative method.

This presentation includes water determinations performed for plant materials including fruit peel, root, rhizome, and bark. The test results of KF direct titration plus external extraction were compared with the results from LOD in different heating times and results from direct titration using different solvents. The validation results confirmed KF direct titration with external extraction method using formamide as solvent to determine water content of plant materials has good accuracy and repeatability.



Chris Hobbs

University of Massachusetts

Re-discovery of Fungi

Christopher Hobbs, Ph.D.

This will be a very concise overview of the laboratory and clinical work that has been published on the health and medical benefits of medicinal mushrooms and mycelium. Medicinal mushroom and mycelium-based products currently on the market will be critically reviewed, specifically focusing on identifying the 5 most important constituent groups intensive world-wide research has identified as providing the intended benefits of these products, and what leading companies as well as startups are doing to insure their products contain them in meaningful amounts.

James Kababick

Flora Research

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

Authentication Of Commercial Mushroom Products

James Kababick, Stacy Wise, Christine Smoak
Flora Research Laboratories, LLC
Grants Pass, OR USA

The popularity of mushroom products has risen dramatically over the last several years with more and more dietary supplement manufacturers incorporating various mushroom raw materials into their formulations. The increased demand has brought new challenges in characterizing and authenticating these ingredients. “Mushroom” can refer to mycelium, fruiting bodies or a combination of these. Additionally, the same fungi can be extracted in different ways which require different profiling methods. We present the strategies employed at Flora Research Laboratories in the quality control of mushroom raw materials and finished products.

Natascha Techen

University of Mississippi

A native of Hamburg, Germany, Dr. Natascha Techen received her BS, MS and Ph.D. in Plant Molecular Biology at the University of Hamburg, Germany.

Dr. Natascha Techen joined Dr. Ihklas A. Khan's team in 2002, where she is working on the identification of genomic markers, also known as 'DNA-barcoding', that can help with the authentication of plant material/dietary supplements and its adulterations by using various molecular methods. In addition her research has helped with the genetic improvement of crops, medicinal or ornamental plants for higher yield and nutrient value, disease and pest tolerance, non-invasiveness, and ornamental traits.

Genetic Identification Of (Edible) Mushroom Species

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The term “mushroom” often refers to the fruiting body of edible and toxic fungi, expanding beyond those that have a stem, a cap, and gills. It also includes microorganisms such as yeasts and molds that are beneficial or damaging to plants, animals, or other fungi. In 2021, the global mushroom market reached a value of USD 50.3 billion, and is anticipated to grow at a compound annual growth rate of 9.7% from 2022 to 2030. Mushrooms are considered a superfood due to four key nutrients namely selenium, vitamin D, glutathione, and ergothioneine. This not only caters to the increasing vegan population but also facilitates a reduction in salt addition for flavor enhancement.

Mushrooms can be cultivated on solid medium or hydroponically. However, their significance extends beyond being a food additive. “Magic mushrooms” contain hallucinogenic metabolites and have been utilized for centuries in various cultures for their psychoactive and therapeutic effects. As the demand for (edible) mushrooms and their metabolites rises, so does the concern for food safety, encompassing issues related to adulteration and poisoning. The presentation aims to provide a concise overview of fungi, emphasizing DNA-based methods for their identification.

Arun Krishnamurthy

Purity IQ

Arun Krishnamurthy is a trained analytical chemist with a masters in Analytical chemistry from the Bangalore University, India, and a PhD in NMR spectroscopy applications from the University of Manitoba, Canada. Arun has several years of experience as a solution- and solid-state NMR spectroscopist, with expertise in metabolomics, and structural analysis of small organic molecules and inorganic systems. Arun is working in the role of NMR Spectroscopist at Purity-IQ which involves metabolomics method development to support science-based solutions in the natural health product industry.

Beyond Appearance: NMR Metabolomics for Mushroom Quality Assurance and Authenticity

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Driven by their prominent health benefits, mushrooms are extremely popular in food and nutraceutical sectors, incidentally attracting food fraud such as species mislabeling and substitution, adulteration, and contamination with synthetic and cheaper substitutes, severely affecting the supply chain and raising concerns among consumers about product safety and quality. Untargeted chemical profiling using Nuclear Magnetic Resonance (U-NMR) spectroscopy, in conjunction with Multivariate Statistical Analysis (MSA) proves to be a superior and universally recognized analytical method in simultaneously addressing these concerns and inadequacies of conventional analytical methods. A comprehensive and robust 1H NMR spectral library is built using validated mushroom samples of different species and product types (extracts, fruiting body, pure mycelium, mycelia on grain, multi-species blends, etc..) and is employed for species authentication and product verification through U-NMR and MSA. Clear assignments of species identification and product verification are achieved, and products with non-conforming chemical fingerprints are identified, attributable to the food fraud aspects listed above. In addition to these examples, the applicability of NMR metabolomics in ensuring the authenticity of mushroom products throughout the supply chain and measures to address food fraud are discussed.

Julie Daoust

M2 Ingredients

Dr. Daoust is the Chief Science Officer at M2 Ingredients. Dr Daoust received her PhD in natural product chemistry from the University of British Columbia and has since worked in the nutraceutical industry with a focus on plant-based products. Her research has been centered on bioprospecting for new functional metabolites in plants, fungi, and bacteria and on clinical outcomes related to plant-based nutrition. At M2 Ingredients, Dr. Daoust brings her passion for mushrooms to life working along the talented M2 mycology and research team. M2 Ingredients is a vertically integrated mushroom ingredient supplier based in Vista, California that grows certified organic functional mushroom for the food and supplement industry.

Decision making towards product efficacy: an untargeted metabolomics and cell based assay approach.

Julie Daoust, PhD, Samuel Andrasko

Mushrooms have a long tradition of use as medicinal and functional ingredients however the lack of development in testing methods currently limits our ability to characterize these products. Selecting the right strain or processing method is currently challenging given the lack of commercially available analytical methods to detect or quantify secondary metabolites with therapeutic endpoints. Very little is known about the variability of these metabolites between strains of the same species and between identical strains grown in different conditions therefore an untargeted analytical method was needed to adequately assess impact of strain genetics and growing methods for M2 Ingredients cultures of Hericium erinaceus and Cordyceps militaris.

To guide decision making in strain selection & processing method optimization, an untargeted metabolomics profiling was performed on strains of Hericium erinaceus and Cordyceps militaris using a Quadrupole TOF mass spectrometer and the Mona, NIST and SCIEX Mass Libraries. The untargeted approach allowed for the identification of bioactive secondary metabolites in each samples and a comparative quantification of these metabolites served to support strain, growing, and processing method selection. In addition, we obtained unexpected matches with molecules that had not been previously reported in the each species.

A comparative analysis of the know bioactive secondary metabolites associated with each set of samples was used to select strains and processing methods for both Hericium erinaceus and Cordyceps militaris. The selected strains and methods were then tested in cell-based assays to assess their bioactivity. Two cell-based assays were used; a cellular antioxidant protection (CAP-e) assay to assess antioxidant potential and a cell based mitochondrial function assay. In both cases, the metabolomics profiling led to the selection of products that had significant biological activity.

Scientific Poster Abstracts

2024

PA-1: Analytical Chemistry Aspects of Botanicals

New Natural Product Certified Reference Material Resources Supported by the NIH Office of Dietary Supplements

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The NIH Office of Dietary Supplements (ODS) Analytical Methods and Reference Materials (AMRM) Program supports the development of tools that promote and facilitate rigorous and reliable characterization of dietary supplement (DS) identity, composition, and purity, as well as assessments of authenticity and contamination of botanical and other natural product raw materials and finished products. AMRM goals are accomplished through development and validation of quantitative and qualitative methods, production of certified reference materials (CRMs), and support of dietary supplement focused laboratory quality assurance programs. Recent advances in DS analytical resources supported by AMRM include an expanded availability of CRM calibration solutions for key bioactive and marker phytochemical constituents of several popular botanical DS ingredients, and the development of two new cyanobacteria biomass CRMs to for the determination of cyanotoxins. The current portfolio of AMRM-supported CRM calibration solutions in partnership with MilliporeSigma includes mixture solutions of ginger gingerols and shogaols, ashwagandha withanolides and withanosides, kavalactones, echinacea phenolic compounds and isobutyl amides, and Silybum silybins, silychristin, and silydianin. AMRM partnered with NRC Canada to support the production of a cyanobacteria CRM with comprehensive non-targeted analyses and value assignments for the major classes of cyanotoxins (i.e., microcystins, nodularins, anatoxins, cylindrospermopsins, and saxitoxins) and a non-toxic Aphanizomenon sp. Control CRM, which are anticipated to be available in 2024. These newly available resources should benefit natural product researchers and industry scientists, expanding the analytical resource toolkit to better support safety assessments or to improve our understanding of how the chemical composition of DS links to their effects their effects on health.

PA-2: Analytical Chemistry Aspects of Botanicals

Benefits and Challenges in Botanical Analysis Using High-Performance Thin-Layer Chromatography (HPTLC)

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In recent years, the total number of herbal supplements (HS) and botanical products, such as plant extracts, have increased with new botanical supplements expected to be introduced to the market in coming years. Dietary supplement manufacturers have the responsibility to use appropriate, scientifically valid methods to identify their ingredients, which can be challenging if their ingredient is a complex botanical extract or plant material. To prove identity and perform specification testing, High-Performance Thin Layer Chromatography (HPTLC) is one of the techniques used by the industry to establish identity of the raw material or final herbal product. HPTLC offers a rapid and reliable technique for quality assurance and offers benefits such as low solvent use, minimum sample clean-up, and low cost compared to gas and liquid chromatography. In addition, identification can be done using visual comparison of HPTLC fingerprints. However, its use as the sole method for identity purposes is challenging, especially when the raw material is mixed with other plant species or when there is the need to differentiate closely related species. Further, the chemical composition of a plant material may vary due to the age of the plant, geographical origin, and harvesting technique with various components potentially hindering accurate identification. Additionally, standard reference materials might not be available for identification using HPTLC, especially for novel herbal ingredients. In this poster we will provide an overview of the benefits of the HPTLC technique and its limitations for the identification of botanical materials.

PA-3: Analytical Chemistry Aspects of Botanicals

Dietary Supplement Laboratory Quality Assurance Program (DSQAP): Natural Product Interlaboratory Comparison Studies at NIST

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The National Institute of Standards and Technology (NIST), in collaboration with the National Institutes of Health, Office of Dietary Supplements (NIH ODS), has developed multiple measurement tools, including natural product reference materials, to support dietary supplement (DS) analytical communities. In addition to reference material development, a Dietary Supplement Laboratory Quality Assurance Program (DSQAP) was initiated in 2007 to provide measurement tools to laboratories for the improvement of measurements of chemical constituents in DS ingredients and products. The DSQAP provides an opportunity for DS testing laboratories to participate in interlaboratory comparison studies aimed at improving comparability and accuracy of their measurements. DSQAP exercises also provide NIST and NIH ODS a means to identify community needs for reference materials, workshops, and other measurement services. This poster will highlight previous and current natural product focused DSQAP studies which includes study design, observations, and overall technical recommendations provided to the dietary supplement measurement community.

PA-4: Quality Aspects of Botanicals

Value Assignment of NIST Reference Material 8210 Hemp Plant

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The National Institute of Standards and Technology (NIST) has prepared a hemp plant reference material (RM 8210) to aid *Cannabis* and forensic laboratories in the validation of their methods, support with the development of new analytical methods, and as a quality control material for routine analysis. RMs play an important role in promoting compliance with current and future legislation, labeling accuracy, and good manufacturing processes. However, RMs are a critical measurement service that is presently lacking in the cannabis industry. RM 8210 has non-certified mass fractions for cannabinoids, total Δ9-THC, total CBD, and toxic elements on a dry-mass basis. The need to accurately measure cannabinoids in hemp plants became significantly important after passage of the 2018 Farm Bill. New legislation legalized hemp in the US by removing hemp from the DEA Scheduled 1 controlled substance list and defined it as *Cannabis sativa* with a total Δ9-THC mass fraction of less than or equal to 0.3 % on a dry-weight basis. Mass fractions (%) were assigned for eight cannabinoids by NIST using LC-UV. Cannabinoids were identified using retention times, absorbance spectra, and peak purity evaluation using a PDA detector to compare absorbance spectra across the entire peak. Contaminants such as toxic elements are the next largest analytical measurements required by *Cannabis* laboratories for hemp plant samples to ensure materials are safe. Across states, regulatory guidelines have been set for toxic elements in hemp plant products to currently include at a minimum As, Cd, Pb, and Hg, while additional toxic elements are on a state-to-state basis. Several of the other RM 8210 toxic elements were selected since identified by the US FDA Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke: Established List. Mass fractions (µg/kg, dry-mass) for toxic elements were assigned at NIST using ICP-MS, ICP-MS/MS, ICP-OES, and direct combustion AAS.

PA-5: Analytical Chemistry Aspects of Botanicals

Characterization and Identification of Sesquiterpene Lactones from *Centaurea benedicta* using Liquid Chromatography/Electrospray Ionization Quadrupole Time-of-Flight Mass Spectrometry

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Centaurea benedicta (L.) L. (Syn. *Cnicus benedictus* L.) of family Asteraceae is an annual herbaceous plant commonly known as blessed thistle or St Benedict's thistle. It is native to the Mediterranean regions of Europe, Africa, and Asia. Liquid chromatography coupled with electrospray ionization quadrupole time-of-flight mass spectrometry (LC/ESI-QToF) was used to identify and characterize eleven sesquiterpene lactones (cnicin), and one lignan (arctiin), in mixed parts of *C. benedicta*. A generalized fragmentation pathway was proposed by comparing the spectra acquired for all classes of compounds. The sesquiterpene lactones in *C. benedictus* have been classified into three groups: germacranolide, guaianolides and eudesmanolides. Using the ESI-QToF method, the major core peak ions generated by germacranolides, eudesmanolides, and guaianolides were investigated. From the QToF-MS/MS spectra, fragmentation reactions of the [M+NH4]+ and [M+Na]+ ions were recorded to provide structural information about the aglycone moieties. The data illustrates the ability of positive mode ESI for the identification of sesquiterpene lactones.

PA-6: Analytical Chemistry Aspects of Botanicals

Use of Statistical Models in Untargeted Metabolomics Analysis of Açaí (*Euterpe oleracea* Mart.) Fruit, Food Powder, and Botanical Dietary Supplement Extracts for Quality and Safety

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Euterpe oleracea Mart., commonly known as açaí, is a palm fruit native to the Amazon region which has gained popularity due to its health benefits including antioxidant and anti-inflammatory activities. The objective of this work is to develop an efficient method for the untargeted characterization of various açaí extracts that can be potentially used for the chemical characterization to evaluate efficacy and safety of açaí botanical dietary supplement (BDS) products.

Açaí fruits, food products, and two BDS brands were extracted with a variety of solvents with varying polarities. Dried extracts were then reconstituted and analyzed with high-resolution LC-MS for in-depth untargeted chemical fingerprinting. The full scan mass spectra were used for multivariate statistical analysis including principal component analysis and hierarchical cluster analysis. Tandem mass spectrometry data obtained using the same liquid chromatography separation were then used to obtain positive and tentative identifications of compounds.

We demonstrate the utility of this method for the characterization of extracts of açaí from multiple origins. This workflow allowed the identification or tentative identification of 173 compounds of which 138 were described in açaí for the first time. Principle component analysis revealed that features obtained using positive mode ESI provided a better model than features obtained in negative mode. This analysis also illustrated that açaí fruits from Hawaii and food products from Brazilian-grown fruits were very similar to each other in chemical composition when extracted with water or acidic methanol but not when extracted with more lipophilic solvents such as ethanol or methanol. For one BDS brand, the two separate lots were very similar in chemical composition for both. However, the second BDS brand showed the greatest difference between lots.

PA-7: Analytical Chemistry Aspects of Botanicals

Development of a Comprehensive Analytical Method for Simultaneous Quantification of Furanocoumarins and Nootkatone in Grapefruit Essential Oils Using UHPLC-MS/MS

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Furanocoumarins and nootkatone are abundant in grapefruit essential oil. These compounds are associated with phototoxicity, raising safety concerns due to their frequent use in cosmetics and perfume. Furanocoumarins have been identified for their interference with several medicines. Their impact on intestinal cytochrome P450 enzymes, especially CYP3A4, can result in increased drug bioavailability, posing a risk of potential overdosing.

The study employed ultra-high-performance liquid chromatography with tandem mass spectrometry (UHPLC-MS/MS) for various grapefruit essential oils. A rapid, robust, and sensitive analytical method was developed to accurately quantify 15 furanocoumarins, named psoralen, 5-methoxypsoralen, 8-methoxypsoralen, 8-geranyloxypsoralen, bergamottin, epoxy bergamottin, byacangelicin, byacangelicol, oxypeucedanin, oxypeucedanin hydrate, imperatorin, isoimperatorin, phellopterin, heraclenin, and isopimpinellin, and one sesquiterpene nootkatone in different types of grapefruit essential oils. The developed method was validated for precision, robustness, accuracy, the limit of detection (LOD), and the limit of quantification (LOQ). The preliminary results demonstrated that the white grapefruit essential oils contained more furanocoumarins than other essential oils. The developed method is economical and can be applied for routine analysis of furanocoumarins and nootkatone in plant samples and various products.

PA-8: Analytical Chemistry Aspects of Botanicals

Quantitative Determination of Cinnamaldehyde and Related Metabolite Cinnamic Acid from Biofluids of Human Liver Microsomes Assay by UHPLC-MS/MS

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Cinnamon bark oil is a unique kind of essential oil because of the pharmacological activities and other health benefits of cinnamaldehyde, which is primarily obtained from the dried bark of *Cinnamomum verum* (syn. *C. zeylanicum*) that belongs to the family Lauraceae. Cinnamon bark contains 1 to 4% cinnamon oil, which comprises the highest quantities of trans-cinnamaldehyde (65–80%), eugenol (5–10%), and (5–10%) trans-cinnamic acid. For centuries, cinnamon oil has been used in traditional medicine, such as Ayurveda, Unani, and Chinese medicine, to manage oxidative stress and stomach diseases, especially gastritis, blood circulation, and liver diseases [1,2].

This study aimed to develop a sensitive method to measure the levels of cinnamaldehyde and its metabolite cinnamic acid in human liver microsomes (HLMs), human liver S9 fraction (HLS9), and primary human hepatocytes (PHHs). We developed an Ultra-High-Performance Liquid Chromatography coupled with a tandem mass spectrometric detector (UHPLC-MS/MS) method for analyzing the cinnamaldehyde and cinnamon oil after a variety of human liver microsomes bioassays. Validation parameters included sample preparation, precision, accuracy, the limit of detection (LOD), the limit of quantitation (LOQ), and the linearity range. The recovery rates ranged between 100% and 112%. Relative standard variations (RSD) of intra- and inter-day studies were below 1.85 % and 2.43 %, respectively. The LOD and LOQ were 0.2 and 0.5 ng/mL for cinnamaldehyde and cinnamic acid, respectively. This method has been successfully applied to the quantitative determination of cinnamaldehyde and cinnamic acid from human liver microsomes assay biofluids.

PA-9: Quality Aspects of Botanicals

Streamlined Sample Preparation for LC-MS and GC-MS Multi-Pesticide Residue Analysis in Botanicals and Oils Using Novel Pass-through Cleanup.

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[1]Now Health Group

One of the biggest challenges in routine pesticide residue analysis in botanicals is addressing the complex and varying nature of those matrices. Historically, separate preparations for LC-MS and GC-MS were necessary to achieve acceptable and consistent recoveries in botanical matrices. The LC-MS method utilized an AOAC QuEChERS extraction followed by a MgSO4, primary secondary amine (PSA), and C18E d-SPE cleanup step. The GC-MS method utilized an original QuEChERS extraction followed by an SPE cleanup containing PSA and graphitized carbon black (GCB). The GCB necessitated an elution solvent containing toluene to free the planar analytes from the GCB. These separate methods come with complications of allocating additional time to sample preparation, high cost per sample due to different sorbents used, and introducing points of contamination by additional interactions with the sample. These points make it difficult to implement on a larger or routine scale. There was a need for sample preparation that can cleanup a diverse number of matrices while not trapping any pesticides. A method was developed with Agilent's Captiva EMR that answered many of the above problems. This was accomplished largely in thanks to the unique composition of these cartridges that can trap pigments without the drawback of also trapping planar analytes. The new method utilizing the Captiva EMR cartridges allowed simultaneous preparation for analysis by both LC-MS and GC-MS, saving on analyst time and cost per sample. This method has shown an increased number of analytes able to be recovered on difficult matrices such as Ginger Root Powder, Peppermint Essential Oil, Turmeric Extract Powder, and various other botanical extracts. All monitored analytes met the SANTE guidelines for analyte recovery and linearity. This streamlined procedure has allowed an uninterrupted workflow that is flexible enough to handle a wide range of botanicals and robust enough to produce consistent data.

PA-10: Quality Aspects of Botanicals

HPTLC identification and differentiation of Juniper species

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[1] NOW Foods

An HPTLC method has been developed to identify juniper (*Juniperus communis*) berries for use in dietary supplements. Presently there is no official method for identification of the fruit of *Juniper communis*; the current methods focus on the identification of essential oil. This method can differentiate between three common *Juniper* species: *J. communis*, *J. virginiana*, and *J. horizontalis*. Samples were a combination of commercially available botanical reference material as well as commercial samples and field collected specimens. In addition to HPTLC, high resolution accurate-mass LC-Orbitrap mass spectrometry with statistical analysis was employed to help identify marker compounds which can be further used to aid in identification of true juniper and discriminate from other species. Several potential markers were identified to aid in differentiation of the species.

PA-11: Quality Aspects of Botanicals

Ramps Metabolomics

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Ramps are wild broadleaf *Alliums* consisting of two primary species, *Allium tricoccum* and *A. burdickii*. These are widely harvested and consumed across Appalachia and the midwestern U.S. They have been used for hundreds or thousands of years as a "spring tonic" herb to promote general wellness and for many other ethnomedicinal uses. They are also a prized ephemeral culinary herb and are popular with chefs. Festivals are held each spring to celebrate these wild vegetables. To date, no phytochemical analyses have been done on the less common species, *A. burdickii*, and only limited research into *A. tricoccum,* with vitamin analysis in the 1970's and sulfur analyses conducted in the 1990's. My research used LCMS (Orbitrap) analysis paired with online metabolomics machine-learning platforms (Metaboanalyst and GNPS) to characterize several classes of important bioactive molecules in both species. Semi-quantitative comparisons (based on peak areas) were performed, and results described here. Many of these compounds are characterized for the first time in both species (anthocyanins, steroidal saponin compounds). The sulfur compounds previously characterized in *A. tricoccum* are described for the first time for *A. burdickii*. Water-soluble vitamins were also quantified via HPLC-UV/DAD and standard calibration curves. The ramps were harvested across Pennsylvania, northern West Virginia, and eastern Ohio in April- May 2023. Instrumental analyses were conducted at Penn State University from May through December 2023.

PA-12: Analytical Chemistry Aspects of Botanicals

Wastewater Whispers: CNS Pharmaceuticals Revealed

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The study of sewage-based epidemiology (SBE) and drug utilization trends has concentrated primarily on large social and public events. High-population events (e.g., intercollegiate sports and concerts) often draw tens of thousands of attendees per event in the southeastern region of the United States of America. Increased drug use has been observed at such events, and the use of illicit drugs and stimulants is a growing socioeconomic burden. These substances are recognized for heightening sensory perception and improving mood over extended periods, ultimately contributing to drug dependency, rising crime rates, and declining human health. Furthermore, the continuous occurrence of CNS drugs in wastewater may result in harmful consequences downstream for fish and other aquatic wildlife.

This study used an LC-MS-MS method to identify CNS stimulants and their metabolites in wastewater from several southern towns and cities and a university campus. Specifically, a novel analytical method involving solid phase extraction of various sludge samples collected in and around Oxford locations was quantified for several CNS drugs, such as fentanyl and alprazolam, in wastewater streams. The details of the sample collection, analytical methodology, results, and findings will be presented. Our efforts are expected to impact the forensic science community significantly and aid law enforcement agencies in implementing such analytical methodologies as a frontline defense to monitor local drug abuse trends.

PA-13: Analytical Chemistry Aspects of Botanicals

Rapid, Accurate Detection of Goldenseal (*Hydrastis canadensis*) Adulteration with Yellowdock (*Rumex crispus*) Using A-TEEM Spectroscopy

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Goldenseal (GS) resources are limited by overharvesting of wild supplies and slow adaptation of cultivation. Hence the availability and price of GS can be a motive to adulterate it with Yellow Dock (YD) roots. GS contains highly colored and or fluorescent isoquinoline alkaloids compounds including berberine, canadine and hydrastine. Standard analysis of these GS compounds involves HPLC-UV and >10 min per sample. Here we investigated GS adulteration using the patented A-TEEM method requiring < 1 min per scan. Matching w:v ethanolic extracts of three individual GS lots were adulterated with extracts from three YD lots from 1 to 100% in a nine-point calibration yielding an 81-sample mixture matrix. The data were evaluated using Gray Classical Least Squares (Gray-CLS), Partial Least Squares (PLS) and Locally Weighted Regression (LWR) (Eigenvector Inc. Solo v9.3). Key performance indicators included the R2, the Root Mean Square Error (RMSE) of Cross Validation and limits of detection/quantification (LOD/LOQ). Pure GS extract exhibited higher absorbance at 345 nm (>9x) and fluorescence EEM intensities (>30x) at ex/em 345/550 nm than pure YD. Unique GS EEM contours resolved using Parallel Factor Analysis were attributed to the aforementioned alkaloids. Using Gray-CLS with the optimized residual weighting value the cross-validated RMSE for all 81 samples was 2.44% with an R2=0.9948; this compared favorably to respective PLS and LWR model solutions of 2.13 and 1.75% with R2 values of 0.996 and 0.997. The best LOD/LOQ values were from LWR at LOD = 3.3 and (SE Intercept/Slope) = 1.45% giving LOQ = 3.3 × LOD = 4.7%. We conclude that GS adulteration by YD can be detected using A-TEEM at levels below commercially relevant adulteration scenarios. Further method improvements with respect to optimizing variable selection, signal to noise and extraction efficiency as well as direct quantification of the alkaloid composition will be discussed.

PA-14: Analytical Chemistry Aspects of Botanicals

Analysis of Absorbance-Transmittance Excitation Emission Matrix (A-TEEM) Data for Natural Product Extracts Facilitated by Linear Correlogram and Gray-CLS Methods

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A-TEEM spectroscopy rapidly (s-min) quantifies specific chemicals from complex natural product extracts. Conventional A-TEEM analyses mostly focus on inverse chemometric methods such as Partial Least Squares (PLS) and other nonlinear machine learning methods including Extreme Gradient Boosting (XGB) and Support Vector Machines (SVM). These methods are prone to the common pitfalls of over- or under-fitting. Diagnosis of these fitting errors is often difficult due to complex interactions among multiple pre-processing and hyper-tuning parameters. Here we evaluate linear, first principles based analytical methods for A-TEEM data with natural product examples. The methods include linear correlogram analysis, where concentration-dependent correlations of the calibration data set are plotted as a function of single or summed A-TEEM variables; the linear slope, intercept and R2 are simply computed and applied to test data. The second linear method is Gray-Classical Least Squares (Gray-CLS) using Eigenvector Solo v9.3. Gray-CLS optimizes a single clutter-removal filter variable based on the CLS model residuals with no additional pre-processing of the spectral or concentration data. Test cases evaluated include anthocyanins in wine, capsaicinoids in chili peppers and cannabinoids in flower extracts. Independent test data are compared for their Root Mean Square Error of Prediction (RMSEP), the Coefficient of Variation (R2) and the Linear Slope and Intercept. When target compound spectral signals are well-resolved and or strong relative to other components in the matrix, linear correlogram models can be fit-for-purpose. In other cases where the matrix spectral components are complex or interfere with the target compound spectra, Gray-CLS models can perform with close to or better statistics than PLS or XGB. In conclusion, linear, univariate solutions can eliminate fitting ambiguity and increase model robustness for A-TEEM applications.

PA-15: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Phytochemical Composition of *Vincetoxicum* Extracts Recovered by Pressurized Acetone, Ethanol and Water and their Antiviral Activity Against Zika Virus

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Vincetoxicum is a genus of flowering plants in the family Apocynaceae, which is native to Europe and Asia. Considering widely documented health benefits (antioxidant, anticancer, anti-inflammatory, antiviral and other bioactivities), there is an interest in a more systematic evaluation of *Vincetoxicum* spp. (poly)phenolic and other bioactive compounds as well as their properties. For instance, quercetin, luteolin and rutin were reported as the strongest antiviral flavonoids, which may have antiviral activity against numerous enveloped RNA viruses including Flavivirus. The present study aimed at preliminary screening of phytochemical composition of extracts isolated from *V. hirundinaria*, *V. nigrum* and *V. luteum* with pressurized acetone, ethanol and water by UPLC-QTOF-MS/MS. In addition, considering possible inhibitory activity of phenolic compounds against different microorganisms, extract activity was evaluated against the Zika virus *in vitro*. Firstly, an MTT assay was performed to determine the non-cytotoxic doses of the extract using human lung epithelial cells A549. Then, the effects of extracts on ZIKV-MR766 (ZIKVGFP) were evaluated by flow cytometry assay. A concentration-dependent toxicity studies revealed that the cytotoxic concentration required to reduce mitochondrial activity by 50% (CC_{50}) was from 200 to 500 µg/mL. Flow cytometry assay showed that extracts demonstrated a dose dependent anti-ZIKV activity. UPLC-QTOF-MS/MS analyses revealed the presence of many compounds, quercetin, isoquercetin, luteolin and rutin being the major flavonoids according to the ion intensity. Several other compounds have also been tentatively identified: chlorogenic acid, quercetin 3-O-pentoside, kaempferol, antofine. In summary, a well-designed extraction process of *Vincetoxicum* spp. leaves enabled to obtain the extracts containing different classes of biologically active compounds with potent antiviral properties.

PA-16: Agrochemical Aspects of Botanicals

Adopting Agro-ecological Zoning Model to Analyse Replacement of Paddy Cultivation with Medicinal Plants in the Indian State of Punjab

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Punjab, an Indian state, heavily relies on agriculture, contributing 29% of the nation's rice and 20% of its wheat. This monoculture is leading to depletion of soil nutrients, necessitating increased chemical inputs. Moreover, paddy cultivation, requiring substantial water, is depleting Punjab's groundwater by 0.5 meters annually. To enhance diversity, scientists propose replacing paddy fields with alternate crops. The Ministry of AYUSH, Government of India is exploring medicinal plant cultivation as a profitable venture. Presently, less than 2% of Punjab's land is dedicated to this. Aim: With no clear policy to suggest the right medicinal plants in the right location, this study is focused on introducing medicinal plants like Andrographis paniculata and Chlorophytum borivilianum to replace paddy. Methods: Agro-ecological zoning, using meteorological data of past 20 years from IMD (Indian Meteorological Department) and PAU (Punjab Agriculture University) stations, determined temperature and rainfall ranges. The soil characteristics were determined using benchmark soil network. GIS Arc.GIS 10.3 helped to create digital soil maps, overlaying native crop requirements to identify suitable areas. Results and discussion: Andrographis paniculata, a Kharif crop, suited Punjab's Roopnagar, Hoshiarpur, and Pathankot districts (Zone I) due to its high-water requirement. With increased irrigation, it can thrive in other zones. In Punjab, the average high and low temperatures during the kharif season varied from 34.4 to 36.7°C and from 22.4 to 26.7°C, respectively. With 500–1500 mm of rainfall during the Kharif season, zones I, II, and III are ideal for *Chlorophytum borivilianum*, while Zone V is less suitable due to lower rainfall and higher soil pH. Conclusion: As per projection by the PRECIS model and given the industrial demand and climatic suitability, these medicinal plants could replace paddy cultivation, contingent on assured marketing connections.

PA-17: Quality Aspects of Botanicals

Reference Standards as Tools for Dietary Supplement Quality Control

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Reference standards are highly characterized substances intended for use in conducting the quality control tests and analytical procedures associated with documentary standards (written monographs that describe specifications and test methods for identity, purity, strength, and limits on contaminants). These materials are critical components of quality systems to help ensure accuracy of labeling. They may also be used for non-quantitative identity testing and as system suitability standards to ensure adequate performance of the chromatographic system. Based on the intended use, reference materials may be pure compounds or matrix materials, such as botanical extracts or enriched fractions. Dietary supplement cGMPs expect specifications including the use of criteria for selecting standard reference materials used in performing tests and examinations [21CFR111.315(d)]. USP and NIST reference materials serve as a widely acknowledged quality benchmark in establishing quality of dietary supplement products and their ingredients.

This session will discuss perspectives from reference standards producers and users on the terminologies, stringency of development, qualification, value assignment, and use of reference standards to exchange views and share experiences on the different issues related to the subject. The information sharing by the panel and the discussion with the participants on reference standards and related topics is expected to provide a better understanding of the use of reference standards.

PA-18: Quality Aspects of Botanicals

USP Standards for Mate (*Ilex paraguariensis*) and Guayusa (*Ilex guayusa*) Leaves: Development and Validation of a UPLC-DAD Method for the Simultaneous Analysis of Methylxanthines and Caffeoylquinic Acids

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[1]US Pharmacopeia (USP)

Mate (or Yerba Mate) (*Ilex paraguariensis*) and Guayusa (*Ilex guayusa*) leaves have been traditionally consumed as infusions in South America. The international market has shown a growing interest in this category of food. Both Mate and Guayusa are rich sources of methylxanthines and caffeoylquinic acids, which confer stimulant and antioxidant properties for applications in novel energy beverages and the formulation of dietary supplements. Mate and Guayusa leaves are very similar botanicals belonging to the Aquifoliaceae family, which creates taxonomic challenges. In addition, different commercial and quality grades exist for both leaves, usually based on the allowable amount (%) of stems and post-harvest processing, which creates additional challenges in the selection of the appropriate materials for DS applications. Ingredients derived from Mate and Guayusa leaves occur in the form of cut leaf, powdered leaf, and aqueous or ethanolic extracts containing different caffeine vs caffeoylquinic acids ratios. Due to the increasing demand for these ingredients, there is an imperative need to create pharmacopeial standards to ensure the quality and safety of these ingredients and to support the specifications for the different articles of commerce. This poster summarizes the work carried out by USP for the development and validation of a UPLC-DAD method for the simultaneous analysis of methylxanthines and caffeoylquinic acids to be proposed as identification and composition tests in the creation of new standards for Mate and Guayusa leaves. Quality by Design (QbD) approach was applied for the sample preparation optimization for the efficient extraction of these compounds in the different matrixes and UPLC method development. The method was validated according to the requirements of USP-NF General Chapter <1225> Validation of Compendial Procedures, regarding specificity, linearity, accuracy, precision, robustness, and stability of solutions.

PA-19: Quality Aspects of Botanicals

Applicability of LC-QToF and Microscopical Tools in Combating the Sophisticated, Economically Motivated Adulteration of Poppy Seeds

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Intentional adulteration of poppy seeds is common, often combined with immature, less expensive, exhausted, or substituted with morphologically similar seeds, viz., amaranth, quinoa, and sesame. For a safer food supply chain, preventive measures must be implemented to mitigate contamination or adulteration. Morphine and codeine are the two principal opiates found in the opium poppy (Papaver somniferum L.) and are therapeutically used for pain management. Poppy seeds with low opiates are primarily used for culinary purposes due to their nutritional and sensory attributes. Moreover, the simultaneous analysis of P. somniferum and its adulterants is largely unknown. Pre- and post-processing further complicate the alkaloid content and may pose a significant health hazard. Considering the challenges, two independent methods were investigated with eight botanically verified and fifteen commercial samples. Microscopical features were established for the authenticity of raw poppy seeds. Morphine, codeine, and thebaine quantities ranged from 0.8–223, 0.2–386, and 0.1–176 mg/kg, respectively, using LC-QToF. In the majority of situations, conventional opiates have a higher content than papaverine and noscapine. The proposed and developed method/s provided a chemical profile of 47 compounds that can be effectively applied to distinguish poppy seeds from their adulterants and may serve as an effective tool to combat ongoing adulteration.

PA-20: Quality Aspects of Botanicals

6-Oxofurostane and (iso)Spirostane Types of Saponins in *Smilax sieboldii*: UHPLC-QToF-MS/MS and GNPS-Molecular Networking Approach for the Rapid Dereplication and Biodistribution of Specialized Metabolites

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Identification of novel phytochemical secondary metabolites following classical pharmacognostic investigations is tedious and often involves repetitive chromatographic efforts. During the past decade, Ultra-High Performance Liquid Chromatography-Quadrupole Time of Flight-Tandem Mass Spectrometry (UHPLC-QtoF-MS/MS), in combination with molecular networking, has been successfully demonstrated for the rapid dereplication of novel natural products in complex mixtures. As a logical application of such innovative tools in botanical research, more than 40 unique 3-oxy-, 3, 6-dioxy-, and 3, 6, 27-trioxy-steroidal saponins were identified in aerial parts and rhizomes of botanically verified *Smilax sieboldii*. Characteristic mass fragmentation patterns of aglycones, diosgenin, sarsasapogenin/tigogenin, or laxogenin were critical to establishing the unique nodes belonging to six groups of nineteen unknown steroidal saponins identified in *S. sieboldii*. Mass fragmentation analysis resulted in the identification of 6-hydroxy sapogenins, considered to be key precursors in the biogenesis of characteristic smilaxins and sieboldins, along with other saponins identified within *S. sieboldii*. These analytes' relative biodistribution and characteristic molecular networking profiles were established by analyzing the leaf, stem, and root/rhizome of *S. sieboldii*. Deducing such profiles is anticipated to aid the product integrity of botanical dietary supplements while avoiding tedious pharmacognostic investigations and helping identify exogenous components within finished products.

PA-21: Quality Aspects of Botanicals

Identification of Botanical Ingredients with Athletic-Performance-Enhancing–Effects in Dietary Supplements

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Since the US Food and Drug Administration (FDA) banned ephedra from dietary supplements in 2004, supplement manufacturers have promoted a complex variety of alternative botanical compounds for athletic performance enhancement. The FDA does not preapprove these ingredients, or any supplement ingredient, for either efficacy or safety before their introduction, but FDA inspections have found that supplement manufacturers often fail to comply with basic manufacturing standards, such as establishing the identity, purity, or composition of the final product. Given the products' potentially complex physiologic effects and concerns regarding manufacturing quality, we determined the accuracy of dietary supplement labels declaring halostachine, octopamine, and turkesterone. Eighty-nine percent of dietary supplement labels did not accurately declare the ingredients found in the products, and 12% of products contained FDA-prohibited ingredients. In the current study, which to our knowledge is the first to quantify these five supplement ingredients, only 11% of products were accurately labeled and three different FDA-prohibited ingredients were found, including an unapproved drug available in Russia (i.e., omberacetam), three drugs formerly available in Europe (i.e., octodrine, oxilofrine, and deterenol), and one drug that has never been approved in any country (i.e., 1,4-dimethylamylamine).

PA-22: Quality Aspects of Botanicals

Determining Quality of Ashwagandha: Current Challenges and Possibilities

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Ashwagandha (*Withania somnifera* (L.) Dunal) has gained significant attention in recent years for its adaptogenic properties that are supported with preclinical and clinical studies. Steroidal lactones and their glycosides, commonly known as withanolides, are generally perceived as the active constituents. Accordingly, the extracts 'standardized' to contain known concentrations of withanolides are used in dietary supplements and complementary medicines across the globe. Pharmacopoeial monographs on Ashwagandha and its extracts are available in USP, EP, BP, IP and API which describe analytical methods based on withanolides, mainly by HPLC and TLC. Our work on Ashwagandha focused on the following points:

1. Can Ashwagandha be evaluated just based on content of withanolides for quality? What are the pitfalls of this approach of excessive focus on content of withanolides?
2. Pros and cons of currently available analytical methods for withanolides.
3. Are the current methods adequate to identify mislabeling and adulteration?
4. Impact of COVID and climate change on supply chain and quality of Ashwagandha roots

We wish to elaborate our findings and thoughts on the above points in this presentation. We expect our findings to ignite further deliberations on the topic towards developing a better understanding on quality of Ashwagandha.

PA-23: Quality Aspects of Botanicals

Development and Validation of Fast GC/FID Method for Cannabinoids Analysis in Cannabis Plant Material of Different Chemovars

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With the legalization of *Cannabis* for medical and recreational purposes in many states, the demand for reliable and accurate cannabinoid analysis has increased. To meet this demand, a simple and fast gas chromatography-flame ionization detection (GC-FID) method was developed and validated for the quantification of the eight main cannabinoids in *Cannabis*. These cannabinoids are cannabidivarin (CBDV), tetrahydrocannabivarin (THCV), cannabichromene (CBC), cannabidiol (CBD), and Δ8-tetrahydrocannabinol (Δ8-THC), Δ9-tetrahydrocannabinol (Δ9-THC), cannabigerol (CBG), and cannabinol (CBN). The method provided baseline separation of the usually coeluted pairs of cannabinoids; CBD /CBC and CBG/CBN. The calibration curve was found to be linear between 5 and 100 µg/mL for all of the target analytes, with a significantly high value of regression coefficient ($r2 > 0.99$). The limit of detection (LOD) and the limit of quantification were 1 µg/mL and 5 µg/mL, respectively. The inter-day and intra-day precisions were less than 15% [relative standard deviation (%RSD)] and the accuracy ranged from 85 to 115 as % recovery. The method was applied for routine analysis of the eight major cannabinoids in different *Cannabis* biomass and *Cannabis* plant extracts. This method provides a reliable and efficient way to analyze the potency of different *Cannabis*-based products and for routine quality control testing for regulatory compliance and can help ensure the safety and consistency of *Cannabis* materials.

PA-24: Quality Aspects of Botanicals

Characterization of Black Cohosh Standard Reference Materials (SRMs) with Mass Spectrometry Detection

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This study presents the characterization of four Black Cohosh Standard Reference Materials® (SRM 3295 – Rhizomes, SRM 3296 – Leaves, SRM 3297 – Rhizome Extract, and SRM 3298 – Solid-Oral Dosage Form) developed collaboratively between the National Institute for Standards and Technology (NIST) and the National Institutes of Health Office of Dietary Supplements (NIH ODS). A targeted liquid chromatography-mass spectrometry (LC-MS) method employing selected ion monitoring (SIM) in negative mode was used for value assignment of key bioactive or marker compounds, including cimiracemoside C, cimigenol-3-β-D-xyloside, 23-epi-26-deoxyactein, cimiracemoside D, 23-epi-26 deoxycimicifugoside, cimicifugoside H-1, and cimicifugoside H-2 within the homogeneous black cohosh matrices. These new SRMs and the validated analytical method employed in their value assignment contribute to the quality assurance and standardization of black cohosh products and preparations used in clinical research, ensuring their reliability and safety in dietary supplement formulations.

PA-25: Quality Aspects of Botanicals

Microscopy, HPTLC, and LC-DAD-Q-ToF Validation of Nut-based Weight-Loss Dietary Supplements, *Aleurites moluccanus* (Candlenut) and *Bertholletia excelsa* (Brazil nut)

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Aleurites moluccanus (candlenut) and *Bertholletia excelsa* (Brazil nut) are marketed as dietary supplements for weight loss. These dietary supplements have been found to sometimes be adulterated with toxic nuts/seeds from *Cascabela thevetia*, commonly known as yellow oleander or lucky nut. This study emphasizes the key identification parameters to differentiate the genuine and adulterated nuts. Samples were obtained from authenticated sources of the nuts and from commercial sources of dietary supplements. The presence of yellow oleander was confirmed in all commercial dietary supplement samples marketed as candlenut as well as in commercial samples of Brazil nut. This study provides simple key identification characters using micro-morphology and histochemical localization of cardio glycosides in the commercial nuts, HPTLC fingerprints, and LC-DAD-Q-ToF analytical parameters to detect and identify adulteration in commercial products.

PA-26: Quality Aspects of Botanicals

Advance Microscopy, GC/Q-ToF, and LC/Q-ToF Characterization of *Salvia mellifera* (Black Sage), *Saliva apiana* (White Sage) and their Varieties

Adams SJ [1], Lee J [1], Avula B [1], Katragunta K [1], Wang M [1], Parveen I [1], Techen N [1], Chittiboyina AG [1], Khan IA [1,2]

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Salvia mellifera (black sage) and *Salvia apiana* (white sage) are known for complex introgressive hybridization. Morphological variations between these two *Salvia* species and their varieties present overlapping characters that may cause confusion in identifying the genuine species in nature. Since these plants may be candidates for investigation of botanical-based drugs, this study aimed to differentiate the two *Salvia* species from each other and to group the closely resembling varieties. With many *Salvia* species offering health benefits, the morphological analysis and chemical fingerprinting of these two species will benefit their potential consideration for further evaluation of their health benefits. Detailed histology, histochemistry, and chemical characterizations were used to identify distinguishing characteristics of genuine *S. mellifera* and *S. apiana* along with two varieties resembling *S. mellifera* or *S. apiana*. Macroscopic and microscopic characterization of leaf lamina and types of trichomes can differentiate the morphology of *S. mellifera* from *S. apiana*. The histochemical analysis of glandular trichomes revealed the presence of flavonoids, terpenes, and other common secondary metabolites. Micropatterns of calcium oxalate crystals were identified as being characteristic and aiding in differentiation. Even though the external morphological characters of the two varieties resemble an intermediate between *S. mellifera* and *S. apiana*, chemical qualitative analyses via LC/Q-ToF and GC/Q-ToF indicate a chemical fingerprint more similar to that of *S. apiana*. This analysis uses various approaches including morpho-anatomy, trichome micromorphology, and chemical similarities to identify and differentiate between *S. mellifera*, *S. apiana*, and their close varieties.

PA-27: Quality Aspects of Botanicals

Using Isotopic Characterization to Identify the Authenticity of *Ilex paraguariensis* Brands Marketed in Southern Brazil

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Yerba mate (*Ilex paraguariensis*) has economic and cultural importance in South America. However, adulteration can occur due to a lack of quality control during processing. The study aimed to measure adulteration of yerba mate brands marketed in southern Brazil with sucrose, through isotopic characterization. Fifteen brands from local grocery stores were analyzed using eight samples of yerba mate derived from plants of different environments. Five samples of other species of *Ilex* genus and *Ligustrum japonicum*, which commonly contaminate yerba mate, were also tested. The isotopic composition of C ($\delta^{13}C$) and % N pointed out that some brands may have been adulterated with sucrose and a combination of % N and $\delta^{15}N$ may be sufficient to identify contamination by leaves from other species. This study shows that isotopic characterization can potentially identify yerba mate that is adulterated with sucrose, and this method can also be used for quality control in the food industry and to warrant further investigation.

PA-28: Quality Aspects of Botanicals

Chemical Characterization and Quantitative Determination of Flavonoids and Phenolic Acids in Yerba Santa (Eriodictyon spp.) Using UHPLC/DAD/Q-ToF

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Eriodictyon species, commonly known as yerba santa, are plants native to the Southwestern US and northern Mexico. The plants are known for their medicinal properties and are used to treat various ailments, in particular, respiratory conditions. Despite a long history of traditional use, many of the species have never been fully chemically characterized, and the constituent range of the species has not been comprehensively reported. In an effort to establish a quality control and chemical characterization method, an extensive set of *Eriodictyon* species including *E. californicum, E. angustifolium*, *E. trichocalyx*, *E. crassifolium*, *E. tomentosum*, *E. traskiae*, and *E. capitatum* were investigated. Fourteen compounds were quantified utilizing a UHPLC/DAD method. The results from the method validation demonstrated excellent linearity (R2 > 0.99) and sensitivity as evidenced by LOD (0.01–0.1 µg/mL) and LOQ (0.05–0.2 µg/mL). Likewise, the method was found to be precise (RSD < 2.78%) with recoveries between 88.9 and 103.2%. To the best of our knowledge, this work encapsulates the most comprehensive data set currently available for the chemical characterization and quantification of the primary constituents in Eriodictyon species. Additionally, results of this study also demonstrated the applicability of the developed method for quality assessment of raw material and commercial herbal products containing different *Eriodictyon* species.

PA-29: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Effect of Light Quality and Natural Ventilation System in Adventitious Roots Induction and Podophyllotoxin Content from *Hyptis suaveolens* (L.) Poit. (Lamiaceae)

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Hyptis suaveolens has podophyllotoxin (PTOX) in its roots, which is a natural product precursor for anticancer chemotherapy, including the semi-synthetic derivatives etoposide, etoposide phosphate, and teniposide. Adventitious roots *in vitro* tissue culture has been increasingly used to produce rare and high-quality medicinal compounds. Aimed to investigate the induction of adventitious roots in *H. suaveolens* leaves under different light qualities and natural ventilation systems. Firstly, the induction of adventitious roots was evaluated under different light conditions and, in a second one light condition were combined with a natural ventilation system. Plantlets of *H. suaveolens* were the explant donors for both experiments, 48 days after seed inoculation. Leaves presenting excised edges at the size of 1×1 cm were used. The Murashige and Skoog (MS) with 0.25 mg/L IBA, 2 mg/L NAA, 30 g/L sugar, and 5.5 g/L agar was used as the basic culture medium. Four explants were inoculated per flask. The first experiment evaluated different light (LED) qualities: T1) red, T2) blue, T3) white, T4) fluorescent, T5) dark (no light). In the second experiment, 6 treatments were evaluated in total: 2 types of ventilation systems (without porous membrane and 4 porous membranes) and 2 qualities of light (monochromatic red and absence of light). The first experiment was evaluated at 42 days and the second at 48 days regarding root dry weight (RDW) and root PTOX content. Direct adventitious roots emerged from *H. suaveolens* leaf explants only in the absence of light and under red monochromatic light. The RDW were statistically equal, on average 25.82 mg per bottle. PTOX content were 10,72 µg/g and 9,93 µg/g, respectively. In the second experiment, the dark condition without membranes accumulated greater RDW (84.02 mg per bottle) and PTOX (46.68 µg/g). In conclusion, adventitious root formation and PTOX accumulation was observed in leaves grown in semisolid MS medium in dark conditions without natural ventilation.

PA-30: Trade Aspects of Botanicals

Chinese Medicinal Herb Production in Southwestern US: Factors Influencing the use of Complementary and Alternative Medicine.

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The use of complementary and alternative medicines, referred to as CAM, has increased significantly over the last several decades. Interest in this growing market from farmers in the Southwestern U.S. has also increased, as medicinal herbs are well suited to the climate and serve existing strong cultural traditions in alternative healing in New Mexico (Moore 2008). CAM therapies include meditation, yoga, herbal medicine and acupuncture, lesser-known products and practices such as Reiki (an energy-healing practice) and biofeedback. Previous works have suggested many factors impacting the rise in alternative medicine such as rising dissatisfaction with traditional medicine and diagnosis of chronic health conditions and new health-conscious individuals demanding organic consumption. To address objectives to support farmers contemplating crop changes to adapt to market and climate challenges, our team sought to contribute to an identified need for a better understanding of the strength and character of the market through identifying the socio-economic factors driving the increased usage of CAM. We used data from a 2019 national consumer survey to assess consumer preferences for CAM after basing the survey on a CDC publication on the increased use of CAM. We used a bivariate logistic regression or binary logic model to identify significant predictors of CAM use while the survey questions focused on participants' use and perceptions of CAM therapies, with an emphasis on herb use. Results show that inclusive socio-economic factors over time have included age bracket, educational level, health conditions and family size. This market characterization helps break the gap between alternative medicine, consumers and farmers who will be growing the herbs. Future research includes an in-depth survey of producers and buyers to better understand crop and production preferences.

PA-31: Regulatory Aspects of Botanicals

Identity Authentication of Botanical Materials for New Dietary Ingredient Notifications

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The Food and Drug Administration (FDA) regulates dietary supplements by the authority outlined in the Food, Drug, and Cosmetic Act (FD&C Act) and the Dietary Supplement Health and Education Act of 1994 (DSHEA). These acts define a dietary ingredient and provide the basis for the FDA to evaluate a new dietary ingredient (NDI) as the subject of an NDI notification. Herbs or other botanicals, as well as their concentrates, metabolites, constituents, and extracts can be dietary ingredients. In order to fulfill the FD&C Act dietary ingredient definition in §201(ff)(1)(C) or §201(ff)(1)(F), the botanical materials from which an NDI is produced must be identified. Challenges can arise in authenticating the identity of botanical materials used to produce an NDI, such as a lack of sufficient detailed information intended to uniquely characterize and verify the taxonomy, origin, supplier, form, and/or composition of botanical materials. This project aims to illuminate common challenges associated with identity verification of botanical materials and propose practical suggestions for ensuring adequate identification of botanical sources. By improving the quality of NDI notifications, and subsequently improving the scientific evidence to support an NDI, the project can contribute to enhancing regulatory compliance within the dietary supplement industry.

PA-32: Quality Aspects of Botanicals

Is There One Method to Rule Them All? Comparing DNA Barcoding, HPTLC, and Untargeted Metabolomics for Herbal Product Identification.

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Botanical identity is a key component of herbal supplement quality programs; however, the innate complexity of plant products complicates testing results and drawing relevant conclusions. There are a few standard approaches to herbal identification testing with a history of success for numerous herbs and formulations, including High-Performance Thin Layer Chromatography (HPTLC) and DNA barcoding. Literature suggests that modern high-resolution mass spectrometry instrumentation is the next step for improving identity evaluations. To date, few studies have directly compared the identification capabilities of these technologies. Thus, we compared the performance of ISSR DNA barcoding, HPTLC, and untargeted metabolomics for identifying *Ocimum* (basil) herbal products. Due to limited reference standards, we generated a reference library by growing 30 *Ocimum* varieties, belonging to three species, in a greenhouse. We first evaluated the ability of each method to separate the three *Ocimum* species using unsupervised statistical models. Next, we investigated which, if any, method can reliably predict the species of commercially available *Ocimum*. Notably, DNA barcoding was unable to reliably produce data for the consumer product, making the approach unsuitable for predictions. Ultimately, each method varied in its classification and prediction capabilities.

PA-33: Agronomical Aspects of Botanicals

The Effect of Nitrogen-fixing Bacteria on Grain and Oil Production of Mustard (*Brassica juncea*) in Rainfed Conditions

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Diazotrophs are the mini-nitrogen factories that convert available atmospheric N2 to ammonia through a process known as “biological nitrogen fixation” which is then taken up by the plants for its metabolic functioning. Free living nitrogen fixing bacteria has been considered as low cost biofertilizer in agricultural production. This study was carried out to investigate the effect of three isolates of nitrogen-fixing bacteria on brown mustard grain and oil production in rainfed conditions .The experiment includes 3 types of nitrogen-fixing bacterial isolates and 7 fertilizer levels; 1) control (no bacteria or chemical fertilizers), 2) bacterial isolate 3MDP-1, 3) bacterial isolate 3MDP-6, 4) bacterial isolate 2MDP-10, 5) chemical fertilizer 250 kg/ha of urea and 150 kg/ha of phosphorus based on soil testing + bacteria 3MDP-1, 6) chemical fertilizer + bacteria 3MDP-6, and 7) chemical fertilizer + bacteria 2MDP-10. The results show that grain yield and yield components, as well as the oil percentage and oil yield of brown mustard grains were not affected significantly by treatments. The results of this research indicate that in rainfed conditions, application of biofertilizers alone or in combination with chemical fertilizers has a similar effect on grain yield and oil production of brown mustard. Therefore, it is possible to reduce the consumption of chemical nitrogenous fertilizers by replacing them with biofertilizers. This could lead to reduced mustard grain and oil production costs and healthier products as well as avoiding environmental pollution.

PB-1: Biological Aspects of Botanicals

Antidepressant Effect of Andrographolide in Chronic Unpredictable Stress Zebrafish Model.

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Recent studies have shown that *Andrographis paniculata* (*A. paniculata*) has an anti-depressive effect on rodents. Zebrafish have also become a valuable complementary model for studying antidepressant drug discovery. This study aimed to investigate the anti-depressive effect of *A. paniculata* extract and andrographolide in a zebrafish model of chronic unpredictable stress (CUS). Four groups of zebrafish (n=10/group) were tested in open-field and social interaction tests 24 hours after treatment: control, CUS (stressed, untreated), CUS+ *A. paniculata* (100 mg/L), and CUS+fluoxetine (0.01 mg/L). After screening the extract, the behavioural and cortisol responses of andrographolide (5, 25, and 50 mg/kg, i.p.) and fluoxetine (10 mg/kg, i.p.) were evaluated. Before the behavioural study, acute toxicity and characterization of *A. paniculata* extract using UHPLC-ESI-MS/MS were performed. The results showed a significant reduction in freezing duration in the *A. paniculata*- (t-test, p=0.0234) and fluoxetine-treated groups (t-test, p<0.0001) compared to the CUS group. Only the fluoxetine-treated group showed a significant increase in total distance travelled and contact duration (t-test, p=0.0007) and (t-test, p=0.0207), respectively. Both treatment groups showed a significant increase in highly mobile duration. Acute andrographolide treatment (50 mg/kg, i.p.) showed a significant reduction in freezing duration (p=0.0042), duration in a dark area (p=0.0338), and cortisol level (p=0.0156), as well as an increase in total distance travelled (p=0.0144). LC-MS/MS detected twenty-six compounds in the *A. paniculata* extract, with andrographolide content at 0.042 µg/g. According to cortisol analysis, *A. paniculata*'s LC50 is 627.99 mg/L, while andrographolide's EC50 was determined as 26.915 mg/kg. Further examination of the cellular and molecular mechanisms of andrographolide's anti-depressive effects is strongly encouraged to assess its potential as an antidepressant.

PB-2: Biological Aspects of Botanicals

Evaluating the Metabolite Profile and Ethnopharmacological Relevance of *Melastoma malabathricum* L. Leaf and Flower Extracts with Reference to Antioxidant and Antithrombotic Capacity: A Comparative Study.

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Melastoma malabathricum L., is an herbaceous shrub, widely used in Indian folklore medicine. This study aims to scientifically validate the traditional claims and explore the medicinal importance of *M. malabathricum* L. by highlighting the metabolite profile and correlating it with the antioxidant capacity, anticoagulant efficacy and in vitro thrombolytic properties of the leaf (MMLE) and flower (MMFE) extracts of *M. malabathricum* L. GC-MS/MS based untargeted metabolite profiling established the presence of 108 and 107 metabolites in MMLE and MMFE, respectively, with only four metabolites in common between the two extracts suggesting their differential pharmacological properties. The major bioactive metabolites identified in MMLE were squalene (12.63%), catechol (6.04%), and beta-sitosterol (5.99%); whereas 5-hydroxymethylfurfural (17.97%), and diosgenin (10.09%) were the core metabolites identified in MMFE. Free radical scavenging activity assays affirmed the strong antioxidant properties of both MMLE and MMFE. It was also observed that MMLE and MMFE had better proteolytic specificity towards the blood coagulation factor fibrinogen than casein. MMLE exhibited αβ-fibrinogenase activity and could also degrade the γ-band of fibrinogen. MMFE also demonstrated αβ-fibrinogenase activity but without any effect on the γ-band of fibrinogen. MMLE exhibited dose dependent anticoagulant properties and inhibited the prothrombin activation property of Factor Xa. However, MMFE showed no significant effect on the blood coagulation process, in spite of its ability to inhibit Factor Xa. Both MMLE and MMFE also had significant *in vitro* clot (thrombus) lysis property. These findings suggest the potential candidature of MMLE and MMFE which can be explored further for the development of conventional antithrombotic and/or thrombolytic agents.

PB-3: Biological Aspects of Botanicals

Anti-inflammatory and Anti-oxidative Effects of STW 42 and Root Extract of *Althaea officinalis* L. on endothelial cells, fibroblasts and macrophages in vitro.

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The root extract of *Althaea officinalis* L. (REAo) has been used since ancient times to treat mild stomach/gut discomfort and dry cough. Application of STW 42 (Phytohustil®), which contains REAo, induces regeneration of the lesioned mucosa. In this context, mucosa wound healing depends on the recruitment of several cell types, e.g., endothelial cells, fibroblasts, and macrophages (MΦ). Reactive oxygen species (ROS)-induced damage is associated with mucosal infiltration of activated leukocytes, such as MΦ, which produce excessive ROS and pro-inflammatory cytokines that may overwhelm the antioxidant defenses and exacerbate mucosal inflammation. Additionally, fibroblasts exhibit a metabolic adaptation to control inflammation-related oxidative stress.

We aimed to investigate the anti-inflammatory/-oxidative properties of STW 42 and REAo on human dermal fibroblasts (NHDF), human umbilical vein endothelial cells (HUVEC), and human acute monocytic leukemia (THP-1) differentiated MΦ, critical cellular components of the gastrointestinal and oral mucosa. Pre-treatment (24 h) of HUVEC, NHDF or THP-1-MΦ with STW 42 or REAo (100–1000 µg/mL) significantly inhibited the H2O2-induced intracellular ROS production by 30.0% to 58.7%. Whereas 24 h (HUVEC, NHDF) or 48 h (THP-1-MΦ) pre-treatment with STW 42 or REAo (10–1000 µg/mL) inhibited the LPS-activated IL6 release by 25.0–67.0%. Additionally, 48 h pre-treatment of THP-1-MΦ with 50–500 µg/mL STW 42 or REAo significantly inhibited LPS-induced TNF-α release by 21.5% (50 µg/mL) to 52.0% (500 µg/mL), in comparison with LPS-treated MΦ. The observed effects of STW 42 or REAo were similar to 25–100 µM diclofenac, which was used as an anti-inflammatory control.

These anti-inflammatory and antioxidant properties may support the benefit of STW 42 in patients during the treatment of irritated laryngopharyngeal diseases; however, they may also have protective/reparative effects on the gastrointestinal mucosa.

PB-4: Biological Aspects of Botanicals

Inhibitors of Multidrug Efflux Pumps from Natural Sources: An *In-Silico* High-Throughput Virtual Screening and *In-Vitro* Validation & Formulation

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Antimicrobial resistance in bacterial pathogens is a challenge that is associated with high morbidity and mortality. Antibiotic resistance happens when germs like bacteria and fungi develop the ability to defeat the drugs designed to kill them. Overuse of antibiotics is the principal cause of resistance evolution. Incorrectly prescribed antibiotics also contribute to the promotion of resistant bacteria. Acquisition of genetic material that confers resistance is possible through all of the main routes by which bacteria acquire any genetic material: transformation, transposition, and conjugation. There are multiple components in the bacterial cell that may be targets of antimicrobial agents, and there are just as many targets that may be modified by the bacteria to enable resistance to those drugs. Efflux pumps allow microorganisms to regulate their internal environment by removing toxic substances, including antimicrobial agents, metabolites and quorum sensing signal molecules. We have screened an *in-sillico* library of natural compounds to evaluate their ability to inhibit MexAB-OprM [PDB ID: 1lnw and 5daj] efflux system of *Pseudomonas aeruginosa* and MepA [PDB ID: 3ECO] efflux system of Staphylococcus aureus by binding specific efflux protein. We employed HTVS (High Throughput Virtual Screening) docking using MOE docking software to identify hits from the Pubchem database subset. A total of 20 compounds were shortlisted against MepA and MexABOprm considering the site of interaction suitable efflux pump inhibitory compounds were selected based on predicted binding energy. Molecular docking calculations identified Hesperidin from *Citrus aurantium* peels and carnosic acid from *Rosmarinus officinalis* leaves as good candidates to inhibit the MexAB-Oprm efflux pump of *P.aeruginosa* and 3ECO efflux pump of *Staphylococcus aureus*. These results are further validated by *in vitro* microbiological assays that showed their activity.

PB-5: Biological Aspects of Botanicals

Antidiarrheal Coumarins from *Psydrax schimperianus* (A. Rich.) Bridson Roots

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Psydrax schimperianus (A. Rich.) Bridson. roots are used for the treatment of diarrhea in the West Arsi zone, Ethiopia. This study aimed to investigate the in vivo antidiarrheal activity of crude extract and coumarins isolated from the roots of *P. schimperianus* to provide a pharmacological basis for its traditional use as an antidiarrheal agent in Ethiopia. The crude root extract of *P. schimperianus* was tested *in vivo* for antidiarrheal efficacy in mice utilizing castor oil-induced diarrhea, gastrointestinal transit time, and enteropooling models at doses of 100, 200, and 400 mg/kg. Phytochemical investigation of the crude root extract led to the isolation of two coumarins, isoscopoletin, and scoparone. Isoscopoletin and scoparone were evaluated for antidiarrheal activity against castor oil-induced diarrhea model at 10 mg/kg and 20 mg/kg doses. The crude root extract of *P. schimperianus*, at doses of 100, 200, and 400 mg/kg, inhibited defecation by 37.5, 46.2, and 61.2%, respectively. At a dose of 20 mg/kg, scoparone and isoscopoletin reduced defecation by 61.2 and 66.6%, respectively. The study warrants further investigation of isoscopoletin and scoparone towards development as a novel treatment for diarrheal diseases.

PB-6: Biological Aspects of Botanicals

Development and Evaluation of Crocetin-containing Nanogel for the Treatment of Skin Cancer

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Skin cancer is a growing health concern with increasing prevalence and mortality rates worldwide. While treatment options exist, they remain limited against aggressive and metastatic cancers. Naturally occurring compounds like crocetin have demonstrated promising anticancer potential; however, their clinical translation remains suboptimal due to poor solubility, instability, and bioavailability. The current study aimed to isolate crocetin from the seeds ethanolic extract of *Nyctanthes arbortristis* Linn to develop crocetin-loaded nanogel to enhance its delivery topically to skin tissues for potential treatment benefits. Biocompatible chitosan nanogels were synthesized to encapsulate lipophilic crocetin using an ionic gelation method optimized by Box-Behnken design. The size of the vesicles for the formulations was between 202 ± 14.2 nm and 374 ± 127 nm, while the entrapment efficiency was between 61.22 ± 0.23% and 85.16 ± 0.24%, and the drug release percentage after 8 h was between 48 ± 0.82% and 76 ± 0.52%. *In vitro* studies demonstrated the potential of the nanogel in significantly inhibiting the proliferation of skin cancer cells, evidenced by its cytotoxic effects on A375 and B16F10 cell lines while exhibiting minimal impact on healthy skin cells. Additionally, *ex vivo* studies of the nanogel showcased efficient penetration into deeper skin layers, promising enhanced drug delivery to the tumor site.

Furthermore, animal studies conducted on DMBA-induced skin cancer animal models corroborated the therapeutic efficacy of the crocetin-loaded nanogel, revealing marked suppression of tumor growth compared to conventional treatment by marketed gel or untreated groups. These findings supported the potential of this crocetin nanogel formulation as a promising strategy for skin cancer therapy, offering targeted delivery, reduced systemic toxicity, and improved treatment outcomes. Preclinical development of this targeted delivery system can facilitate the clinical advancement of this natural bioactive.

PB-7: Biological Aspects of Botanicals

Red Ginseng Extract Inhibits Platelet-leukocyte Aggregates in LPS-induced Septic Mice.

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Platelet–leukocyte aggregates (PLAs) play important roles in cardiovascular disease and sepsis. Red ginseng extract (RGE) has been well-studied for its antiplatelet and anti-inflammatory activities. However, the potential inhibitory effects of RGE on PLA have not been investigated. Six-week-old ICR mice were given oral gavage of RGE for 7 days, followed by an intraperitoneal injection of 15 mg/kg of lipopolysaccharide. Mice were euthanized 24 hours later, and blood samples were collected for further analysis. Flow cytometry was utilized to sort populations of PLAs and platelet–neutrophil aggregates (PNAs). PNAs were validated using confocal microscopy. Morphological changes in platelets and leukocytes were visualized with scanning electron microscopy. Tissue factor (TF) and platelet factor 4 (PF4) expressions were investigated using enzyme-linked immunosorbent assay. Populations of activated platelets, PLAs, and PNAs were significantly increased. Treatment with 200 and 400 mg/kg of RGE decreased platelet activation.

Moreover, the populations of PLAs and PNAs were reduced. PNAs were visible in the septic mice's blood, which was attenuated by treatment with 400 mg/kg of RGE. Morphologically, sepsis-induced platelet activation and fibrin formation in the blood. This was reduced with RGE treatment. Sepsis-induced increase in the plasma levels of TF and PF4 was also reduced with RGE treatment. This study shows that RGE is a potential therapeutic that reduces the activation of platelets and targets PLA and PNA formation. Detailed inhibitory mechanisms of RGE should be studied.

PB-8: Biological Aspects of Botanicals

Histomorphometric Lung Density Evaluation of Immulina™ Treatment Using a Murine Influenza Pneumonia Model

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Histomorphometric lung density measurements were used to evaluate the effects of Immulina™ on mouse pneumonia. Mice were intra-nasally exposed to the H1N1 influenza virus at a dose of 50,000 PFU/50 µL/mouse. Lung density was measured using the NIH ImageJ software program. Density values were compared to semi- quantitative pneumonia severity scores. Lung photomicrographs were evaluated at 25-×, 40-×, and 400-× magnification. The study included viral inoculated con- trols (IC) and non-inoculated controls (NC) and mice either treated or not treated with Immulina. Three doses of Immulina were included (25, 50, or 100 mg/kg) and administered using 3 protocols: prophylactic treatment (P), prodromal treatment (PD), and therapeutic treatment (TH) (note that in most of the evaluations of the data for the three treatment protocols were combined). Groups of mice were evaluated on days 3, 5, 7, 10, and 15 following exposure. The “digital pneumonia” (DP) occurrence was defined as a density measurement above the 95% confidence limit of the corresponding NC values. A significant reduction in the occurrence of DP with Immulina treatment at the higher doses compared to IC was seen as early as day 3 and persisted until day 15. There were also statistically significant dose-variable reductions in lung density in response to Immulina. The study suggests early administration of Immulina (P or PD protocols) may enhance resistance against influenza-induced viral pneumonia. A moderate correlation between pneumonia severity scores and lung density was observed for the 25-× and 40-× images (R = 0.56 and 0.53, respectively), and a strong correlation (R = 0.68) for 400-× images.

PB-9: Biological Aspects of Botanicals

The Comparison Studies of Protopanaxadiol and Protopanaxatriol: Efficacy in Blood Circulation

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Ginsenosides can be grouped into protopanaxadiol (PPD)- and protopanaxatriol (PPT)-types of molecules. Previous reports have shown that many ginsenosides exhibit anti-platelet activity. However, the comparison of the anti-platelet activity of PPD and PPT was not investigated previously. We conducted *in vitro* and *ex vivo* platelet aggregation studies in Sprague-Dawley rats. For *in vitro* studies, rat blood was collected via cardiac puncture, and platelets were collected after treatment with an agonist and samples. For *in vivo* studies, PPD and PPT were treated orally in rats for 3 consecutive days, and platelet aggregation was induced by collagen or ADP. Granule secretion, cAMP, cGMP, and TXB2 were investigated via ELISA; fibronectin adhesion was also investigated using fibronectin-coated plates. Our findings revealed that PPT was more effective than PPD regarding platelet aggregation in vitro. However, ex vivo experiments revealed that PPD was more effective than PPT; PPD effectively prevented platelet aggregation induced by collagen and ADP, reduced ATP secretion, serotonin release, and fibronectin adhesion. This is an interesting finding, and we hypothesize that the different delivery routes of PPD and PPT have affected its efficacy. PPD consists of Rb1, Rc, Rb2, Rb3, and Rd, whereas PPT consists of Rg1, Re, Rf, and Rg3. Ginsenosides were widely studied for their anti-platelet activities, and most ginsenosides from PPT (Rg1 and Rg3) were reported to prevent platelet aggregation. We hypothesize that the metabolism of PPD ginsenosides has affected its anti-platelet activity. In conclusion, PPD has more effective anti-platelet activity than PPT when administered orally.

PB-10: Biological Aspects of Botanicals

The Protective Effect of *Hypericum ascyron* L. Extract on Airway Inflammation.

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Industrialization has caused an increase in particulate matter and fine dust in the air we breathe and at the same time increases the risk of asthma and breathing difficulties. We aim to investigate the analgesic properties of *H. ascyron L.* (HA) in airway inflammation and unravel its mechanism of action. HA reduced CFA-induced NO without exhibiting cytotoxicity in MH-S cells. HA also reduced the mRNA expression of pro-inflammatory cytokines and increased the expression of proteins in the NFkB and MAPK pathways. In a mice model of CFD-induced airway inflammation, HA effectively reduced neutrophil infiltration in BALF and increased the amount of T cells in the BALF, PBMC, and blood while reducing all other immune cell subtypes to reduce the airway inflammatory response. CXCL-1, IL-17, MIP-2, and TNF-α expression in the BALF was also reduced and HA effectively reduced MIP-2 and TNF-α mRNA expression in the lung tissue of the mice. In a nutshell, HA is effective in preventing airway inflammation induced by CFA in MH-S cells as well as inflammation induced in mice by a combination of particulate matter and diesel particulate matter.

PB-11: Biological Aspects of Botanicals

Anticancer Activity of *Annona squamosa* Seed Isolate in Ovarian Cancer

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Cancer is a broad category of illnesses that can originate in nearly any organ or tissue in the body when aberrant cells proliferate out of control, cross normal boundaries to infect other body parts, or spread to other organs. In India, the Indian Council of Medical Research (ICMR) has disclosed in its bi-annual study that more women than males are receiving cancer diagnoses. The disease is expected to affect 1.57 million people in 2025, up from 1.46 million this year. Ovary, cervix, and corpus uteri were the next most common cancers in women, with breast cancer having the greatest prevalence. The study's main aim is to determine the anticancer activity of isolate derived from hydroalcoholic extract of *Annona squamosa* (AS) seeds and identify the compound responsible against Ovarian cancer lines.

Hydroalcoholic extract of *Annona squamosa* seeds was purified using column chromatography to yield two isolates, I1 and I2, and tested using the sulforhodamine B assay method on ovary cancer cell lines where phytochemical analysis was performed using the LCMS method. The phytochemical characterization was done using the LCMS method, which showed 15 different molecular weight compounds. The extract showed an average *in vitro* anticancer activity at 100 µg/mL concentration against ovary cancer cell lines. The phytochemical analysis using the LCMS method showed a wide range of phenols and flavonoids, which show anticancer activity of AS seeds isolate I2.

PB-12: Biological Aspects of Botanicals

Regioselective Claisen–Schmidt Adduct of 2-Undecanone from *Houttuynia cordata* Thunb as Insecticide/Repellent against *Solenopsis invicta* and Repositioning Plant Fungicides against *Colletotrichum fragariae*

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The U.S. Department of Agriculture (USDA) has established research programs to fight the phytopathogen *Colletotrichum fragariae* and the invasive red imported fire ant, *Solenopsis invicta*. *C. fragariae* is known to cause anthracnose disease in fruits and vegetables, while *S. invicta* is known for its aggressive behavior and painful stings and for being the cause of significant damage to crops, as well as harm to humans and animals. Many plants have been studied for potential activity against *C. fragariae* and *S. invicta*. Among the studied plants, *Houttuynia cordata* Thunb has been shown to contain 2-undecanone, which is known for its antifungal activity against *Colletotrichum gloesporioides*. Based on the mean amount of sand removed, 2-undecanone showed significant repellency at 62.5 μg/g, similar to DEET (N,N-diethyl-meta-toluamide), against *S. invicta*. The 2-undecanone with an LC_{50} of 44.59 μg/g showed toxicity against *S. invicta* workers. However, neither *H. cordata* extract nor 2-undecanone had shown activity against *C. fragariae* despite their known activity against *C. gloesporioides*, which in turn motivates us to reposition 2-undecanone as a selected candidate for a Claisen–Schmidt condensation that enables access to several analogs (2a–f). Among the prepared analogs, (E)-1-(3-methylbenzo[b]thiophen-2-yl) dodec-1-en-3-one (2b) and (E)-1-(5-bromothiophen-2-yl) dodec-1-en-3-one (2f) showed promising activity against *C. fragariae*, revealing a distinctive structural activity relationship (SAR). The generated analogs revealed a clear regioselectivity pattern by forming the C=C alkene bond at position C-1. These data open the window for further lead optimization and product development in managing *C. fragariae* and *S. invicta*.

PB-13: Biological Aspects of Botanicals

Comparative Study on Sub-critical Extracts of *Elaeocarpus sylvestris* var. *ellipticus* Leaves as Potential Cosmetic Ingredients

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Elaeocarpus sylvestris var. *ellipticus* (Thunb.) H.Hara (Elaeocarpaceae) is an evergreen tree with shiny and oblanceolate leaves. Since it is susceptible to cold weather, the distribution area is limited to subtropical regions such as Jeju Island (Korea), Japan, Southern China, and Taiwan. *E. sylvestris* contains polyphenolic compounds such as tannins and flavonoids, which exhibit antioxidant, antiviral, and antibacterial activities. In this study, we prepared extracts from each part (fruits, leaves, stem) in *E. sylvestris* by using the sub-critical extraction method and fermentation method by *Latilactobacillus curvatus* extracted with 70% EtOH to determine the efficient extraction conditions for *E. sylvestris*. The HPLC profile showed that each extract had similar patterns, but the sub-critical water leaf extract had the highest peak intensity at 280 nm. Gallic acid, the active and major compound in the extract, was quantified by HPLC, showing the highest content in the sub-critical water leaf extract among six samples. The antioxidant, anti-acne, and whitening effects were proportional to the gallic acid content. The findings suggest that subcritical leaf extracts of *E. sylvestris* have the potential to be effective materials for cosmetic applications such as skin whitening and anti-acne applications.

PB-14: Biological Aspects of Botanicals (OSD)

Menthalactone, a Potential Natural-product–based Bioherbicide Selective Against Creeping Bentgrass

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The persistent challenge of managing invasive weed species continues to confront the agricultural industry, presenting ecological, economic, and agronomic hurdles causing over $100 billion in annual crop losses globally. One such concern is the management of *Agrostis stolonifera*, commonly known as creeping bentgrass, which is particularly concerned due to its ability to form hybrids. This scenario underscores the urgent need for innovative, effective, and environmentally sustainable herbicides, steering the focus toward natural substances as potential candidates. In collaboration with USDA-ARS, we report a promising natural lactone, known as menthalactone, derived from *Mentha cordifolia*. The phytotoxic activity was assessed against the monocot, bentgrass (*A. stolonifera* - Penncross variety), and dicot, lettuce (*Lactuca sativa*—Iceberg A Crisphead cultivar, Burpee Seeds). Menthalactone displayed outstanding activity against the monocot bentgrass and was further evaluated for in-depth phytotoxic characteristics. The germination of *A. stolonifera* seeds was significantly inhibited with an IC_{50} value of 4.9 ± 1.2 µM.

Contrary to bentagrass seeds, *Lemna pausicostata* plants did not respond greatly to menthalactone with an IC_{50} of 293.4 ± 70.6 µM. Both species are monocots, and the results suggest that menthalactone might have a destructive effect on seed germination but does not effectively impact the metabolism in green tissues. The susceptibility of menthalactone on three common, obnoxious weed species, i.e., ryegrass (*Lilium perenne*), barnyard grass (*Echinochloa crusgalli*), and crabgrass (*Digitaria sanguinalis*) was assessed. Menthalactone at 1000 µM completely hampered the germination of all three grass species, while 330 µM was ineffective at inhibiting germination in less than 50%. Post-emergence application of menthalactone at 1% did not produce a significant effect against ryegrass, barnyard grass, or crabgrass.

PB-15: Biological Aspects of Botanicals

Pyrrolobenzodiazepines: Natural Sources, Therapeutic Uses, and Future in Neurological Treatments

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Pyrrolobenzodiazepines (PBDs) are a potent class of compounds that have been analyzed since the 1960s and are found naturally in a wide variety of species. They may be obtained through extraction from natural sources or through synthetic routes. Various studies have indicated remarkable anti-tumor, anti-bacterial, analgesic, and anti-neurodegenerative activities of PBDs. This review will examine natural sources of PBDs, their biological activities, newer synthesis strategies, and the effect of structural modifications, specifically from a neurological standpoint. Emerging studies on pyrrolobenzodiazepines offer encouragement for further research on their neurological activities, potentially leading to therapeutic uses in addition to that as an oncological agent.

PB-16: Biological Aspects of Botanicals

Bioaccessibility and Metabolic Stability of Cinnamaldehyde: A Major Constituent of Cinnamon Oil and its Interaction with Xeno-receptors

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Cinnamon has been used for a long time as a condiment in various food delicacies as well as an ingredient in herbal formulations. Cinnamaldehyde is a primary constituent of cinnamon, which substantially contributes to the food additive and medicinal properties of cinnamon. To understand its ADME properties, the present study evaluated cinnamaldehyde's bioaccessibility, metabolic stability, and interaction with xeno-sensing receptors (PXR and AhR). The results of dissolution studies showed that over 100% cinnamaldehyde was bioaccessible in fasted and fed-state simulated gastric and intestinal fluids. Metabolic stability studies suggested that upon incubation with HLMs and HLS9 fraction, cinnamaldehyde (in its pure form or the form of cinnamon oil) rapidly oxidized into cinnamic acid. However, incubation with primary human hepatocytes revealed moderate stability. Cinnamon oil dose-dependently activated AhR in human AhR-reporter cells, but cinnamaldehyde or cinnamic acid (in pure form) did not affect AhR. In addition, cinnamaldehyde significantly activated PXR in human hepatic (HepG2) and intestinal (LS174T) cells. On incubation with translationally matured CYPs, tested compounds partially inhibited the catalytic activity of CYP3A4 and 1A2. Our findings indicated that highly bioaccessible cinnamaldehyde possesses moderate hepatic stability with a reasonable PXR activation. Hence, controlled ingestion of cinnamon-containing foods or dietary supplements can boost health, but overconsumption may induce modest HDIs, especially in chronic pathophysiology.

PB-17: Biological Aspects of Botanicals

Fatty Acids from Natural Sources as Potential Moisturizing and Anti-aging Agents.

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Oxidized saturated fatty acids, a relatively unexplored category of oxidized lipids in the realm of food science, are investigated for their potential impact on skin hydration and anti-aging properties. While the conventional belief suggests that oils can enhance skin hydration by reducing trans-epidermal water loss, this study delves into the specific effects of oxidized saturated fatty acids derived from natural sources on key moisturizing and anti-aging mechanisms.

The primary objective of this research is to elucidate whether the observed skin hydration attributed to oxidized saturated fatty acids is linked to the upregulation of Hyaluronic Acid Synthase (HAS) and Cluster of Differentiation 44 (CD44) expression in human monocytes and keratinocytes. The study involves testing seven fatty acids on CD44 expression using human keratinocytes and THP-1 cells. Results indicate that 9-oxo-2-decenoic acid and 8-oxodecanoic acid significantly elevate HAS2 and HAS3 mRNA expression in human keratinocytes by Reverse Transcription Quantitative Polymerase Chain Reaction (RT-qPCR). Other fatty acids examined were found to be inactive in this regard. Furthermore, 8-oxodecanoic acid demonstrated a noteworthy increase in CD44 expression, as evidenced by fluorescence microscopy and flow cytometry analyses in human keratinocytes and THP-1 cells.

In conclusion, our findings suggest that 8-oxodecanoic acid, an oxidized saturated fatty acid derived from natural sources, holds promise as a potential moisturizing and anti-aging agent. These results contribute valuable insights for developing functional foods and cosmetic applications to enhance skin hydration and combat aging effects.

PB-18: Biological Aspects of Botanicals

Anti-obesity and Anti-diabetic Effects of Damiana (*Turnera diffusa*) Leaf Extract through Inhibiting Adipocyte Differentiation and Enhancing Glucose Uptake in Myocytes.

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Turnera diffusa leaf has been used in traditional medicine as an aphrodisiac, tonic, and in the management of diabetes. Based on the traditional use and recent evidence of antidiabetic activity, we investigated the effects of hydroethanolic extract of *T. diffusa* leaf extract (TDE) on a series of ligand-activated transcription factors, namely PPARα, PPARγ, LXR, and NRF2, which are involved in the regulation of metabolic pathways associated with obesity, diabetes, and inflammation. Further, the effects of TDE on lipid accumulation in adipocytes (adipogenesis) and glucose uptake in myocytes were also evaluated.

TDE demonstrated strong agonistic effects on LXR, resulting in an increase of >2-fold in LXR activity, while the activation of PPARα, PPARγ, and NRF2 was in the range of 1.15 to 1.82 folds under similar experimental conditions. At a 100 µg/mL concentration, TDE decreased lipid accumulation in adipocytes (55.3%) and increased glucose uptake in muscle cells (91.3%). The adipogenic effect induced by a full PPARγ agonist (rosiglitazone) was antagonized by TDE, showing a decrease of 57.6% in lipid accumulation. This is the first report to reveal the agonistic action of TDE on multiple nuclear receptors along with its glucose uptake enhancing and antiadipogenic effects. The results indicate the potential utility of TDE in alleviating metabolic syndrome symptoms and preventing the undesired adipogenic effects of antidiabetic drugs of the glitazone class. Phytochemical analysis of TDE to identify potential bioactive constituents is underway. Further studies in type II diabetes animal models would further corroborate our initial findings.

PB-19: Biological Aspects of Botanicals

Comprehensive Investigation of Psilocybin Mushrooms.

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Neuropsychiatric disorders (ND) pose significant challenges in the US, affecting various aspects of society, including the economy. Individuals with untreated neuropsychiatric disorders are at higher risk of involvement with the criminal justice system and face increased suicide rates. Non-hallucinogenic psilocybin-related metabolites could be transformative for the treatment of ND devoid of abuse liability. ND therapeutics, such as opioids, carry high abuse liability and unsafe drug-drug interactions. Psychedelic psilocybe mushrooms, also known as “magic mushrooms”, contain the psychedelic compound psilocybin and consist of over 200 species and have been used for centuries for their psychoactive and therapeutic effects. Psilocybin is the main active component in psilocybe mushrooms that metabolizes to the hallucinogenic psilocin. They target the human serotonin 2A receptor (5-HT2AR) and have shown promise in treating ND; however, their associated hallucinogenic effects are hampering their use. FDA granted "Breakthrough Therapy" status to psilocybin-assisted therapy for the treatment of resistant depression. We studied three selected strains of *Psilocybe cubensis*, namely Golden Halo, Hillbilly, and B+, at 3, 5, and 9 weeks of growing stages. Chemical analysis revealed at least a 20% increase in the psilocybin content at week 5 compared to 3 in the B+ strain, while considerable variation has been noticed for B+ and Hillbilly strains between week 5 and 9. LC/MS analysis has revealed the tentative identification of 14 compounds from B+, 12 from Hillbilly, and 9 from Golden Halo. Many non-reported related minor metabolites have been detected that warrant further large-scale investigation.

PB-20: Biological Aspects of Botanicals

Morphine Dependence is Attenuated by a Combination Treatment of Red Ginseng and Polygalae Radix in Mice.

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As part of ongoing efforts to alleviate morphine dependence, we screened for the anti-narcotic effects of natural products through behavior experiments. In addition, microRNAs, small noncoding RNA molecules that regulate post-transcriptional gene expression, and various genes in the brain of morphine-addicted mice. Polygalae radix is the dried rhizome of *Polygala tenuifolia* Wild. We compared each treatment alone with ginseng, polygalae radix, and a combination of the two in various ratios for morphine-induced dependence on mice. Mice were pretreated with red ginseng, polygalae radix, and a combination in various ratios once a day, 30 minutes before the morphine treatment. Morphine was injected twice a day at 12-hour intervals for 9 days to induce morphine dependence. Physical dependence was assessed using a naloxone-induced morphine withdrawal jumping behavior, and psychological dependence was measured by conditioned place preference (CPP) score. The scores of naloxone-precipitated jumps and CPP were significantly suppressed by the combination treatment of a specific ratio rather than the single treatment of red ginseng or polygalae radix. In addition, PCR and western blot experiments confirmed that the combination of red ginseng and polygalae radix in a specific ratio decreased morphine dependence. Therefore, this study suggested that a specific combination of red ginseng and natural products has more potential for the treatment of morphine dependence than treatment with either product alone.

PB-21: Biological Aspects of Botanicals

The Effects of Gintonin on the Activation of Macrophage through the MAPK Pathway

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The objective of the study is to examine the effect of macrophage activation by gintonin isolated from *Panax ginseng*. Macrophages are known as immune cells responsible for innate immunity. *Panax ginseng* has been traditionally used for a long time in Asia, including Korea and China, to remedy various diseases. One of the functions of polysaccharides is thought to increase immunity in the body by activating immune cells. Recently, we have isolated the gintonin compound with about 17 kDa as a novel compound of *Panax ginseng*. Gintonin consists of constituents of lysophosphatidic acids and ribonuclease-like protein. Therefore, we verified whether gintonin could increase the activation of macrophages. As a result, gintonin treatment increased the expression of CD11b, CD80, and MHC-II, a common marker for macrophage activation. Also, gintonin increases mRNA expression of TNF-α, IL-6, IL-1β, NF-kB, IkBα, p65, NOS2, COX-2, JNK, p38, Ephb1, PERK, NLRP3, and caspase-1. Gintonin increased protein levels such as iNOS, COX-2, IL-1β, caspase-1, TNF-α, TGF-β, MAPK, and NF-kB signaling. Namely, the treatment of gintonin up-regulated the protein expression of iNOS and COX-2 almost 2-fold in the present study. IL-1β, caspase-1, TNF-α, TGF-β, and MAPK phosphorylation had significantly increased compared to the control. Our findings showed that gintonin can increase macrophage functions by influencing gene or protein expression. Specifically, we observed that the NF-kB/MAPK signaling pathway plays an essential role in the upstream of cytokines.

PB-22: Biological Aspects of Botanicals

Activation of Natural Killer Cell by Korean Red Ginseng and its Mechanism

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Recently, studies have shown that Korean red ginseng has anti-inflammatory, antioxidant, and anticancer effects. However, the effects of Korean red ginseng and its immunomodulatory function on porcine are poorly understood. The pig (*Sus domesticus*) has very high similarities to humans in immune system functions (more than 80% in contrast to the mouse with only about 10%), e.g., the presence of tonsils, which are absent in rodents. Therefore, in the present study, we aimed to examine the immune functions of Korean red ginseng by natural killer (NK) cell activation as well as signaling molecules and cytokines on porcine. Korean red ginseng was supplied by Korea Ginseng Corporation (KGC, Daejeon, Korea). For the study, about 20 kg pigs were divided into four groups in each group. In the KRG groups, animals were treated with 3 and 6 g KRG because if 3 or 6 g Korean red ginseng is administered to a 20 kg pig, it corresponds to 150 or 300 mg/kg concentration, corresponding to the doses commonly treated in rodents. The results showed that Korean red ginseng treatment increased the CD4+CD8+T cell population and CD3-CD172-CD8+NK cells. These results indicated that Korean red ginseng affected these immune cells in porcine. The cytotoxic property target cells were analyzed. A significant increase in cytotoxic function was observed. These results show Korean red ginseng could have more cytotoxic activities against target cells. IL-4, IL-6, and IL-10 levels were also increased after treatment with Korean red ginseng. Also, we have studied NK cells' surface marker expression, i.e., NKp46, NKp44, and NKp30. As a result, our data showed that NKp30 and NKp46 were significantly more abundant than the normal group. NKp44 significantly increased in the 6 g KRG group. Taken together, we have concluded that when Korean red ginseng is administered on porcine, immune responses of NK cells increase, which is thought to be due to the mechanism of cytokine secretion.

PB-23: Biological Aspects of Botanicals

Pharmacology and Micro-morphological Analysis of *Houttuynia cordata* Thunb.

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Houttuynia cordata Thunb is widely distributed as an edible plant in many Asian regions. It plays a key role in traditional health care management, where its stems and leaves have been used in China to treat pneumonia and lung abscesses. Micro-morphological analysis of the stem using an Olympus BX53 fluorescence microscope shows two different structural outlines. The stem internodes are circular and symmetrical, whereas in the nodal region, the stem shows a concave shape on one side and a circular to oval on the other. The transverse section of heart-shaped leaves comprises an outer epidermal layer covered with a thin cuticle layer. In our in vivo study, rats infected with acute pneumonia caused by intravenous administration of oleic acid into their tail veins were treated with a combination of *H. cordata* and Immunorm® for 12 days. Rats were sacrificed 3, 7, and 14 days after acute pneumonia was simulated. On day 7, uneven thickening of the interstitium appears in the lung tissue due to cellular infiltration. On day 14, uneven narrowing of the lumen due to spasm is noted in the lung vessels. Our data suggested that combinational therapy of *H. cordata* and Immunorm® reduced the inflammatory histopathology of the lungs, as evidenced by the decrease in interstitial inflammation and an increase in the interstitial area, resulting in the restoration of lung tissue. HR-MS analysis of *H. cordata* methanol extract has revealed the tentative identification of four compounds commonly named as imenine; 5-methoxy, houttuynoid A, houttuynoid C, and strigol, 5-ketone, where the detailed biological contribution of the identified metabolites to the overall activity is undergoing.

PB-24: Biological Aspects of Botanicals

MR Antagonism of Rg3(R) Modulates FLG Expression via SIRT1 to Mitigate Excessive Skin Barrier Disruption Induced by Glucocorticoids.

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Panax ginseng root, widely embraced in traditional herbal medicine throughout Korea, China, and Japan, is renowned for its immune-enhancing properties. Ginsenosides, its primary pharmacological components, exhibit structural resemblance to nuclear hormone receptors(NRs), allowing them to modulate activation or inhibition by binding to NRs. Notably, glucocorticoids(GCs) can bind to mineralocorticoid receptors (MR) with high affinity due to their structural similarity. MR, inappropriately activated by excessive GC levels, significantly contribute to developing GC-mediated skin side effects. As highlighted by previous studies, the NAD-dependent protein deacetylase SIRT1 plays a crucial role in cell survival, aging and stress response, particularly in GC-induced skin complications. Our prior research confirmed Rg3(R) as an MR antagonist, illustrating its efficacy in mitigating GC-induced skin barrier breakdown by regulating FLG expression. In this study, HaCaT cell experiments showed decreased SIRT1 expression and increased acetyl p53 and p21 expression following GC treatment. Strikingly, treatment with the MR antagonist Rg3(R) reversed these trends, underscoring its potential to modulate FLG expression through the SIRT1 pathway, thereby alleviating GC-induced skin barrier disruption. These findings offer valuable insights for effectively managing skin complications associated with excessive GC exposure using herbal remedies and molecular modulators at the molecular level.

PB-25: Biological Aspects of Botanicals

Antimicrobial Evaluation of Various Extracts of *Hypsizygus ulmarius* (Bull. ex Fr.) Redhead: A Cosmeceutical Important Mushroom

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A variety of medicinal products from mushrooms may be used in cosmeceutical products applied topically, such as creams, lotions, and ointments. Cosmeceuticals incorporating mushrooms include those for skin care, such as anti-aging, antioxidants, skin revitalizing, skin whitening, and hair products. In some cases, topical preparations can also be prepared from the topical extraction of mushrooms. A mushroom polysaccharide has increased interest as a skincare ingredient due to its high moisture content in the epidermis and stratum corneum and its ability to retain moisture. Additionally, these compounds hydrate the stratum corneum and improve the physical and chemical properties of the skin, providing a smooth-soft texture. The *Hypsizygus ulmarius* species possess several nutritional and medicinal properties such as antitumor, immunomodulatory, antioxidant, anti-inflammatory, anti-allergic, hypocholesterolemic, and antimicrobial activities. The powdered *H. ulmarius* mushroom was successively extracted with various solvents such as ethanol, water, and ethanol/water through an orbital shaker. The mushroom extracts were tested for antimicrobial activity against *E. coli*, *P. aeruginosa*, *S. aureus*, *S. pneumonia,* and *C. albicans* by 96 well method at various concentrations (0.20 to 1.56 mg/mL) of extracts. All the extracts were effectively tested against microorganisms and compared with standard antibiotics (Ciprofloxacin and Amphotericin B). The maximum antimicrobial activities were obtained in water (200 mg/L to 6.25mg/mL), followed by ethanol/water and ethanol extracts. All three extracts were active against all the microorganisms, and strong activity was recorded against *C. albicans*. The present results indicated the potentiality of this mushroom extract, which can be utilized as a cosmeceutical product to control several skin infectious diseases caused by microorganisms.

PB-26: Biological Aspects of Botanicals

Examination of Essential Oil Combinations Against Bacteria Underlying Nosocomial Infections

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Nosocomial infections are causing an increasing problem in healthcare. In the case of hospital-acquired infections (HAI), it is common for the planned nursing time to be extended, and the patient needs to spend more time in the hospital ward, thus multiplying the probability of infection and increasing the use of antibiotics. Essential oils are complementary therapeutic possibilities, so their popularity is constantly increasing. The antibacterial effect of essential oils is known, but we have less information about the combined effect of essential oil samples used in different combinations.

Our studies aimed to test essential oil combinations against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Our essential oil samples included cinnamon bark essential oil, thyme essential oil, and clove essential oil. To carry out our research, we performed an *in vitro* checkerboard titration. The fractional inhibitory concentration index (FICI) value was calculated from the obtained values.

Based on our results, it can be said that all three strains of bacteria reacted sensitively to the essential oil treatment. During our combination studies, the essential oil of thyme and cinnamon bark proved synergistic for all three bacteria. In the case of *P. aeruginosa*, the combination of clove and cinnamon bark essential oil showed an additive effect, similar to the *S. aureus* clove-thyme and thyme-Ceylon cinnamon bark essential oil combination. In the case of *E. coli*, the combined use of clove and thyme essential oil resulted in an additive effect. During our research, we proved that different essential oils and their combinations show a higher degree of effectiveness in the case of different strains of bacteria. Furthermore, it was confirmed that certain essential oils can enhance each other's activity when used together, and a synergistic effect can be detected among them.

PB-27: Biological Aspects of Botanicals

The Combination of Natural Compounds Crila® and Epigallocatechin Gallate Showed Enhanced Antiproliferative Effects on Human Uterine Fibroid Cells Compared with Single Treatments

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Crila® and epigallocatechin gallate (EGCG) combined effects were investigated on human uterine fibroid cells (HuLM). HuLM cells were treated with different concentrations of Crila, alone or in combination with EGCG. Cell proliferation, drug synergy, protein, and gene expression of a proliferation marker and an apoptosis marker using western blot and qPCR were performed. Results showed that tested Crila concentrations, combined with 25 and 50 µM EGCG, exerted synergistic growth inhibitory effects on HuLM viability. This inhibitory effect on HuLM cell viability was mainly due to decreased cell proliferation, as shown by a decrease in the proliferation marker, proliferating cell nuclear antigen, at mRNA and protein levels. Our study concludes that further investigation is warranted for the combination treatment as a potential therapy for uterine fibroids. The utility of natural compounds may provide a safe and cost-effective alternative to currently used short-term hormonal therapies against uterine fibroids.

PB-28: Biological Aspects of Botanicals

Natural Molluscicides to Control the Intermediate Host Snails for the Trematode *Bolbophorus damnificus* in Catfish Aquaculture

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Infection by the digenean *Bolbophorus damnificus* causes substantial economic loss to catfish aquaculture in Mississippi and Louisiana. The catfish acquires the infection from the intermediate hosts, ramhorn snails (*Planorbella trivolvis*), and the invasive snail, *Biomphalaria havanensis*, prevalent in catfish production ponds. The infection is controlled by reducing the snail population, mainly using copper sulfate. Even though copper sulfate effectively controls the snail population, its usefulness is limited due to its accumulation in the environment, toxicity towards phytoplankton, and a small margin of safety between molluscicidal and ichthyotoxic concentrations.

This study aims to identify inexpensive natural molluscicides with limited toxicity to fish and phytoplankton. Saponins have been shown to possess potent molluscicidal activity. We evaluated the molluscicidal activity of five commercially available saponin extracts from plants (tea, alfalfa, yucca, English ivy, soya) listed by the US Food and Drug Administration as generally recognized as safe (GRAS). One of these commercial extracts showed potent molluscicidal activity, and the major compounds isolated from this extract showed activity comparable to copper sulfate. The molluscicidal activity of these extracts and compounds and their structure-activity relationships will be presented.

PB-29: Biological Aspects of Botanicals

Pharmacological Effects and Mechanism of Action of Xuetongsu in Alleviating Bone Destruction: Targeting RANKL-Related Osteoclastogenesis

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Rheumatoid arthritis (RA) is a progressive autoimmune disease that causes joint inflammation and bone destruction. Long-term severe bone destruction can cause joint deformity and disability, which seriously damages the health. Osteoclasts play a crucial role in bone destruction, as their excessive activity leads to cartilage matrix degradation. Currently, conventional anti-RA drugs used in long-term treatment often cause various side effects including gastrointestinal discomfort, hepatic and renal toxicity, and cardiovascular complications. This study was to examine the anti-bone destruction effects of Tujia ethnomedicine Xuetongsu on RA and explore ability to inhibit RANKL-mediated osteoclast differentiation and promote osteoclast apoptosis. RAW264.7 cells were cultured with 50 ng/mL RANKL to differentiate into osteoclasts. 36 SD rats were injected subcutaneously with complete Freund's adjuvant emulsion containing heat inactivated Mtb at the base of the tail to establish an AIA rat model. Osteoclasts were treated with different concentrations of Xuetongsu (0, 4.5, 9, and 18 μM) or methotrexate (4.5 μM). The Xuetongsu group received varying doses of Xuetongsu (1.0, 2.0, and 4.0 mg/kg), while the normal and model groups were treated with the same volume of 0.3% CMC-Na. The rats in positive control group were given 1.0 mg/kg methotrexate solution. Xuetongsu effectively mitigates RA-induced bone destruction in AIA rats by inhibiting osteoclast differentiation through direct targeting of RANKL and promoting osteoclast apoptosis via the activation of the Caspase-3/Bcl-2 pathway. Importantly, Xuetongsu exhibits favorable biosafety profiles in vivo. In conclusion, Xuetongsu inhibits RA bone destruction by targeting RANKL-Related osteoclastogenesis.

PB-30: Biological Aspects of Botanicals

Acupuncture and Moxibustion Modulate Gut Microbiota and Metabolism to Alleviate Colonic Inflammation in Crohn's Disease Rats: Implications for Therapeutic Mechanisms

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The mugwort in Hunan Province possesses significant medicinal value. The practice of igniting moxa sticks, made from the processed leaves of mugwort, for therapeutic purposes is known as moxibustion. Moxibustion is extensively employed in Asian regions and demonstrates efficacy in treating gastrointestinal disorders. In this study, we explored the effects of acupuncture and moxibustion on colonic inflammation in Crohn's disease (CD) rats and investigated the underlying mechanisms involving gut microbiota and metabolism modulation. CD rats were induced using 2,4,6-trinitrobenzene sulfonic acid (TNBS) and treated with acupuncture and moxibustion at specific acupoints for 7 days. We observed significant improvements in disease symptoms and colonic inflammation, accompanied by changes in the colonic microbiota composition and metabolic profiles. Treatment increased Proteobacteria and reduced Firmicutes abundance, along with alterations in key metabolites involved in various metabolic pathways. Our findings suggest that acupuncture and moxibustion alleviate inflammation in CD rats by modulating gut microbiota and metabolism.

PB-31: Biological Aspects of Botanicals

GOQDs-loaded Sinomenine Hydrochloride Nanocomplexes Synergistically Target Macrophage Repolarization and Proliferation of Rheumatoid Arthritis Fibroblast-like Synoviocytes for Treatment of Adjuvant-induced Arthritis and Collagen II-induced Arthritis in Rats

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The characteristic features of the rheumatoid arthritis (RA) microenvironment are synovial inflammation and hyperplasia. Therefore, there is a growing interest in developing a suitable therapeutic strategy for RA that targets the synovial macrophage and fibroblast-like synoviocytes (FLSs). In this study, we used graphene oxide quantum dots (GOQDs) to create a nanomedicine system (GP@SIN NPs) by loading anti-arthritic sinomenine hydrochloride (SIN). Our molecular mechanism studies demonstrated that this nanomedicine system was effective against RA by promoting the transition of M1 to M2 macrophages and inhibiting the abnormal proliferation of FLSs in vitro. To assess its therapeutic potential, we employed two preclinical models of RA: adjuvant-induced arthritis and collagen-induced arthritis in rats. Importantly, we modified the surface of the hybrid membrane (RFM)-coated biomimetic nanomaterial with hyaluronic acid (HA) (HA@RFM@GP@SIN NPs) to target inflammatory articular lesions. This modification allowed for the synergistic regulation of macrophage polarization and synovial hyperplasia, ultimately preventing cartilage destruction and bone erosion in vivo. Metabolomics demonstrated that HA@RFM@GP@SIN NPs exerted their anti-arthritic effects through the regulation of steroid hormone biosynthesis, ovarian steroidogenesis, tryptophan metabolism, and tyrosine metabolism. More notably, transcriptomic analyses and protein validation revealed that HA@RFM@GP@SIN NPs inhibited the abnormal proliferation of RA-FLS by interfering with the PI3K/Akt/SGK/FoxO signaling pathway, leading to a decrease in cyclin B1 expression and cell cycle arrest in the G2 phase. Additionally, HA@RFM@GP@SIN NPs exhibited favorable biocompatibility and biosafety in both in vitro and in vivo experiments. Overall, these multifunctional nanoparticles offer a promising therapeutic approach for patients with RA.

PB-32: Biological Aspects of Botanicals

Microbial Metabolism of the Sesquiterpene Carotol: Cytotoxicity Evaluation and *In Silico* Studies of its Metabolites

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Microbial cultures serve as efficient biocatalysts, offering a diverse array of derivatives that are often challenging to obtain from mammals or through synthetic methods. This technique has facilitated the study of xenobiotic metabolism. Carrot (*Daucus carota* L.) is a root vegetable where its seed essential oil is a common aromatic component in cosmetics and perfumes. Beyond its fragrance applications, it boasts therapeutic uses, particularly in treating skin conditions. Notably, carotol, a sesquiterpene alcohol, stands as the main compound found in carrot seed oil. This study aimed at exploring the microbial capacity to metabolize carotol into various derivatives, producing quantities sufficient for assessing their cytotoxic effects. All initial screening and preparative-scale experiments followed the standardized two-stage protocol. Carotol, prepared as a 10% solution in DMF, was introduced into the 24-h-old stage II culture medium of the microorganisms at a concentration of 0.1 mg/mL of medium. Substrate and culture controls were also prepared. Following a 2-week incubation period, each test and control underwent harvesting and subsequent analysis. Metabolites were isolated and purified using Si gel columns and identified through NMR and X-ray diffraction spectroscopy. The pure metabolites' cytotoxic activities were assessed against HepG-2, HTC-116, MCF-7, A-549 carcinoma cells, and the normal cell line MRC-5, in comparison to those of carotol and the control cis-platin. Molecular docking of carotol and the metabolites was conducted using MOE. Out of the seventeen microbial cultures screened for their capability to biotransform carotol, Absidia coerulea ATCC 6647 produced three hydroxylated metabolites (CM1, CM-2, and CM-3). Among these metabolites, CM-2 exhibited the highest activity against all tested cell lines. However, all metabolites demonstrated lower activities with high affinity and free binding energy to NADPH oxidase compared to carotol.

PB-33: Biological Aspects of Botanicals

Betulin Exhibits Antimigration Activity Against MCF7 Cells

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This work examines the antimigration activity of betulin against MCF7 breast cancer cells using a scratch wound assay. Betulin was isolated from the bark of *Parartocarpus venenosus* (Zoll. & Mor.) Becc. It precipitated out as a white powder from the fraction that eluted out of the crude ethyl acetate extract in a normal phase vacuum liquid chromatography using 7:3 (v/v) hexane: ethyl acetate. It was purified with reverse phase HPLC and characterized via 1D- and 2D-NMR, UPLC-HRMS, FTIR, and melting point. This is the first report of the isolation of betulin from *P. venenosus*. Prior to the scratch assay, betulin toxicity was evaluated against liver (HepG2), kidney (HK-2), and heart (H9c2) cells with an LDH quantification assay. It exhibited low cytotoxicity against the three cell lines at 1, 5, and 20 uM but was already nephro- and cardiotoxic at 50 uM. Betulin inhibited the migration of MCF7 cells at 22.6 uM. Although betulin has been shown to exhibit anticancer properties, this is the first report of its antimigration activity against MCF7 cells, suggesting its potential against HR+ breast cancers.

PB-34: Biological Aspects of Botanicals

Studies of St. Johns's Wort (*Hypericum perforatum*) Dry Extracts: No Hints on Mutagenicity

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The genotoxic safety of herbal medicinal products (HMPs) from preparations of *Hypericum perforatum* L., herba have already been assessed and reviewed over the last years. These HMPs play an important role in the treatment of e.g. mild to moderate depressive episodes and of mental exhaustion. One traditional form is the comminuted or powdered herbal substance alone. The way to test their genotoxic potential is the so called "bracketing and matrixing concept", where three extracts with different polarity are tested. The purpose of this concept is to obtain a representative sample of all components of the drug in these three extracts as a whole. Additional data on the genotoxic potential are therefore desirable to assess the therapeutic safety of these HMPs, using the Ames test according to the genotoxicity guideline of the Herbal Medicinal Product Committee HMPC of the European regulatory agency EMA. Three dry extracts of *Hypericum perforatum*, representing the whole spectrum of polarities of the extraction solvents (water – 50 % ethanol (v/v) – n heptane) were tested in the Ames test, according to the OECD and HMPC guidances.The extracts showed no mutagenic effect, even not in the highest concentrations according to the OECD guidance. The results of the three tested dry extracts can be extrapolated by a "bracketing and matrixing concept" for other dry extracts of *Hypericum perforatum* in the tested polarity range of the extraction solvents. The data support the therapeutic safety of the extracts and the drug powder and add the assessment in the HMPC monograph of *Hypericum perforatum*.

PB-35: Biological Aspects of Botanicals

Antimicrobial, Antibiofilm and Cytotoxic Assessments of Pakistani Traditional Medicinal Plants

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Traditional medicinal plants are a primary source of natural products which are used for the prevention and treatment of various infections throughout the world. This study documents the ethnobotanical investigation and bioactivities of 17 traditional medicinal plants belonging to 12 families from the Swat region of Pakistan. The plants were collected after interviewing local ethnomedicinal knowledge holders and confirmation of their effective use by the local population. The extracts (85) were prepared in five different solvents (hexane, acetone, ethanol, methanol, and water), and were tested for bioactivity such as antibacterial (5 Gram-positive and 9 Gram-negative bacteria), antifungal (6 yeasts), and cytotoxicity (cancerous and non-cancerous cell lines). Results demonstrated that 25.06% extracts showed pronounced activity (IV>50%) against different planktonic microbes, 35.3% extracts showed pronounced activity against biofilm strains of bacteria and fungi. Cytotoxicity was often observed against a tumor cell, but rarely against non-tumoral cell lines. Moreover, ethanol was found to be the best extractant solvent compared with other solvents. Based on the bioactivities observed in the study, plants like *Juglans regia*, *Punica granatum*, *Artemesia maritima*, *Aesculus indica*, *Thymus linearis*, *Nasturtium officinale*, *Berberis lyceum*, *Dysphania ambrosioides*, and *Mentha spicata* are recommended for further studies to be used as a potential source of novel drug discovery. The comprehensive pharmacological studies including extraction, bioassay guided fractionation, isolation, characterization, in vitro and in vivo assessments, understanding mechanism of actions and synergistic effects of the bioactive compounds from the mentioned plants could pave the way for the development of various drugs for various health conditions.

PB-36: Biological Aspects of Botanicals

Natural Products and Herbal Medicine from Dong Ethnic Medicine

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Dong minority is one of 56 races in China, with a population of 3 million scattered in the mountain areas of southwestern China, about 90 percent of Dong people living in the boundary of Hunan, Guangxi and Guizhou provinces. Due to the inconvenient traffic situation and poor medical health system. Dong people developed and inherited their own herbal medical knowledge based on the abundant natural plant/animal resources and the widespread basic TCM ideas. There are more than 300 kinds of herbal medicines summarized in total, while only parts of the resources have been researched currently. Here several kinds of herbal medicine with good therapeutic effects were subject to pharmacological research with modern technology. Such as Madengai, the rhizome of *Potentilla freyniana* Bornm. (Rosaceae), been used as a folk medicine in clearing heat, treating canker and external bleeding. Investigations disclosed that the plant contained lots of ursolic and oleanolic type triterpenoids, especially A-ring contracted triterpenoids madengaisu A and B, the structures were elucidated on NMR, HRESI-MS and other spectrum methods. Bioassay on isolated compounds showed good anti-inflammatory and anti-tumor activity.

PB-37: Biological Aspects of Botanicals

Ecological Momentary-assessment Study of US Adults who use Kratom Accompanied by Kratom Product Assay

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Aim: 1) to characterize proximal motivators, effects, and patterns of kratom use and to assess whether use frequency is associated with motivations, effects, past-year substance use disorder for kratom; 2) to quantify alkaloid content of the kratom products participants used.

Between July-November 2022 US adults regularly using kratom were screened and enrolled into a national convenience sample. Following baseline survey completion, participants underwent ecological momentary assessment (EMA) for 15 days.

Of the 2,235 candidates screened, 395 were enrolled. A total of 13,401 distinct kratom use events were recorded. Whole leaf/loose powder was most commonly used. Peak effects were 40–80 minutes post-dosing. Participants reported overall motivators of use on the baseline survey that involved managing psychiatric and SUD problems, but proximal motivators evaluated with EMA were situation-specific (increasing energy, alertness, productivity; decreasing pain). Acute effects were considered congruent with daily obligations. Use patterns, despite having some distinguishing features, were generally similar in their motivators and effects; participants used kratom predominantly during the daytime. Higher use patterns were associated with symptoms of physical dependence (withdrawal, tolerance). Co-used substances included caffeine, nicotine, tea, vitamins, and cannabis. The 330 kratom products collected were analyzed for 10 major and minor kratom alkaloids using a validated ultraperformance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method. Among the analyzed commercial kratom products, mitragynine, paynantheine, speciogynine, and speciociliatine were found to be major alkaloids, and very low concentrations (<0.02%) of 7-hydroxymitragynine, corynoxine, corynoxine-B, and mitraphylline were observed. Corynoxine and corynoxine-B were correlated, with all remaining alkaloids correlated with one another.

PB-38: Biological Aspects of Botanicals

Discovering Antiviral Agents from Plant Sources

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Infectious diseases caused by emerging or re-emerging pathogens pose serious health problems and viral diseases dominate the World Health Organization (WHO)'s list of ten threats to global health. The recent Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) and monkeypox/mpox outbreaks have unmasked the urgent need for antiviral drugs that can be rapidly deployed to combat viral infections before a vaccine is developed. Thus, there is an urgent need for new and readily affordable drugs against viral infections and drug-resistant pathogens. Medicinal plants have been used against viral infections for centuries, but several of these plants remain uninvestigated both pharmacologically and chemically. Our work investigating the anti-mpox, and anti-COVID-19 activities of medicinal plant extracts will be presented as well as some biologically active compounds we isolated and characterized.

PB-39: Biological Aspects of Botanicals

Moringa oleifera Anticancer and Radio Sensitizing Agent on Cervical and Aero-digestive Cancer Cell Lines

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In this study, we evaluated the anticancer effect of the methanolic extract of *Moringa oleifera* leaves. Tested on HeLa and FaDu cancer cell lines, the leaf extract showed remarkable cytotoxic, antiproliferative and radio-sensitizing properties. Cell survival was significantly low in both cell lines when treated with the extract followed by irradiation at 2 Gy. Furthermore, a striking reduction (approximately 70–90%) in cell proliferation was observed when they were treated with the extract plus irradiation than with the extract alone. In addition, the radiosensitivity test carried out on these cervical and aerodigestive cancer lines showed a remarkable reduction in the repair of double-strand breaks after irradiation at a dose of 4 Gy. In addition, the analysis of the cell cycle showed an enrichment in G2/M indicating that the extract effectively blocks cell multiplication at the G2/M phase. Finally, GC-MS analysis of the spectrum of the total extract revealed the presence of numerous compound peaks. This suggests that the anticancer properties of *Moringa oleifera* could be attributed to bioactive compounds present in the methanolic extract of the plant's leaves. This is a unique study because no article has yet been published on the radio-sensitizing effect of *Moringa oleifera* extracts on the HeLa and FaDu lines. Thus, our study is the first of its kind to evaluate the cytotoxic, antiproliferative and radio-sensitizing properties of the methanolic extract of *Moringa oleifera* leaves. These results suggest that the leaves of *Moringa oleifera* collected in Senegal have anticancer activity, therefore a candidate drug for developing new anticancer drugs.

PB-40: Biological Aspects of Botanicals

An *In Vitro* Evaluation of Botanical Extracts on CES1 Catalytic Activity

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Carboxylesterase 1 (CES1) is the most abundant hepatic drug metabolizing enzyme and is capable of metabolizing endogenous and exogenous compounds including an array of medications such as cardiovascular, anticancer, and antiviral agents. CES1, a serine hydrolase, catalyzes the cleavage of amides, esters, and thioesters resulting in the activation of prodrugs (i.e., oseltamivir), and deactivation of active drugs (i.e., methylphenidate). Concerns have been raised over botanical-drug interactions (BDIs) and their potential to impair enzymatic function. Indeed, BDIs have been investigated with the cytochrome P450 superfamily of enzymes; however, CES1 BDIs have remained largely uninvestigated. This study aimed to assess the in vitro inhibitory potential of popular botanical extracts using an established CES1 incubation assay and LC-MS/MS analysis. Botanical extracts were generously provided by Finzelberg & Co. KG (Andernach, Germany) and the National Center for Natural Product Repository (University of Mississippi). Of the investigated extracts, ashwagandha, saw palmetto, St. John's wort, turmeric, and yohimbe all demonstrated significant impairment of CES1 metabolism. These extracts reduced CES1's catalytic activity by 50% or more, with turmeric having an astonishing 95% inhibition of CES1 at 10 µg/mL. Echinacea, ginseng, green tea, pitcher plant, and valerian also produced notable CES1 impairment by 20% or more. Turmeric demonstrated a lack of irreversible inhibition of CES1; however, it had a potent inhibitory effect on CES1 with an IC50 of 1.01 µg/mL. All other extracts that demonstrated a 50% inhibition of CES1, like ashwagandha, will be assessed for irreversible inhibition. Further in vitro work will explore the inhibitory potential of the individual constituents of the botanical extracts. These in vitro investigations are a necessary step in elucidating BDIs that may be clinically relevant and informing further in vitro, modeling, and clinical work.

PB-41: Biological Aspects of Botanicals

GC-MS Based Metabolites Profiling, *In-silico* Analysis and *In-vitro* Antiproliferative Activity of Bioactive Phytocompounds from the Ethanolic Extract of *Evolvulus alsinoides* L. Aerial Parts on MCF-7 Human Breast Cancer Cell Lines

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The study was designed to identify main bioactive phytocompounds and to evaluate the in-vitro antiproliferative effect of the ethanolic extract of Evolvulus alsinoides aerial parts against MCF-7 breast cancer cell lines using the MTT colorimetric assay. Flash chromatographic separation technique was used to isolate the main bioactive components followed by Gas Chromatography– Mass Spectrometry (GC–MS) analysis. A commercial mass spectral library was used for the depiction of individual phytocomponents. Fatty acids, phytosterols, alkaloids and flavonoids were identified from E. alsinoides. Bioassay analysis against breast cancer cell lines and molecular docking studies revealed the potential medicinal activities of active compounds like narcissidine, 9- methoxycamptothecin, dasycarpidanone from the plant. In addition, the binding energies were found to be -4.42, -4.71, -7.49 respectively, indicating their affinities towards Estrogen (PDB ID: 6CBZ) receptor alpha. The results showed a significant ($p < 0.01$) antiproliferative activity against MCF-7 cells breast cancer cell lines using the Micro Culture Tetrazolium (MTT) assay. From the present study it was concluded that the herbal drugs can be potentially used to control the proliferation rate of cancer cells. The present investigation may be quite useful as these medicinal plants are highly valued in traditional systems of medicine.

PB-42: Biological Aspects of Botanicals

Study on Chemical Constituents and Bio-activity of *Andromeda polifolia*

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The chemical constituents and antitumor activity ofthe methanol extract of *Andromeda polifolia* L. were investigated in this paper. *A. polifolia* belongs to *Andromeda* genus in Ericaceae family, which is mainly distributed in northern North America, northern Europe and northern Asia. It was first discovered in China in 2012, and was mainly growing on wetland, swamp and towers. At present, there are few studies and only nine compounds have been reported in this genus. Therefore, we decided to conduct systematic research on the chemical compositions in *A. polifolia*. To obtain a series of compounds with novel structure and significant activity, we will provide a theoretical basis for the subsequent pharmacodynamic substance base. In this study, the methnol extract of *A. polifolia* were separated and purified by normal phase silica gel and ODS column chromatography and Sephadex LH-20 gel column chromatography. Resulted in the discovery of 17 compounds and their chemical structures were elucidated by the physical and chemical properties, spectral data (1H-NMR and 13C-NMR), as well as by comparison of the spectral data with the literature. They were identified as quercetin (1)、quercetin-3-O-α-L-arabinopyranoside (2)、querce-tin-3-O-β-D-galactoside (3)、avicularin (4)、quercetin-3-O-α-L-(5 ″ -O-acetyl)-arabinofuranoside (5) 、 quercetin-3-O-α-L-arabinopyranosyl-(1→2)-β-D-galactopyranoside (6)、myricetin (7)、myricetin 3-O-ga-lactoside (8)、betmidin (9)、myricitrin (10)、syringin (11)、dehydrosyringin (12)、vanillic acid 4-O-β-D-glucoside (13)、lyoniside (14)、nudiposide (15)、(7R, 8S)-3',4,7,9-tetrahydroxy-3-methoxy-8-O-4'-neolignan-9'-O-α-L-rhamnopyra- noside (16)、(7R, 8R) -3', 4, 7, 9 - tetrahydroxy-3-methoxy-8-O-4'-neolignan-9'-O-α-L-rhamnopyranoside (17). To sum up, the chemical contituents of *A. polifolia* were enriched, which provided a theoretical basis for the development and utilization of *A. polifolia*.

PB-43: Biological Aspects of Botanicals

Screening Approach to find Natural Products that can be Utilized to Treat or Prevent Metabolic Syndrome

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Metabolic syndrome (MS) is a rising global health concern. MS is comprised of obesity, typeII diabetes, and hypertension which is also associated with a high degree of chronic inflammation. Nuclear receptors (NRs) are ligand activated transcription factors that regulate various metabolic pathways as well as inflammatory signaling. This study was carried out to screen a collection of medicinal plants for potential agonistic effects on selected NRs (LXR, PPARα, PPARγ, and NRF2) that are involved in the progression of metabolic syndrome using a series of high throughput reporter gene assays performed in hepatic cells. PPARα, PPARγ, and LXR play key roles in lipids, glucose, and energy homeostasis. NRF2/KEAP pathway is known to protect cells from oxidative stress and inflammation. The hydroethanolic extracts of a number of plants showed strong agonistic effects toward select NRs. Potential candidates were selected and further screened for their effects against obesity and diabetes based on established in vitro models that utilize differentiated adipocytes and muscle cells.

Out of about one hundred plant extracts screened, twenty extracts exhibited significant agonistic effects on multiple NRs indicating a modulation of multiple pathways. *Hydrastis canadensis* (root) and *Piper nigrum* (fruit) showed agonistic effects towards all four NRs. *Serenoa repens* (fruit) activated PPARα only while *Nigella sativa* (seed) activated PPARγ only. *Pueraria lobata* (root) was specific for LXR and *Withania somnifera* (leaf) was specific for NRF2. In the follow up assays, *Withania somnifera* (leaf) showed capability to reduce fat accumulation in adipocytes, and *Tribulus terrestris* (fruit) was effective in enhancing the glucose uptake in differentiated muscle cells. The study suggests the potential utility of selected medicinal plants in treating symptoms of MS. Further investigations are warranted in animal models of type II diabetes and obesity.

PB-44: Biological Aspects of Botanicals

In Vitro Antibacterial Activity of Crude Extracts of Some Fresh Water Cyanobacteria

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Antibiotics are increasingly becoming ineffective due to the astronomic rise of antimicrobial resistance (AMR), therefore, there is a need for the discovery of new antibiotics and antioxidants from natural products. This study aimed at exploiting the potential metabolite reservoir of cyanobacteria towards the development of novel antimicrobial compounds. Freshwater cyanobacteria, *Cylindrospermum alatosporum* NR125682.1 and *Loriellopsis cavenicola* NR117881.1, were utilized in this study and isolated from Vulindlela area, KwaZulu-Natal, SA. They were propagated on BG-11 and identified through 16S rDNA sequencing. The cyanobacteria biomass was sequentially extracted with hexane, dichloromethane (DCM) and ethanol, then screened for their antioxidant capacity using artificial and biological radicals, *in silico* molecular interactions against β-lactamase and *in vitro* antibacterial potential against some select gram-positive and gram-negative clinical isolates. The effect of the extracts on the bacterial membranes was also evaluated using the lactate-dehydrogenase assay, and the efflux-pump inhibitory potential was investigated by measuring the percentage of cytoplasmic accumulation of rhodamine. *In-vitro* beta-lactamase inhibitory potential was investigated along with synergistic potential when combined with erythromycin, their effect on DNA damage was also evaluated.

PB-45: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Antifatigue, Memory Enhancing and Blood Circulation Effects of Korean Red Ginseng

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Korean red ginseng (KRG) had been reported in many *in vivo* and clinical studies to exhibit various beneficial biological effects such as immunologic, antifatigue, antineoplastic, neuroprotective, hepatoprotective, antidiabetic, antistress, lowering blood pressure, memory enhancing, anti-inflammatory, antihyperlipidemic, improve blood circulation and antioxidative properties, etc. In this study, we share the antifatigue, memory enhancing and blood circulation effects of KRG.

KRG has been used in Asian countries to enhance vital energy since ancient times. Many *in vivo* and clinical studies have demonstrated that Korean red ginseng exhibited anti-fatigue activities (Brekhman, 1960; Chang, 1989). Li Zhang et.al 2019 evaluated the safety and antifatigue effect of KRG through a randomized, double-blind, and placebo-controlled clinical trial and found that KRG has a potent antifatigue effect disprove the common conception of “fireness” related to KRG.

KRG had been reported to be helpful for brain related diseases such as Alzheimer’s disease (AD), memory deficits in both *in vivo* and clinical studies. Young rats with hippocampal lesions displayed significant deficits in place learning tasks (PLT). Treatment with KRG significantly ameliorated place-navigation deficits in young rats with hippocampal lesions in the PLT. The results suggest that KRG ameliorates learning and memory deficits through effects on the central nervous system, partly through effects on the hippocampal formation (Nishijo et. al. 2004).
KRG platelet aggregation by regulating the synthesis of prostacyclin (PGI2), which has an antagonistic mechanism toward platelet aggregation, as well as thromboxane A2 (TXA2) and serotonin, which promote platelet aggregation, thus suppressing the generation of thrombi and improving blood circulation (So et al., 2018). Administration of KRG to healthy subjects significantly inhibited ADP-induced and collagen-induced platelet aggregation. KRG has a potential

PB-46: Molecular Biology Aspects of Botanicals

Advances in Biotechnology of Cannabis Mass Propagation

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Cannabis is a source of unique group of compounds called cannabinoids. So far, more than 550 constituents have been isolated from *Cannabis*, of which 125 are cannabinoids. Among phytocannabinoids, D9-tetrahydrocannabinol (D9-THC) is reported to be the most psychoactive compound with a wide spectrum of therapeutic potential in cannabis. On the other hand, cannabidiol (CBD), a non-psychoactive compound, is reported to contain very promising pharmacological activities as an antiepileptic agent, particularly for the treatment of intractable pediatric epilepsy. *Cannabis* is a dioecious and wind-pollinated species. A significant plant-to-plant variation in its cannabinoids profile and content is observed within a single *Cannabis* variety. For the production of a biomass product that is consistence in phytocannabinoids, sinsemilla (seedless female) plants are preferred. To obtain sinsemilla, male plants are removed from the cultivation site as soon as they appear, female plants with desirable profiles are screened and selected as mother plants for the future. Selected mother plants are then multiplied by using vegetative propagation or by using biotechnological techniques including micropropagation. In this presentation, we focus on our efforts on conservation and mass propagation of elite *Cannabis* plants using the biotechnological tools.

PB-47: Molecular Biology Aspects of Botanicals

Cultivation of Magic Mushrooms for Psychoactives

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Psychedelic fungi have experienced a surge in interest in recent years due to the therapeutic potential based on the fungal secondary metabolite, psilocybin. The psilocybin mushrooms also referred to as "magic mushrooms", have the potential to treat addiction, depression, anxiety, and other mental health concerns. This has escalated the demand for the natural products derived from the mushrooms. In the United States, psilocybin and psilocin are listed as Schedule 1 Drugs. There are hundreds of species belonging to at least 7 genera of psilocybin producing fungi of which *Psilocybe cubensis* is the most well-known *Psilocybe* species. With the growing interest in the medicinal benefits of psilocybin for treating mental health problems, an attempt has been made in our laboratory to cultivate different strains of *P. cubensis* which include B+, Hillbilly, and Golden Halo. The different stages of growth involved a selection of suitable commercial spores, development of spawn, substrate preparation, optimizing different growth conditions for fruiting and harvesting. Biomass produced for the three strains will be used for further research activities at NCNPR. All the growing activities were performed under the DEA (License # 18185/8.2) compliance.

PB-48: Agronomical Aspects of Botanicals

Effect of Magnesium on Cannabis Biomass Yield and Cannabinoids Content: Evaluating Different Application Rates and Methods

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Magnesium deficiency (MGD) is a severe problem in plants. Magnesium (Mg) is one of the important nutrients involved in many enzymatic activities and rarely studied in cannabis plats. In this study, the effect of application of different concentrations (2 mL/L of 'Advanced Hemp Factor X' equivalent to 10 mg/L of Mg and 4mL/L of 'Advanced Hemp Factor X' equivalent to 20 mg/L of Mg) and methods of application (drench vs. foliage application) of Magnesium was studied on useable biomass yield and cannabinoids content on two chemotypes (high CBD and high CBG) of *Cannabis sativa* L. Plants grown through feminized seeds, from the beginning, were divided into two groups, control (no treatment) and treated with different concentrations of Mg (10 mg/L of Mg drench, 20 mg/L of Mg drench and 3.75 mg/L of Mg foliage spray). Plants of both groups were grown side by side in an identical environmental condition in a polytunnel and, were watered and fertilized normally. Application of different concentrations of Mg was started from the first week of flowering until maturity. At maturity, both groups of plants were harvested and processed for usable dry biomass. Plants of both groups were compared for biomass production per plant and cannabinoids content.

Our results show that among all the treatments (drench and foliage application), in 'CBD chemotype' plants, maximum increase in cannabis biomass/plant was achieved by the application of 10 mg L-1 Mg whereas, it was achieved highest by the application of 10 mg/L Mg in 'CBG chemotypes'. On other hand, among all the treatments, maximum increase in CBD content/plant (in 'CBD chemotype' plants) and CBG content/plant (in 'CBG chemotype' plants) was observed by the application of 10 mg/L Mg drench as compared to those as 'control' plants.

PB-49: Technological Aspects of Botanicals

Utilization of GlyCORE Imaging Core in Advance Plant and Animal Biological Research

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The Glycoscience Center of Research Excellence (GlyCORE) is a Phase I Center of Biomedical Research Excellence sponsored by the NIH. It was established in 2020 at the School of Pharmacy, University of Mississippi. GlyCORE comprises three core facilities: Analytical and Biophysical Chemistry Core, Computational Chemistry and Bioinformatics Core, and The Imaging Core. The GlyCORE Imaging Core offers a range of services such as live cell imaging, FRET, FLIP and FRAP photobleaching measurements, immuno- and lectin staining, SEM coupled with EDS, and other imaging and image processing services. GlyCORE houses state-of-the-art instruments such as Stereomicroscopy, Epi-fluorescent and Bright Field Microscopy, Imaging Flow Cytometer, and Field-Emission Scanning Electron Microscope (FESEM) with multiple detectors: Energy Dispersive X-Ray Spectrometer (EDS). Confocal Laser Scanning Microscopy (CLSM). The Core's Leica SP8 CLSM has powerful multichannel capabilities with a resonant scanner (faster scanning) and HyD PMTs (super sensitive). It has an excitation of 405 nm, 442 nm, and a white light laser (WLL). The white light laser has continuous excitation lines from 470 nm up to 670 nm, and is pulsatile with a frequency of 80 Hz, allowing excitation to be tunable in 1 nm increments up to 8 laser lines simultaneously, such that almost any visible dye or fluorescent protein can be excited. This scope is highly sensitive, multispectral, and fast, enabling many advanced confocal techniques, such as FRET and FLIM. The JSM 7200FLV FESEM is another cutting-edge instrument found in the GlyCORE Imaging Core. The FESEM is highly versatile; it offers a new level of expanded performance using an in-lens Schottky Field emission gun. Advanced nanostructure analysis and determining the sample's elemental composition through X-ray spectroscopy (EDX) is possible. The GlyCORE Imaging Core specializes in supporting glycoscience research and advanced botanical research.

PB-50: Biological Aspects of Botanicals

Korean Red Ginseng Alleviates Choroidal Neovascularization and Fibrosis by Regulating Crystallin Alpha B Function

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Age-related macular degeneration (AMD) is a disease that leads to vision impairment as a result of the deterioration of the macula's function, which is located in the central part of the retina. It is a major cause of vision loss in old age. The current treatment for AMD not only involves the inconvenience of intravitreal injection of anti-vascular endothelial growth factor (VEGF), but also has a 45% risk of fibrosis within three years. Korean Red Ginseng (KRG, *Panax ginseng* C.A. Meyer) is recognized for its protective effects against fibrosis in various diseases. In this study, we investigated the anti-fibrotic and anti-neovascularization effects of Korean Red Ginseng water extract (RGWE) and ginseng total saponin (GTS) in both *in vivo* and *in vitro* AMD models. Additionally, the study measures the binding affinity of ginsenosides and crystallin alpha B (Cryab), a small heat shock protein to understand the mechanism underlying KRG effects. In ARPE-19 cells, RGWE, GTS, and ginsenosides decreased vascular endothelial growth factor (VEGF) and α-smooth muscle actin (αSMA). Furthermore, we showed that RGWE and GTS reduced CNV lesion area and VEGF and αSMA expression in laser-exposed mouse eyes. Additionally, we showed that ginsenosides interact directly with Cryab, as demonstrated by the pull-down assay. In conclusion, these results suggest that KRG may play a role in preventing the deterioration of macular degeneration through the regulatory effects of ginsenosides on Cryab function.

PB-51: Toxicological Aspects of Botanicals

Predicting Human Liver Injury and Botanical-drug Interactions with 3D Liver Microtissues and High-throughput Transcriptomics

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Human liver injury from botanical products and food additives continues to be a leading concern around the world, which is complicated by the vast array of varied compositions of commercially available products and related claims for health benefits. In order to address these challenges, an international, cross-sector consortium was formed with the goal of identifying useful test systems to study these complex mixtures being intentionally exposed to humans with little-to-no information on their potential for adverse health effects. In recent years, advances with physiologically relevant culture models and assay platforms revealed important opportunities to extend these systems to transform methods for evaluating natural products to predict human toxicity and drug interactions. In this study, we describe our use of patient-derived 3D spheroid cultures of primary human hepatocytes and high throughput transcriptomics to evaluate botanical safety with 13 botanical mixtures alongside 9 reference drugs with established clinical outcomes. Our work has demonstrated the translational utility of this integrated omics platform, in combination with benchmark concentration modeling, to predict human liver injury, estimate the potencies botanical-drug interactions, identify mechanistic signatures of biological response similarity across botanical extracts, and accurately estimate the potencies for in vivo liver weight increases. Ultimately, these data will be integrated with other toxicity endpoints to identify efficient methods for rapidly assessing the safety of natural products.

PB-52: Toxicological Aspects of Botanicals

Inter-strain Variability in Response to a Single Administration of Cannabidiol-rich Cannabis Extract in Mice

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Cannabidiol (CBD) has gained widespread popularity; however, its pharmacological and toxicological profiles in the context of human genetic diversity remain largely unexplored. Here, we investigated the variability in metabolism and toxicity of CBD-rich cannabis extract (CRCE) in genetically diverse mouse models: B6C3F1, C57BL6J, and NZO/HlLtJ strains. Mice received a single dose of CRCE containing 58.9% CBD at dosages of 0, 246, 738, and 2,460 mg/kg of CBD. All strains showed minor weight loss at 24 h post dosing. No significant alterations were detected in the organ-to-body weight ratios, nor were there appreciable histomorphological changes in these organs. However, plasma bilirubin levels increased markedly in all strains at the highest CBD dose, with C57BL6/J mice showing a significant increase at the 738 mg/kg dose. Elevations in liver enzymes ALT and AST were particularly pronounced in NZO/HlLtJ mice at the 738 mg/kg dose. C57BL6/J mice displayed significant increases in ALT levels at the two higher concentrations. While B6C3F1 and NZO/HlLtJ mice had negligible plasma CBD levels at 738 mg/kg, C57BL6J mice exhibited levels exceeding 7,000 ng/mL. At 2,460 mg/kg, high CBD concentrations were found in B6C3F1 and C57BL6J mice, but markedly lower levels were seen in NZO/HlLtJ mice. These patterns were mirrored in the plasma concentrations of CBD metabolites. Gene expression profiling showed a significant increase in Cyp2b10 across all strains, but varying responses in Cyp1a1 expression, indicating strain specific CYP dysregulation. Genetically similar and diverse mice exhibited differential pharmacological and toxicological responses to CRCE as evidenced by significant variations in CBD and its metabolites' circulation levels, metabolism, and liver injury biomarkers. Our results suggest a high potential for inter-individual variability in the pharmacology and toxicology of CBD in humans, underscoring the importance of considering genetic diversity in future research.

PB-53: Toxicological Aspects of Botanicals

An Evaluation of the Interaction Risk between Herbal and Pharmaceutical Medicines Used Concurrently for Disease Management in Blantyre, Malawi

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Herbal medicines have been used globally for centuries for myriad health benefits. These ubiquitous and readily available natural products are often used concurrently with pharmaceutical drugs, which can lead to altered drug efficacy or increased toxicity. Therefore, understanding potential herb-drug interactions (HDIs) is imperative to improve patient safety. Previous research in this field examined interactions between certain herbal medicines and antiretrovirals. The evolving global disease scenario and growing reliance on herbal medicines for non-communicable diseases necessitated a broader investigation into HDIs, particularly within the context of the healthcare system in Malawi. The objective of this study was to investigate the concurrent use of herbal and pharmaceutical medicines as treatment for diabetes and hypertension in Blantyre, Malawi, where this practice was identified as widespread. Through patient-reported data and literature-based case studies, results highlight the potential for HDIs, calling attention to the urgent need for more research and data collection, particularly within Malawi and other low- and middle-income countries. Examples of potential HDIs include those involving the popular herbal medicine moringa and anti-diabetes drug metformin. Results from this study could help inform the documentation of herbal medicine use in healthcare records and increase education for healthcare providers and patients about potential safety and efficacy concerns regarding HDIs. This survey and analysis could be adapted and expanded to other African regions and low- and middle-income countries. This approach will foster a comprehensive understanding of HDIs, ultimately contributing to safer and more effective integrated healthcare practices worldwide.

PB-54: Toxicological Aspects of Botanicals

Investigating the Pharmacodynamic Interactions of Açaí Extracts and Anticancer Drugs

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Açaí, *Euterpe oleracea* Mart., is a fruit native to Central and South America that has many bioactive compounds that contribute to many beneficial health effects in humans. Açaí is on the list of the top 40 botanicals currently used in the US. To study the pharmacodynamic interactions between açaí botanical dietary supplements (BDS) and anticancer agents, açaí extracts were tested in combination with methotrexate and tamoxifen to determine synergism, antagonism, or additive effect from concomitant use. Açaí fruit powder and two botanical dietary supplement capsule formulations were extracted using an aqueous, ethanolic, methanolic, and acidic methanolic solution, respectively. Preliminary dose-response experiments on three cell lines, MCF-7, MDA-MB-231, and MCF-10A were completed using Tamoxifen, Methotrexate, and seven standardized açaí extracts. These extracts, based on cyanidin-3-glucoside (C3G) content, were tested against the three cell lines in a range of 10 pg/mL to 1000 ng/mL which includes the human equivalent dose (HED) of 2.321 ng/mL of C3G. All the açaí extracts caused slight toxicity in the normal breast cell line, MCF-10A, at high concentrations (1000 ng/mL C3G). There was no toxicity from the extracts in the two breast cancer cell lines. A combinatorial screening was conducted across all three cell lines by testing a range of the anticancer drug and a HED concentration of the respective extract. The combinations with the most statistically significant ($p < 0.05$) differences in each comparative dose were chosen for a full combinatorial assay which was performed using a 7x7 combination matrix of anticancer drug and selected açaí extract. The data obtained was analyzed via SynergyFinder+. All combinations exhibited an additive or synergistic effect with one or both anticancer drugs on all three cell lines. This study aims to highlight the pharmacodynamic interactions of açaí extracts and anticancer drugs to determine safety and efficacy of concomitant use.

PB-55: Toxicological Aspects of Botanicals

Case Studies Comparing *In vitro* and *In vivo* Toxicological Data to Inform Botanical Safety Assessment

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Evaluation of botanical ingredient safety has traditionally relied upon either a history of safe use or toxicological data from animal studies. Challenges in incorporating data from New Approach Methods (NAMs; i.e., *in silico*, *in vitro*, and alternative animal tools) in botanical safety assessments include addressing complex botanical chemistries; accounting for absorption, distribution, metabolism, and excretion; and distinguishing bioactivity from adversity in sensitive systems. To build confidence in the application of NAMs, case studies are needed to compare traditional human and animal data to NAM based data. Orthogonal datasets containing *in vivo* rodent data and *in vitro* data will be discussed for botanicals including black cohosh (*Actaea acemose*), *Ginkgo biloba*, ephedra (*Ephedra sinica*), and wormwood (*Artemisia absinthium*). In each case, botanical ingredients were evaluated using *in vitro* studies that mimic the biological target identified in *in vivo* toxicological studies. For example, *Ginkgo biloba* extract was found to be hepatotoxic and carcinogenic in the liver of mice and rats with mechanistic studies implicating constitutive androstane receptor (CAR) and pregnane X receptor (PXR) pathways. A human-cell–based liver model measuring metabolizing enzymes reflective of CAR and PXR activity was then used to evaluate multiple *Ginkgo biloba* extracts. Correlation of findings in human cell-based systems confirmed that the mechanism of action was conserved, although species differences in receptor activity indicated that similar outcomes would not be anticipated in humans. Additional in vivo targets in case studies include cardiotoxicity (ephedra), genotoxicity (black cohosh), and neurobehavioral effects (wormwood). Careful evaluation from case studies will be useful in assessing the utility of NAM assays for botanical safety and identifying biological targets that require additional methods development.

PB-56: Toxicological Aspects of Botanicals

Nature's Weaponry: A Study on the Molluscicidal Potential of Saponin-rich Root Extract of Aleppo Milk-vetch collected from the Jordan Rift Valley

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The digenetic trematode *Bolbophorus damnificus* (formerly *B. confusus*) has been associated with high catfish mortality and poor economic returns from catfish ponds in Mississippi, Arkansas and Louisiana. These qualitative and quantitative losses exceeded $1,236/ha in moderate to severely affected ponds (>34% of the fish infected). Ramshorn and Biomphlaria are the intermediate hosts of these trematodes in the catfish pond. One of the strategies is to control the intermediate host using copper sulfate ($CuSO_4$), but, being non-selective, it is equally toxic to fish and to the environment as well. Active alternatives may be identified from the GRAS list. As part of collaborative project to search for selective and eco-friendly solutions, we tested the root saponins from *Astragalus aleppicus*. Saponins are one of the groups that are used to control snails, earthworms, etc. In basic screening, the sample induced 100% mortality in Ramshorn (3 d exposure) and 53% mortality in Biomphlaria (1 d exposure) at 100ppm.

PB-57: *Regulatory* Aspects of Botanicals

Empowering the Healthcare Ecosystem with Budsinfo™ and Cerium™ for Comprehensive Data Collection

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This research project addresses a critical gap in healthcare practitioner (HCP) knowledge, attitudes, and documentation concerning adverse events associated with non-FDA approved products. National pharmacovigilance guidelines predominantly focus on FDA-approved substances, leaving non-FDA approved products devoid of proper AE reporting guidance for HCPs. This deficiency is amplified by existing challenges HCPs face in reporting AEs across various approved drugs and consumer products. AEs for non-FDA approved products remains notoriously underreported in the US and throughout the world. This issue is especially concerning regarding cannabis & hemp-derived stuffs, amid their widespread market presence. Our innovative proposal empowers patients and HCPs to initiate AE reporting incidents, overcoming barriers, enhancing data collection, and fostering a more comprehensive understanding of adverse events related to non-FDA approved products in the healthcare ecosystem.

We conducted a pilot study featuring a K&A survey and an education intervention for HCPs. The intervention, Cerium education, includes modules on essential topics like pharmacology, dosing, safety, drug interactions, data collection, and AE reporting. It offers interactive features such as education blogs and one-on-one discussions to address specific concerns. In response to these AE reporting limitations, we also developed Budsinfo, a platform for consumers to report adverse events linked to non-FDA approved products, for example, cannabis and hemp-derived products. Budsinfo and Cerium together provide a comprehensive solution bridging critical gaps in adverse event reporting, enabling data-driven decision-making for regulatory agencies and empowering healthcare professionals and the public. Budsinfo streamlines adverse event reporting, creating a user-friendly environment, while Cerium equips healthcare professionals with knowledge and skills to contribute to data collection.

PB-58: Regulatory Aspects of Botanicals

Budsinfo: A User-Friendly Platform for Reporting the Effects of Cannabis and Cannabis-Derived (hemp) Products

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A significant gap exists in systematic data collection for cannabis and cannabis-derived (hemp) products (CCDP) limiting the public's ability to assess their risks and benefits. Products like tetrahydrocannabinol isomers (e.g., D8-THC) derived from hemp are increasingly available in stores and boutiques. Despite their accessibility, the assumption of safety often differs from the reality of potential risks. A publication using data from the Food and Drug Association adverse event system (FAERS) highlighted potential health concerns associated with D8-THC.1 In response, an adverse event reporting tool (AERT) was developed to better inform individuals about the risks associated with CCDP products. This anonymous questionnaire, accessible through a QR code or website link, was distributed at conferences, online webinars, registry newsletters, music festivals, and medical offices. Presented here are preliminary data from the pilot of the CCDP tool on the Budsinfo platform. Currently there are over 350 scans. Overall, 51 reports have been submitted to date. Of the respondents who experienced adverse effects, most were between 50 and 65 years old (32%) and female (66%). Regarding their experiences, 12% reported "getting too high"; 56% obtained their product from legal dispensaries. Most adverse effects were of moderate intensity, lasting 1 to 6 hours, and resolved with self-care at home. The most common reactions were dizziness and anxiety. Inhalation was the most common administration method. These preliminary findings from the CCDP AERT indicate that consumers are willing to share their experiences using regulated and unregulated products. This tool provides an important avenue for individuals to report and access information about the effects of CCDP. The tool can be accessed at www.budsinfo.com. Further analysis and expansion of this tool could significantly contribute to our understanding of the safety profile of these products.

PB-59: Regulatory Aspects of Botanicals

Selling with Science – An Epidemiological Assessment of Herbal Supplementation

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What is the evidence to support the use of herbal supplements and how does that impact the sales of certain products? For example, the use of elderberry syrup to shorten the duration or lessen symptoms of a respiratory infection. A recent article published in HerbalGram reports the sales of herbal supplementation in 2022 as $12 billion. The aim of this study is to understand the strength of the evidence for top selling products. Using the published HerbalGram sales data as a proxy to exposure, we estimated the cost of products using Amazon marketplace, total volume / purchase and computed the cost per dose, and cost for a year supply. This allowed an estimate of per year exposure values. We performed a PubMed and CFSAN Adverse Event Reporting System (CAERS) search using the following terms: psyllium, elderberry, turmeric, apple cider vinegar, ashwagandha, cannabidiol, and cranberry. These top selling herbal products in 2022 contributed to over $1.0 billion in sales. Product recall, and label claim searches were also performed. The data was used to determine potential factors associated with driving or affecting sales. The table shows that apple cider vinegar had the highest ratio of publications the year prior to record sales being achieved. The overall proportion of adverse event reports by product compared to prior years was highest for cannabidiol followed by turmeric. A few notable publications were published in 2021. 1-4 These data may be prone to several biases. Cognitive biases may be driving sales. Notoriety bias, a type of selection bias, may be affecting the number of events reported in CAERS. There are a number of limitations: Social media could be an avenue that drives sales and product advertisements with false claims. In summary, consumers should be aware of herbal supplement product recalls and evidence supporting any claims, and ultimately be aware they are consuming many products, which have an undisclosed level of risk.

PC-1: Chemistry Aspects of Botanicals

O-Aroyl-β-aminopropioamidoximes; Synthesis and Biological Evaluations

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O-Aroyl-β-aminopro-pioamidoxime compounds are insufficiently studied despite their importance in drug research and being potential pharmacophores and building blocks in medicinal chemistry. The synthesis has been conducted according to Kayukova L. et al. (ISRN Organic Chemistry, 2012, pp.945893-945893). Several leads have shown promising *in vitro* antitubercular activity with MIC values of 1–100 µg/mL, which inspired further evaluations. Several analogs have been synthesized given the previously addressed structure-activity relationship (SAR), and the chemical structures of the newly synthesized compounds have been established via NMR and LC/MS analysis. Moreover, amidoximes functionality suggests potential herbicidal activity, as they are known for their coordination abilities with metal ions and form metal complexes that can disrupt plant enzyme functions, leading to growth inhibition. The synthesized analogs are undergoing in-depth evaluation for their antimicrobial and herbicidal activities.

PC-2: Chemistry Aspects of Botanicals

Development of PBD Small Molecules for the Treatment of Proinflammatory Pain States

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Chronic pain affects more than 116 million adults, with a cost of $636 billion annually in the United States. However, currently, available pharmacotherapy can control pain in only a fraction of patients. This clinical reality drives an urgent need to develop safe and effective analgesics. One approach is to identify novel analgesic drug targets. Agonists of cannabinoid receptor 1 (CB1) are non-optimal given their psychoactive effects; however, CB2 agonists are devoid of these liabilities and can sharply reduce inflammatory and neuropathic pain in rodents. Using structure-based rational drug design, we have synthesized CB2-selective pyrrolo[2,1-c][1,4]benzodiazepine (PBD) analogs with outstanding oral bioavailability, biodistribution to the central nervous system and good efficacy in a rodent model.

A strong preliminary data package has been catalyzed by NIGMS COBRE funding and has revealed at least one lead compound (4k) that is stable (up to 240 min at physiological pH), has a positive pharmacokinetic profile (t1/2 in brain ~23 h following oral administration), is efficacious against acute visceral pain (equipotent to oxycodone in an acetic acid writhing assay). Our lead compounds have been evaluated at the NIMH Psychoactive Drug Screening Program (PDSP) against a battery of drug targets, and the lead compounds (4k) do not show appreciable binding affinity on any of these targets. Further, our in vivo data in the conditioned-place preference paradigm suggests the absence of rewarding effects. PBD analogs could be transformative for the treatment of visceral pain and other pro-inflammatory pain states.

PC-3: Chemistry Aspects of Botanicals

Resveratrol and Piperine Loaded Cubosomal Drug Delivery: A Novel Approach for the Management of Melanoma

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Melanoma is one of the most aggressive types of skin cancer, with a high incidence rate and mortality throughout the world. The present study aimed to develop, characterize, and evaluate the resveratrol and piperine-loaded cubosomes (RPC) for targeting melanoma. A novel, self-assembled RPC nanoformulation was developed using glycerol monooleate and Pluronic F-127 by homogenization technique. Optimization of RPC using 2-factor 3-level factorial design indicated cubic-shaped structures, having a mean particle size and zeta potential of 110 ± 3.30 nm and -34.3 ± 1.04 mV, respectively. The entrapment efficiency of resveratrol (RV) and piperine (PI) entrapped inside the RPC was 88.12 ± 1.54 and 85.17 ± 0.25%, respectively. *In vitro* drug release of optimized RPC demonstrated biphasic drug release with diffusion-controlled release of resveratrol (RV; 92.7 ± 2.08%) and piperine (PI; 72.48 ± 3.36%). Optimized RPC was further formulated into cubosomal gel (RPC-Gel) by using carbopol (1.5% w/v), and the gel was evaluated for ex-vivo permeation and deposition, which shows better drug permeation and deposition in mice skin layers in comparison to resveratrol and piperine gel (RP-Gel). Biocompatibility of optimized RPC was observed towards L929 (mouse fibroblast), with better anticancer activity against A375 (human melanoma) cell lines compared to pure RV and PI. A stability study showed the ability of RPC to maintain stability at room temperature. The composition of RPC-Gel has been proven non-irritant to the skin of mice. An in vivo local bioavailability study depicted the potential of RPC-Gel for skin localization compared to resveratrol and piperine gel (RP-Gel). Topical application of RPC-Gel into melanoma-bearing BALB/c mice for up to six weeks resulted in tumor regression, thereby proposing the RPC-Gel as a promising drug delivery system through transdermal application for melanoma treatment.

PC-4: Chemistry Aspects of Botanicals

Development and Evaluation of a Novel Quercetin-loaded Nanostructured Liquid Crystalline Dispersion (NLCD) for Targeting Skin Cancer.

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Melanoma is the most aggressive and lethal kind of skin cancer, with an increased rate of incidence and around 75% of all skin cancer-related deaths every year. Quercetin, a naturally occurring glycoside, exerts its potential activity in melanoma skin cancer. Owing to its poor pharmacokinetic properties, a novel topical nano-formulation is required, which has more potential to cross the skin's stratum corneum barrier. A novel nanostructured liquid crystalline dispersion (NLCD) has been used in the current study to improve the applicability of quercetin. Quercetin-loaded NLCD was prepared using a top-down approach followed by high-speed homogenization and probe sonication technique. The optimized NLCD (QNLCD5) contains cubic-shaped nanoparticles with a particle size and zeta potential of 123.6 nm and -36.7 mV, respectively. The entrapment efficiency of quercetin entrapped inside the NLCD was 95.06%. Quercetin was estimated in developed QNLCD using the developed RP-HPLC technique. *In vitro* drug release of optimized QNLCD5 demonstrated biphasic drug release with diffusion-controlled release of quercetin 71.63%. Cell compatibility studies of free quercetin and QNLCD5 were evaluated against a mouse fibroblast cell line (L929), which showed no significant difference in cell viability, which confirms its cytocompatibility. *In vitro* cytotoxicity studies in the human melanoma cell line (A375) demonstrated an improved anticancer activity of QNLCD5 in comparison with free quercetin. The results of an *in vitro* anti-melanoma study demonstrated QNLCD to be a promising drug delivery system for melanoma treatment and could be a promising topical nanocarrier for melanoma treatment.

PC-5: Chemistry Aspects of Botanicals

Semi-synthetic Modification of Labdane Diterpenoid Andrographolide Isolated from *Andrographis paniculata* for PPAR-γ Agonism

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Owing to the important pharmacological activities and structural flexibility, andrographolide suffers serious limitations of water solubility and low bioavailability; therefore, an attempt has been made to synthesize novel derivatives of the natural product by incorporation of the spiro-isoxazoline ring via 1,3 dipolar cycloaddition to give candidates with better lipophilicity and bioavailability for the treatment of diabetes mellitus as PPAR-γ agonists. In this work, novel isoxazolyl analogs of natural product andrographolide have been synthesized, out of which four compounds, 5b, 5c, 5d, and 5e, exhibited significant *in vivo* blood-glucose-lowering comparable to standard drug Rosiglitazone. These compounds also exhibited significant *in vitro* PPAR-γ transactivation activity. Compounds 5b, 5c, 5d, and 5e recovered the activity of serum AST, ALT, and ALP and did not cause any damage to the liver. Compounds 5e significantly affect PPAR-γ gene expression as it increases the PPAR-γ expression by 2.0-fold, compared to standard drugs Rosiglitazone (1.0-fold) and Pioglitazone (1.5-fold). Moreover, the semi-synthetic analogs displayed better lipophilicity than andrographolide, as observed from octanol-partition coefficient data. It can be concluded that the semi-synthetic analogs 5b, 5c, 5d, and 5e may be considered potential candidates for developing new antidiabetic agents.

PC-6: Chemistry Aspects of Botanicals

Harnessing Nature's Defense: Mediterranean Flora Bioprospecting to Search for Potential Antimalarial Compounds in Plant Extracts

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Malaria is a parasitic disease that represents a major public health problem worldwide, particularly in developing and African countries. According to the World Health Organization (WHO) in 2022, there were an estimated 249 million malaria cases and 608 thousand death cases in 85 countries. *Plasmodium* is the parasite genus responsible for malarial infection involving five *Plasmodium* species. The most significant are *P. vivax* and *P. falciparum*, where the latter is the most clinically relevant. In this study we have screened a selected library of fifteen plant extracts against two clones of drug-resistant strains of *P. falciparum* parasite D-6 and W-2. The in vitro test is done in parasitized whole blood using the parasite lactate dehydrogenase assay. The polar ethanolic extract of *Inula viscosa*, *Salvia dominica*, and *Bellevalia zohari* showed antiprotozoal activity. These extracts showed more activity against W-2 strain. The IC50 against W-2 strain were 14, 15, and 35 µg/mL respectively, compared to 30, 21, 40 µg/mL against D-6 strain. *Bellevalia zohari* and *Salvia dominica* are reported here for the first time. Further investigation of fractions and unique compounds from *Bellevalia zohari* will be presented.

PC-7: Chemistry Aspects of Botanicals

Deciphering Triglyceride Complexity in Wild Eastern Mediterranean Echium Seed Oil via Application of Paterno-Büchi Modulated Lipidomics Profiling

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There is a growing emphasis on unraveling the intricacies of the fabric of triglycerides (TG) found in oils, specifically, those rich in ω-3 polyunsaturated fatty acids (PUFA). While conventional methods such as gas chromatography are capable of detecting fatty acid classes, it is inadequate to specify the double bond position in these fatty acids. Echium oil, rich in α-linolenic acid (ALA, 18:3ω-3) and stearidonic acid (SDA, 18:4ω-3), surpasses many other plant-resourced seed oils due to their anti-inflammatory and cardio-protective effects. In this study, a pseudo-targeted approach was implemented to profile the fatty acid and triglycerides found into two echium species *Echium glomeratum* and *Echium judaeum*. The TG characterization is feasible with high resolution mass coupled to high performance liquid chromatography (HRMS-HPLC). Additionally, the positioning of double bonds in these fatty acids can be accessed via Paterno-Büchi acetyl pyridine derivatization of TG. This study shows that *Echium glomeratum* and *Echium judaeum* have different fatty acid and triglycerides (TG) profiles, with (ω-3: ω-6) ratio being 3.5 and 1.5 respectively, corresponding to higher ALA (45.50%) and SDA (12.59%) in *E. glomeratum*. TGs comprise 93% of lipids in echium oil. The most abundant TGs (50-60 carbons) were profiled in both species with comprehensive and simultaneous assignment of the double bond structure. The superior *E. glomeratum* oil profile, was further assayed for its cytotoxicity, cell migration assay, and antioxidant activity.

PC-8: Chemistry Aspects of Botanicals

Molecular and Structural Insights of Boswellic Acid Analogues as Potent Anti-diabetic, Antioxidant, Anti-hyperlipidemic and α-Glucosidase Inhibitors

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Boswellic acid and its derivatives are known for their potential anticancer, anti-inflammatory and α-glucosidase inhibitory activities. Olibanum has been reported for the presence of *β*-Boswellic acid (*β*-BA) and 11-keto-*β*-boswellic acid (*β*-KBA). Here in this study chemical composition of oleo gum resin was investigated by 1D and 2D NMR techniques viz., 1H, 13C, DEPT, HSQC, HMBC, and COSY, and NEOSY, ESI-MS. Moreover, the isolated chemical components were evaluated for their anti-diabetic, *in silico* pharmacokinetic and α-glucosidase inhibition activities. Chemical analysis revealed the presence of one new triterpene, called 3α-hydroxyurs-5:19-diene (1) with 12 reported components such as 8 triterpenoids (2–9), 2 diterpenoids (10 and 11) and 2 straight chain alkanes (12 and 13). Likewise, 10 reported components were isolated from *B. sacra.* Moreover, *β*-BA and *β*-KBA were isolated from gum resin of *B. sacra.* Our findings showed that *β*-BA and *β*-KBA demonstrated anti-diabetic, antioxidant, and anti-hyperlipidemic effects recommending these components as potent candidates for diabetes. Moreover, other isolated components such as 1, 3, 10, 11, 15, and 17–19 showed significant effects against α-glucosidase. It is obvious from our overall results that these chemical components had an efficient therapeutic effect on the blood glucose level and blood biochemistry.

PC-9: Chemistry Aspects of Botanicals

Fatimanols Y and Z: Two Neo-clerodane Diterpenoids from *Teucrium yemense*

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Teucrium L. (Lamiaceae), commonly known as germander, is a cosmopolitan genus of about 300 species mainly distributed in South and Central America, Southern Asia, and the Middle East but predominantly prevalent in the Mediterranean basin. The *Teucrium* genus is a rich source of diterpenoids, particularly neo-clerodanes which are used as chemotaxonomic markers for *Teucrium* species. *Teucrium* species have been used traditionally as diuretic, diaphoretic, antipyretic, and antiseptic agents for centuries in many parts of the world. *Teucrium yemense* (Defl.), a medicinal plant, grows in Yemen and Saudi Arabia and is also referred to as Reehal Fatima. The plant has a long history of use in these regions for the treatment of diabetes, rheumatism, and renal conditions. Phytochemical investigation of the aerial parts of *T. yemense* yielded two previously undescribed neo-clerodane diterpenoids, namely fatimanols Y and Z (1 and 2) along with the known teulepicephin, 8-acetylharpagide and teucardosid. Structure elucidation was accomplished from their 1D and 2D NMR and MS characteristics as well as by comparing them to related reported compounds. The new molecules expand understanding of secondary metabolites of this genus.

PC-10: Chemistry Aspects of Botanicals

New Bisprenylated Benzoic Acids from Yerba Santa (*Eriodictyon californicum*)

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Eriodictyon californicum, commonly known as Yerba Santa, is a plant native to western North America. Its leaves have traditionally been used to treat asthma, upper respiratory infections, allergic rhinitis, and other disorders by indigenous people. The diverse array of medicinal properties, including anti-inflammation, antioxidation, bronchodilation, immune modulation, and wound healing, makes it a subject of interest in herbal medicine and scientific research. The plant is rich in bioactive compounds such as flavanones, flavones, and phenolic acids, contributing to its therapeutic potential. To explore the healthcare function and to fully utilize this plant, a chemical investigation was carried out, and 22 bisprenylated benzoic acids were isolated and identified from the plant. Among them, 17 were new compounds that had not been previously reported in the literature.

PC-11: Chemistry Aspects of Botanicals

Alkamides from the Roots of *Echinacea angustifolia* and Their Anti-inflammatory Effects Compared to Alkamides from *E. purpurea*, Evidence of Synergism

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Echinacea products are among the most commonly used herbal supplements in the U.S. They are medicinally useful mainly for their immunostimulatory and anti-inflammatory effects. The anti-inflammatory effects of Echinacea have been attributed to their content of alkamides, while the alkamides contribute in part, beside other constituents to the immunostimulation. The medicinally used *Echinacea* species include *E. purpurea*, *E. angustifolia*, and E. *pallida*.

In a previous study, we isolated ten alkamides including a novel lkamidesated lkamides from *E. purpurea*. Herein, the isolation methodology and structural determination of five alkamides (1-5), from a commercial sample of *E. angustifolia* roots, are presented. Of these are two previously unreported alkamides. The isolation was carried out employing multiple chromatographic techniques. The isolates were identified based on 1D and 2D NMR, HRESIMS, and FTIR spectral data. In addition, the anti-inflammatory effect of these alkamides and others isolated from *E. purpurea* in our laboratory, hexanes, DCM, and ethanol extracts from both species of *Echinacea*, and a partially purified fraction belonging to *E. angustifolia* were assessed using the *in vitro* assay that measures the level of inhibition of iNOS in LPS induced macrophages.

The IC50 of iNOS for the pure alkamides isolated from *E. angustifolia* and *E. purpurea* are close to each other with a range of 18.0–25.0 µM. The IC50 of the hexanes extracts of *E. angustifolia* and *E. purpurea* were 8.0 and 14.0 µM, respectively. The IC50 of the ethanol extract of *E. purpurea* was 44.0 µM, while the ethanol extract of *E. angustifolia* was inactive. Further, a column chromatography fraction of *E. angustifolia* exhibited the most potent inhibition of iNOS with IC50 5.65 µM. The anti-inflammatory activity observed in the current study is presumably a result of synergistic effect of multiple alkamides of the extract or the partially purified fraction rather than contribution of the individual compounds.

PC-12: Chemistry Aspects of Botanicals

Hyperforin-like Polycyclic polyprenylated acylphloroglucinols from *Garcinia gummi-gutta*

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Garcinia gummi-gutta is a well-known plant belonging to the family Clusiaceae and is considered native to Southeastern Asia and India. *G. gummi-gutta* fruit extracts or its botanical dietary supplements, have gained immense popularity in the United States as a remedy for weight loss. As a result, its supplements are available over the counter with attractive slimming aids and a substantial human population consumes them with the notion that being of natural origin they have no side effects. Parallelly, the cases of *G. gummi-gutta*–associated hepatotoxicity have markedly increased. In response, the United States Food and Drug Administration (US FDA) and the Centers for Disease Control and Prevention warned the consumers and manufacturers of these products (e.g., Hydroxycut and OxyElite Pro). The rind of *G. gummi-gutta* fruit has several phytochemicals including organic acids, polyisoprenylated benzophenones, and polyprenylated acylphloroglucinols (PPAPs), but hydroxy citric acid is thought to be the essential constituent responsible for weight loss effects and liver toxicity.

PPAPs possess various pharmacological activities and they fascinated us as they structurally resembled hyperforin, a potent agonist of human pregnane X receptor (hPXR) that leads to herb-drug interaction (HDIs), especially in chronic pathophysiology. Subsequently, studies also suggested that overactivated PXR significantly contributes to liver toxicity. Recently, we revised the chemical structure of guttiferone J which has substantial potency for PXR activation. Herein, we present the isolation and characterization of eight PPAPs, including four previously undescribed ones, from *G. gummi-gutta* and their PXR activation potential.

PC-13: Chemistry Aspects of Botanicals

Molecular Docking of Kratom Alkaloids Including their Metabolites at μ-Opioid Receptor: A Systematic Computational Study

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Mitragyna speciosa, a plant grown in Asia and Africa's tropical and subtropical regions and commonly known as kratom, has traditionally been used for medicinal treatments for centuries. Kratom's growing civilian popularity has also generated increased scientific interest as a potential opioid withdrawal treatment or as a potential analgesic due to its purported pain-relieving effects. Concern in the forensics and healthcare community has subsequently escalated due to the potential addictive properties associated with kratom's euphoric effects. Over 40 Kratom alkaloids have been determined to be primary contributors to the plant's psychoactive effects. Despite its potential therapeutic value, kratom use has been scrutinized for many adverse effects, including multiorgan toxicity and cardiotoxicity. However, no experimental information is available at the molecular level on the binding mechanism or putative binding site of kratom alkaloids and their metabolites at the μ-opioid receptor (MOR) (PDB ID: 5C1M). In the present study, we investigated the possibilities of MOR activation by kratom alkaloids and their metabolites by studying their binding mechanism and interaction profiles at the active-state MOR X-ray crystal structure, in concert with molecular docking, binding free-energy calculations, and all-atom molecular dynamics (MD) simulations. The results of the docking studies have proposed unique binding poses for the kratom alkaloids compared to traditional opioids, and MD studies are in progress. Identification of key interactions between kratom alkaloids, their metabolites, and the MOR will help to elucidate the relationship between kratom compounds and the MOR, as well as allow for the design of new analogs.

PC-14: Chemistry Aspects of Botanicals

Phytochemical and Biological Investigation of *Peucedanum guvenianum* from West Anatolia

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Peaucedanum is represented by more than 120 species in the Apiaceae family, widely distributed in Europe, Asia, and Africa. Various extracts of aerial and underground parts of several *Peucedanum* species well-known traditional medicine and have been used in folk medicine for treatment of various conditions, such as cough, cramps, pain, rheumatism, asthma and angina. Phytochemical and pharmacological studies have shown that several secondary metabolites, including coumarins, phenolic acids, flavonoids, phenylpropanoids, chromones, fatty acids, steroids, and a number of volatile oils (monoterpenoids, sesquiterpenoids) have been identified from the *Peucedanum* species. The major constituents of this plant are furanocoumarin and pyranocoumarins and these compounds have various beneficial effects such as anti-inflammatory, anti-asthma, chemopreventive, smooth muscle relaxan, cytotoxic, antiplatet, neuroprotective, and anti-osteoclastogenic properties. *Peucedanum guvenianum* Yıldırım & H.Duman is a newly described species endemic to the West Anatolia region of Türkiye. Herein, we report the isolation and characterization of ten coumarin derivatives from the roots of *P. guvenianum* and their biological activities assessment.

PC-15: Chemistry Aspects of Botanicals

Discovery of Potential hNaV1.1 Inhibitors for the Treatment of Drug-resistant Epilepsy

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Epilepsy is a neurological illness characterized by recurrent spontaneous epileptic seizures. Epileptic adverse effects include cognitive, psychological, social, and neurodegenerative consequences. More than 65 million people around the world and about 3.4 million people in the United States have active epilepsy. Many epilepsy patients do not respond to conventional antiepileptic drugs and therapies. Recently, the FDA has approved cannabidiol (CBD) (Epidiolex) as a treatment for two rare forms of childhood epilepsy that are resistant to current drugs; namely Dravet syndrome (DS) and Lennox Gastaut syndrome (LGS). Many researchers have tested CBD and its derivatives in rat and mouse models of epilepsy and have found anticonvulsant effects with differing levels of potency. CBD showed promising effects in patients with drug-resistant epilepsy. However, the major disadvantages of CBD are poor solubility, chemical instability, excessive metabolic instability, low oral bioavailability (approximately 5-6%), fast accumulation in fatty organs such as the brain, and very high plasma protein binding (>99%). Given these findings, we started our journey to identify novel CBD analogs or other minor constituents of cannabis with superior and sufficient efficacy and enhanced drug-like properties (such as water solubility, low lipophilicity, chemical, and metabolic stability as key properties). The identified hits may have a substantial impact on the treatment of epilepsy. There is no CBD bound hNav1.1 complex available either NMR or X-ray crystal structure; therefore, we first constructed and validated CBD bound hNav1.1 complex using computational approaches such as docking, Prime-MMGBSA calculations and all-atom molecular dynamics simulations. In addition, we identified potential hits from minor constituents of cannabis and CBD analogs by docking them at hNav1.1 channel. The *in vitro* results are pending, and potential results will be presented.

PC-16: Chemistry Aspects of Botanicals

Application of Molecular Dynamics to Assess the Binding Orientation of CBD within hNav1.1 Receptor

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Epilepsy is a devastating disease with severe adverse effects and pprox.. 65 million people around the world and about 3.4 million people in the United States have active epilepsy. CBD showed promising effects in patients with drug-resistant epilepsy. Previously, molecular modeling and site-directed mutagenesis studies have been employed to investigate the mechanism of Nav1.1–CBD binding interactions; however, the precise orientation of CBD within hNav1.1 is not well established. In the present study, we explored the potential binding-site orientation and interactions of CBD within Nav1.1 using computational approaches including docking, Prime-MMGBSA and molecular dynamics. To gain insight regarding potential binding orientations of CBD within Nav1.1, we performed Induced-Fit Docking of CBD on cryo-EM structure of the human Nav1.1 (hNav1.1) (PDB ID:7DTD). We evaluated two orientations of CBD within Nav1.1: one in which the terpene moiety is directed towards the extracellular region and another in which the terpene moiety is directed towards the key residue Phe1772. In addition, we performed 500 nanosecond molecular dynamics simulations of the commencing from the best docked pose for each of the two orientations for CBD within Nav1.1, including POPC membrane, water and appropriate ions. The molecular dynamic is in progress and results will be presented in the conference. The results of this work may be helpful for the design of novel CBD analogs that fit optimally into the Nav1.1 binding pocket.

PC-17: Chemistry Aspects of Botanicals

Phytochemical Profile of *Elephantorrhiza elephantina* Rhizome

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Elephantorrhiza elephantina (Burch) Skeels (Fabaceae), commonly known as elephant root, is widely used by southern African indigenous people as a source of food, medicine, and tanning /dyeing materials. The tuberous red rhizome is the most commonly used part of the plant in traditional medicine for the management of various metabolic and infectious diseases in both humans and animals. Twenty-two compounds mainly catechin, taxifolin, and proanthocyanidin derivatives were isolated and characterized from methanolic extract of *E. elephantina* rhizome. Elephantinaside A-F were found to be undescribed compounds. Structure elucidation was mainly based on 1D- and 2D-NMR and HRESIMS data. The absolute configuration of isolates was determined via NOESY NMR and experimental and calculated ECD data analyses.

PC-18: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Design and Synthesis of Structurally Novel Acylphloroglucinols Against *Cryptococcus* Species

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Cryptococcus neoformans is an invasive fungus, transmitted through the inhalation of spores and causes cryptococcosis, an infection commonly associated with immunosuppressed patients with AIDS, cancer, or organ transplants. Naturally occurring acylphloroglucinols provide a large range of structurally diverse compounds. A number of compounds within this structural class are known to be active against various fungal and bacterial pathogens, but only a few compounds were reported to show activity against *Cryptococcus* spp. The synthetic compound 2-methyl-1-(2,4,6-trihydroxy-3-(4-isopropylbenzyl)-phenyl)propan-1-one, classified as an acylphloroglucinol, has exhibited potent in vitro antifungal efficacy against two strains of *C. neoformans* (ATCC 90113 and H99) and one strain of *C. gattii* (ATCC 32609). This promising activity suggests its potential as a lead compound for subsequent structure and activity optimization. In our approach, we strategically designed and synthesized acylphloroglucinols, mimicking a lead compound. This involved the incorporation of n-butyryl and n-pentanoyl groups into the phloroglucinol core, coupled with the introduction of a heterocyclic aromatic ring in the side chain. These designed compounds are anticipated to exhibit reduced lipophilicity, increased antifungal efficacy, and decreased cytotoxicity. Our work presents a collection of potential compounds characterized by potent antifungal activity and enhanced chemical stability against *Cryptococcus* species.

PC-19: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Design, Synthesis and Biological Evaluation of Coumarin Based TRKA Activators as Anticancer Agents

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Coumarins are an important class of natural plant metabolites that offer a variety of biological activities. The coumarin scaffold is widely used for the development of highly effective anticancer agents with minimum side effects. The tropomyosin receptor kinase (TRK) family of receptors are encoded by neurotrophic tropomyosin receptor kinase (NTRK) genes and plays a role in the development and normal functioning of the nervous system. The TRK receptor family comprises three members (TrKA, B, & C) encoded by the genes NTRK1, 2, & 3, respectively. NTRK gene fusions have shown different rates of occurrence in rare cancers (frequency >80%), and common cancers (frequency <25%). Following its prevalence in both rare and common cancers, NTRK gene fusions have emerged as a viable target for anticancer drug therapy. Several of the currently used chemotherapeutics induce autophagic cell death. Activation of TrkA in human glioblastomas might be beneficial therapeutically.

Seven compounds were investigated with possible activity on the NGF/TrkA pathway with a coumarin-scaffold (5c-g, 5j, and 5k) that exhibited significant growth inhibition in the glioma SF539 cell line. Their effect was investigated on TrkA activation at three doses (10 µM, 5 µM and 2.5 µM) in the Indigo Bioscience, Human Tropomyosin Receptor Kinase A reporter assay system (TrkA). All samples except 5k showed activation on TrkA at either 10 uM or 5 uM. 5c and 5d were able to cause ~2-fold induction of TrkA (~100% increase in activity). Moreover, 5e, 5f, 5g, and 5j showed a parabolic effect, with the highest activity at the middle concentration 5 µM. These data suggest that the glioblastoma growth inhibition detected by the coumarin-scaffold derivatives investigated in this study could be at least in part working through TrkA activation.

PC-20: Chemistry Aspects of Botanicals

Butanolides from the Twigs of *Casearia grewiifolia*

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Casearia grewiifolia Vent. (Salicaceae) is a shrub or small tree that grows in tropical and subtropical areas such as Southeast Asia and some Pacific islands. The extracts of this plant have been used traditionally to treat diarrhea, fever, and itching. Previous investigations for this plant have reported the presence of amides, clerodane-type diterpenoids, lignans, other phenols, and steroids as chemical constituents, and bioactivities such as antimycobacterial, antimalarial, and cytotoxic effects. To explore new chemical constituents from this plant, the twigs of *Casearia grewiifolia* were investigated and as a result, three butanolides derivatives (1–3) were isolated. The chemical structures and absolute configurations were established by detailed NMR spectroscopic data including 2D 13C–13C Incredible Natural Abundance DoublE QUAntum Transfer Experiment (13C–13C INADEQUATE), mass spectra, hetero half-filtered TOCSY (HETLOC), Mosher esterification procedure, and electronic circular dichroism (ECD).

PC-21: Chemistry Aspects of Botanicals

Revisiting *Mandragora officinarum* L.: From Magic to Phytochemistry and Bioactivities

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Mandragora officinarum L. (mandrake) is a perennial herbaceous plant from the nightshade (Solanaceae) family, native to the Mediterranean region. The plant has a rich history of uses from ancient times for its healing and psychotropic properties. However, its wider use has declined due to the presence of tropane alkaloids, which can lead to poisoning, if used improperly. In general, the number of publications on *M. officinarum* chemical composition and bioactivities is rather scarce. The majority of the previously performed studies were focusing on its alkaloids. The aim of this study was to fractionate oven and freeze-dried *M. officinarum* fruits (berries) and roots in to the lipophilic and higher polarity fractions by using consecutive extraction with supercritical CO2 and pressurized liquids using the increasing polarity solvents and to evaluate the phytochemical composition and antioxidant potential of the fractions obtained. First of all, proximate composition of *M. officinarum* berries and roots was evaluated by using standard methods

	Proteins, %	Fats, %	Insoluble fibers, %	Minerals, %	Moisture, %
Roots	10,18 ± 0,41	4,7 ± 0,6	8,33 ± 0,05	4,35 ± 0,01	9,7 ± 0,35
Dried at 60°C fruits	13,27 ± 0,51	13,63 ± 0,31	21,77 ± 0,2	5,35 ± 0,02	6,24 ± 0,18
Freeze-dried fruits	13,67 ± 1,55	13,26 ± 0,4	22,47 ± 1,3	4,92 ± 0,02	8,27 ± 0,13

The content of lipophilic fractions isolated at 350 Mpa pressure and 50°C temperatures was approximately 0,5% for the roots and 8% for fruits. Additionally, the total amount of phenolic compounds and ABTS radical scavenging activity were also determined in the roots, fruits and leaves of this plant. The same assays were also carried out not only with dry raw material but also with various extracts: CO_2, ethanolic, acetone and water.

PE-1: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Research on Natural Sunscreens Based on Medicinal Plants.

Dramé A [1], Guèye B [1], Bop MC [1], Tall AB, SowPG', Diop, KAO[1], Diop CT[1], Fall SE [1,2], Leve MMM [1], Niang MN, Diop PA[3]

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Research on natural solar filters (sun creams for albinos) based on medicinal plants. Protecting the skin from the sun is a public health issue. Due of the growing awareness of the risks of skin cancer due to damage from UV-A and UV-B rays, UV filters are now found in many beauty products applied daily. Our skin cells have essential fatty acid barriers, and when UV arrive, they penetrate this barrier by manufacturing oxygen molecules called “singlet oxygen”, which can be harmful to the cell and to the cell nucleus and attack DNA.

Thus, the sun is responsible for sunburn and premature aging of the skin as well as the appearance of skin cancers. "At a certain time, when their DNA has been frequently attacked, cells end up having abnormal DNA, which can then give rise to a cancer cell", notes Dr. Gaucher. Outside of cancer, cells that are repeatedly damaged age faster. A solution: protect yourself from the sun by applying protection solar filters.

This involves verifying the natural sun filter effect based on medicinal plants. In presence of significant activity certain medicinal phytochemicals such as flavonoids could be used in the production of natural sun protection (plant-based sunscreen) in accordance with WHO guidelines according to traditional medicine and the European Union cosmetics directive. The study of toxicity *in silico*, *in vitro* and/or *in vivo* make it possible to cover all the potential problems linked to the molecule, such as the identification of its potential irritant, sensitizer and/or photo irritant and/or sensitizing effects as well as its embryotoxic and reprotoxic potential and finally carcinogenicity and genotoxicity.

PE-2: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Sustainable Cultivation of Spicy and Aromatic Plants Applying Green Manure

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Understanding the effects of green manure on the development and quality of plants can contribute to the promotion of more sustainable agricultural practices and the maximization of the economic and medicinal potential of species such as *Ocimum basilicum* L. and *Origanum majorana* L. The objective was to evaluate the potential of *Crotalaria juncea* and *Cajanus cajan* as green manure in the production of biomass and in the essential oil metabolism of *O. basilicum* and *O. majorana*. Six treatments and four replications were used, each containing five plants per replication, totaling 120 plants. The treatments consisted of five green manure doses (0, 3, 6, 9, and 12 kg/m²) and a chemical control. After 120 days of cultivation, the dry weight of leaves, stem, roots, and total plant, as well as the oil content and yield, and the chemical composition of the essential oil were analyzed. The use of *C. juncea* and *C. cajan* as green manure demonstrated a positive and significant impact on the production of dry weight in vegetative organs, as well as on the yield and chemical composition of the essential oil. The green manure management exerted a positive influence on the essential oil production, showing contents and yields comparable to chemical fertilization. α-Terpineol stood out as the major compound in the essential oil of *O. majorana*, reaching higher concentrations in plants treated with 12 kg/m² of *C. cajan*. In conclusion, the application of the dose of 12 kg/m² of *C. juncea* or *C. cajan* resulted in the best performances in terms of growth and nutrient accumulation. It also affirmed the effectiveness of sunn hemp and pigeon peas as a fundamental green manure strategy for the sustainable production of aromatic plants.

PE-3: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Quality Assessment and Authentication of Lavender Essential Oil

Wilson TM[1], Murphy BJ[1], Bowerbank CB[1], Carlson RE[1], Smith BL[1]

[1]Young Living Essential Oils

The pleasant aroma of lavender (*Lavandula angustifolia*) essential oil, combined with its purported health benefits, makes it a popular choice for aromatherapy, cosmetic, flavor, and fragrance applications. The widespread use of lavender essential oil lends itself to potential adulteration. To assess the quality and authenticity of lavender essential oil, it is vital to also understand which factors influence the essential oil profile and which analytical techniques are optimal for analysis.
To investigate authentication of lavender essential oil, samples (n = 41) were procured directly from farmers/distillers and used as reference materials. These essential oils were analyzed to determine profiles and related data by GC, enantioselective GC, and GC/IRMS. Said analysis resulted in the identification of 43 authentic marker compounds, enantiomeric ranges for 15 compounds, and stable isotope ranges for four prominent compounds in authentic lavender essential oil. This dataset was used to assess the quality of commercially available lavender essential oil samples (n = 12) purchased from online retailers. Nine of the twelve (75%) commercial samples studied were adulterated, and 17 adulteration marker compounds were identified from these commercially available samples. These studies stress the importance of understanding factors contributing to natural variation and establish the utility and importance of using a multifaceted analytical approach to differentiate quality and determine authenticity of lavender essential oil.

PE-4: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Characterization of Cannabis Smoke Condensate and its Inhibitory Effects on CYPs in Human Lung

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Smoked cannabis flower is the most commonly utilized form of cannabis for medical and recreational purposes. Cannabis is typically used in the treatment of various chronic conditions and diseases including amyotrophic lateral sclerosis, cancer, Crohn's disease, epilepsy, glaucoma, and others. These conditions typically require the use of one or more conventional medications including lung therapeutics concurrently which leads to concerns over botanical-drug interactions (BDIs). Combusted cannabis leads to the formation of thousands of compounds and this study focuses on the collection and characterization of cannabis smoke condensate (CSC) and an assessment of its in vitro inhibitory effects on six major cytochrome P450 enzymes (CYP) in the lung. Three standardized cannabis cigarettes sourced from the US National Institute of Drug Abuse Drug Supply Program were consecutively combusted in an enclosed smoke exposure system. Generated smoke was routed through an ultra-cold condenser permitting the collection of CSC. CSC was weighed and analyzed for the presence of 8 major cannabinoids (CBs) via LC-MS/MS. *In vitro* enzyme inhibition studies were conducted/ongoing using human lung S9 to evaluate the potential inhibitory effect of CSC on CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2B6, and CYP2E1. A total of 14.6 mg (4.87 mg per cigarette) of CSC was collected, containing 0.022% CBD, 1.163% CBN, 9.317% THC, 0.193% CBG, and 0.008% 11-OH-THC of the total weight. The half-maximal inhibitory concentration (IC50) of CSC for CYP3A inhibition was determined to be 17.85 µM with Δ9-tetrahydrocannabinol (THC) as the index substrate. The study revealed that the relative CB content of cannabis smoke is substantially different from that of non-combusted cannabis flowers. Furthermore, CSC produced a mild inhibitory effect on CYP3A activity. Further investigations are ongoing to elucidate the inhibition mechanisms and assess the inhibitory effects on other CYPs and drug metabolizing enzymes.

PE-5: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Discovery of Selective Cannabinoid Receptor Type II Ligands from Sandalwood Oil

Paudel P [1], Pandey P [1], Paris JP [2], Ashpole NM [2], Mahdi F [2], Tian J-M [1], Lee J [1], Wang M [3], Xu M [4], Chittiboyina AG [1], Khan IA [1,2], Ross SA [1,2], Li X-C [1,2]*

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Bioassay-guided fractionation of the essential oil of *Santalum album* led to the identification of α-santalol and β-santalol as a new chemotype of cannabinoid receptor type II (CB2) ligands with Ki values of 10.49 and 8.19 μM, respectively. Nine structurally new α-santalol derivatives were synthesized to identify more selective and potent CB2 ligands. The synthetic compound with a piperazine structural moiety demonstrated a Ki value of 0.99 μM against CB2 receptor and did not show binding activity against cannabinoid receptor type I (CB1) at 10 μM. α-Santalol, β-santalol, and the synthetic α-santalol derivative increased intracellular calcium influx in SH-SY5Y human neuroblastoma cells that were attenuated by CB2 antagonism or inverse agonism, supporting the results that these compounds are CB2 agonists. Molecular docking showed that α-santalol and the synthetic α-santalol derivative had similar binding poses exhibiting a unique interaction with Thr114 within the CB2 receptor, and that the piperazine structural moiety is required for the binding affinity of this synthetic compound. A 200 ns molecular dynamics simulation of CB2 complexed with the synthetic α-santalol derivative confirmed the stability of the complex. This structural insight lays a foundation to further design and synthesize more potent and selective α-santalol-based CB2 ligands for drug discovery.

PE-6: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Micro-Morphology Characterization and HS-SPME-GC-MS Analysis of Floral Part of *Quararibea funebris* (La Llave) Vischer, Traditionally Known as Rosita de Cacao

González-Anduaga GA [1], Adams SJ [4], Dueñas-Deyá A [1], Pérez-Vásquez A [1] , Avula B [2], Katragunta K [2], Khan IA [2,3,4], Navarrete A [1,2]

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The flowers of *Quararibea funebris* (La Llave) Vischer are used to make a traditional drink called tejate, to which it adds aroma, flavor, and consistency. The aim of this work is to describe the morphoanatomy of the flower of *Q. funebris* and analyze the change of its volatile chemical composition during the drying process from 0 to 180 days using headspace solid-phase microextraction (HS-SPME)-gas chromatography-mass spectrometry (GC-MS). The cross-section of the calyx, corolla, androecium, and gynoecium, the presence non-glandular fused stellate trichomes, calcium oxalate crystals and large secretory ducts are very characteristic. The chemical analysis revealed that the most abundant compounds of the essential oil (yielding 0.04%) were trans-farnesol and geraniol. HS-SPME analysis revealed a more complex composition in the fresh flower than the dry flower. A total of 31 components were identified, □□-ocimene, linalool, citronellol, geraniol, methyl geranate, and trans-farnesol with the highest relative abundance. Nonanal and geranyl acetone as distinctive components in the 180- day-old, dried flowers. These results can help in identification and volatile chemical profiling of dry flowers and also be used as quality control parameters to confirm the raw materials sold commercially in the name of Rosita de Cacao.

PE-7: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Chemical Composition and Biological Activities of *Eugenia sellowiana* DC. (Myrtaceae) Essential Oil

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Federal University of Goiás PD&I de Bioprodutos -Bioproduct Research, Development and Innovation Laboratory

Myrtaceae is an important and promising class of plants with sources of plant bioactives. This family is widely distributed in Brazil's Cerrado biome, a vast ecoregion of tropical savanna in eastern Brazil. While some species in this biome are well-characterized, others, like *Eugenia sellowiana*, remain less known. This research aims to investigate the biological potential of *E. sellowiana* leaf essential oil as an insecticide and antifungal agent and to conduct a toxicological screening for hemolytic potential. *E. sellowiana* leaves were collected from the Cerrado area in Hidrolândia, Goiás (16°54'02" S and 49°15'34" W), dehydrated, and the sample powdered, then submitted to hydro-distillation with a Clevenger apparatus for 2 hours. Gas chromatography-mass spectrometry (GC/MS) elucidated the chemical composition. Larvicidal activity against third-instar *Aedes aegypti* larvae was investigated. The potential antifungal effect was examined by microdilution in broth against ten fungal strains. Potential hemolysis was assessed using commercially obtained sheep erythrocytes. The extraction process yielded 0.36% of essential oil (OE) comprised of 25 substances, with limonene, z-caryophyllene, germacrene D, and bicyclo germacrene showing better percentages. Larvicidal activity was promising, with significant lethality in *Aedes aegypti* larvae (LC_{50} 100 µg/mL). A substantial antifungal effect was observed against various strains (MIC/MFC 32/1024 µg/mL). In evaluating hemolytic potential, the essential oil of *E. sellowiana* demonstrated a hemolysis rate of less than 9% at the highest concentration tested (244 µg/mL), suggesting the material is non-toxic. The results indicate that the biopotential of *E. sellowiana* is promising and warrants further investigation. Additionally, the study underscores the importance of preserving plant species like *E. sellowiana* in the Cerrado biome.

PE-8: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Dereplication of The *Aaronsohnia factorovsky* Phytochemicals and Essential Oil: A Thriving Daisy in The Heart of Salty Moab Mountains-Eastern Dead Sea.

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Aaronsohnia factorovskyi Warb. & Eig (AF) is a rarely investigated herb that belongs to the daisy family Asteraceae. It has been traditionally used as an herbal tea with a medicinal value. In particular, it is used for kidney stones, toothache, anemia, cancer, and diabetes. AF has a strong and pleasant aroma and desirable hot stinging taste. In this study, we have explored the chemical composition of the plant employing various analytical techniques. The chemical composition of the essential oil was analyzed by gas chromatography-mass spectroscopy (GC-MS), and the secondary metabolites of the polar methanolic extract were analyzed with liquid chromatography-high resolution electrospray ionization mass spectrometry (LC-HRESIMS). The cytotoxicity of the essential oil was carried out by MTT assay in T47D, and A549 cell lines for ductal cell carcinoma and non-small cell lung cancer. Our results demonstrated a cytotoxic effect of the volatile oil at 2.517 µl/mL, and 1.844 µl/mL respectively. Myrcene was the major compound identified in the hydro distilled volatile oils, with concentration of 26.65%; and together with ocimene <(Z)-β-> and capillene, they accounted for about half of the oil. Furthermore, the untargeted profiling of the AF methanolic extract has detected the alkamide thienyl-hexadien-isobutylamide as the major compound. Comprehensive chemical composition of AF oil and polar extract will be presented.

PE-9: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Electrophysiological Assessment of the Essential Oil of *Murica gale*, an Irish Wetland Plant on Seizure Activity

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The literature has reported on many plant metabolites, volatile extracts and whole fresh material exhibiting anti-seizure activity, with evidence of administering these directly to tissue having anti-convulsant effects [1]. Seizure activity can be reduced via the inhalation of certain essential oils (EOs) [1,2]. Myrica gale (MG) is a native Irish bogland shrub and has been known as a natural remedy for fits in dogs [3]. This study aimed to assess the acute anti-epileptic potential of 2 Irish wild MG EOs (EO1M, EO15C) and 1 commercial Canadian EO (COM) using in vitro electrophysiology. Extracellular local field potential (LFP) recordings measured ictal-like events (ILEs), in adult Lister hooded rat brain slices (400ym). ILEs were elicited using the proconvulsant 4-aminopyridine (26.7mM). Following establishment of baseline ictal activity (5 ictal events), the EOs were individually applied to slice via perfusate (0.5%v/v). LFP recordings of ILE activity were recorded from the superficial layers (II-III) of the medial entorhinal cortex (mEC). The effects of each EO on ictal duration (ID), inter-ictal duration (IID), first spike amplitude (FSA), spectral power density (SPD) and number of seizures (NoS) were analysed. Acute application of EO1M significantly reduced ID ($n=9$, $P < 0.01$), IID ($P < 0.01$), NoS ($P < 0.01$), PSD ($P < 0.01$) and FSA ($P < 0.05$). EO15C, significantly reduced ID ($n=9$, $P < 0.01$), IID ($P < 0.01$) and NoS ($P < 0.01$). COM did not demonstrate any significant activity for all parameters measured, ID, IID, NoS, PSD, and FSA ($n=9$, $P > 0.01$).

We demonstrate that EOs extracted from Irish MG samples, can reduce seizure like activity in this model. The variance in plant metabolites for each sample are assumed to bear some significance in the variation of activity assessed. Future work aims to reveal the mechanistic nature of individual terpenes and/or complex mixture of EOs on seizure activity in brain tissue.

PE-10: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Quality Evaluation of Peppermint Oils and Commercial Products: An Integrated Approach Using Conventional and Chiral GC/MS Combined with Chemometrics

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The herb peppermint (*Mentha* x *piperita* L) is a perennial aromatic herb which is a natural hybrid of *Mentha aquatica* L. (water mint) and *Mentha spicata* L. (spearmint). Peppermint essential oil (EO) has a multitude of applications such as a fragrance in cosmetics, personal care, and industrial products; or as a flavoring ingredient in food and beverages. Despite its popularity and economic significance, peppermint EO is often adulterated in order to reduce production costs and to increase profits. Peppermint EO can be adulterated by one or a combination of four methods: 1) the addition of synthetic compounds which are not naturally present in the EO; 2) the addition of synthetic compounds which are present in natural EO; 3) the addition of natural compounds from other sources (i.e. plants) or enzymatic production; and/or 4) the addition of EO fractions or oil which have a similar composition to all or part of natural peppermint EO. Although ISO standards for peppermint EO using conventional GC techniques exist, detecting sophisticated forms of adulteration remains challenging. In order to address these issues, the goal of our investigation was to develop and utilize both conventional and chiral GC/MS techniques to analyze samples of known and unknown provenance. Next, the data obtained from the chiral analysis of known provenance samples was averaged and used to establish a point of comparison for unknown samples. In addition, data obtained from the GC/MS analysis was also subjected to chemometric analysis in order to detect outliers.

PE-11: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Unlocking the Aromatic Symphony: Terpenes and Furanocoumarins in Grapefruit Essential Oil Orchestrate Metabolic Harmony

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The essential oils (EOs) of *Citrus* (Rutaceae) fruits have been utilized for centuries and remain popular due to their numerous beneficial health effects. Particularly, grapefruit EO has been touted for topical and internal administration due to the abundance of limonene, which some scientific literature has identified to modulate metabolism. While the major constituents of grapefruit EO are monoterpenes, sesquiterpenes have been identified in minor quantities. Indeed, many botanicals have been demonstrated to affect metabolism through the pregnane X receptor (PXR). Activation of PXR can result in the increased transcription of metabolic enzymes, such as cytochrome P450s (CYP450s). Additionally, grapefruit isolates have been shown to contain a wealth of oxygenated heterocyclic compounds (OHCs) with scaffolds similar to the prototypical bergamottin. Such furanocoumarins are heavily implicated or have been demonstrated in modulating inhibitory activity at CYP450s, principally CYP450 3A4. Considering not only the concomitant administration of both terpenoids and furanocoumarins in grapefruit EO but also the interplay between PXR and CYP450s, it is critical to assess the potential effects on the metabolism of the phytoconstituents. In the context of metabolism, the harmful effects of grapefruit furanocoumarins may be mitigated by the upregulation of PXR from volatile grapefruit compounds in the matrix of essential oil. A computational approach was implemented to assess the plethora of grapefruit EO volatile organic compounds (VOCs and OHCs) to support this hypothesis. Parent grapefruit EO VOCs and furanocoumarins were docked with Schrödinger Glide to select PXR and CYP450s 1A1, 2C9, 2D6, and 3A4 crystal structures. The findings suggest that activation of PXR and inhibition of CYP450s may happen concurrently. This necessitates additional validation through experimental techniques that involve coincubation of both prioritized grapefruit volatile and furanocoumarin compounds.

PE-12: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Chemical Analysis and Antibacterial Efficacy of *Cinnamomum camphora* (L.) Nees et Eberm. Essential Oil Against *Klebsiella pneumoniae*: *In vitro* and *In silico* Study

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The essential oil of *Cinnamomum camphora* (Campor) stands out in the literature for its antimicrobial, insecticide and antioxidant properties, but it has high volatilization and low stability, hence to overcome these limitations nanoencapsulation of this oil could be the desired alternative. The objective of this work was to identify the volatile compounds from *Cinnamomum camphora* (L.) Nees et Eberm., leaf essential oil from India and to establish its antibacterial effect against *Klebsiella pneumoniae* (Schorete) Trevisan (MTCC 618). The essential oil was extracted by hydrodistillation and chemical constitutes were identified by using GC-MS. Chitosan based nanoformulations of the essential oil were prepared using ionic gelation method and characterized by UV, SEM, XRD, FTIR, in vitro release and by encapsulation efficiency. The antibacterial activities were evaluated against Gram-negative bacteria *K. pneumonia* by agar well diffusion assay and its mode of action was predicted by *in silico* studies. Major content identified by gas chromatography-mass spectrometry (GC-MS) were Carvone (55.71%), limonene (18.83%), trans-carveol (3.54%), cis-carveol (2.72%), beta-bourbonene (1.94%), and caryophyllene oxide (1.59%). The essential oil displayed antibacterial effects against *K. pneumonia* with IC50 of 0.087 mg/mL. Further, results confirmed the successful encapsulation of the *Cinnamomum camphora* essential oil with 94.7% encapsulation efficiency and 90% of loading capacity. Nanoparticle size analyzer, scanning electron microscope (SEM) showed that CSNPs were spherical particles with a range of 200 to 220 nm. The results of in vitro release study indicated that the release of essential oil was phased, and chitosan encapsulated essential oil had certain sustained-release properties.The *in silico* ADMET and molecular docking studies confirm that the results have a greater affinity with the *in vitro* tests carried out for the selection of new antibacterial products of natural origin.

PE-13: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

Antidiabetic Activity of Standardized *Geranium robertianum* and *Geranium subcaulescens* Extracts and their Major Compound Geraniin

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In the last 10 years, diabetes mellitus has risen from 14th to 10th place among global causes of death with a mortality. Although the use of conventional drugs in treating diabetes is widespread, plants have been a therapeutic source in traditional treatment. There are 350 *Geranium* L. species worldwide and 39 in Turkey. *Geranium* species are popular in Turkey, Northern Peru, Morocco and Algeria for andiabetic purposes. In light of this information, the aerial parts of *G. robertianum* and roots of *G. subcaulescens* were investigated for antidiabetic effect. α-Glucosidase, α-amylase for antidiabetic activity, cholesterol esterase, pancreatic lipase enzymes have been studied due to the association between diabetes and obesity. The main compound in the extracts was determined to be geraniin by RP-HPLC, and both extracts were standardized based on geraniin and methylgallate as markers. *G.subcaulescens* showed higher activity than *G.robertianum* in all four enzyme models. When all enzyme inhibitory activity results were compared, it was concluded that both species showed strong inhibitory activities, especially against α-glucosidase and α-amylase enzymes. Standardization of the extracts by RP-HPLC revealed that geraniin (20.90 ± 0.06 mg/100 mg) and methyl gallate (10.65 ± 0.02 mg/100 mg) in *G. subcaulescens* were higher than geraniin (16.33±0.02mg/100 mg) and methyl gallate (0.72 ± 0.07 mg/100 mg) in *G.robertianum*. Geraniin particularly strongly inhibited the enzymes α-glucosidase and α-amylase. On the other hand, it was observed that the activity increased as the amount of methyl gallate increased in the extracts, but it was not effective as a single compound. The results showed that geraniin is the effective compound of *Geranium* species and methylgallate also contributes to the synergistic effect. In light of all these findings, future *in vivo* activity and molecular docking studies on geraniin are planned.

PE-14: Chemistry, biology, and safety of volatile organics from aromatic and medicinal plants

α-Copaene and its Oxidation Products: NMR Analysis and Fire Ant Repellent Activity

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University of Mississippi

As part of a natural product discovery program for identifying fire ant control agent, the essential oil extracted from Gurjun balsam (*Dipterocarpus turbinatus*) was screened and demonstrated repellent effects against imported fire ants. Bioassay-guided isolation of the oil resulted in the identification of α-copaene (1) as the major phytochemical responsible for the activity. Surprisingly, α-copaene, a highly strained tricyclic sesquiterpene with one double bond, is susceptible to autoxidation in the presence of air, producing a previously undescribed hydroperoxide [5-hydroperoxy-α-copaene (2)] and copa-2-en-4-ol (3). Chemical epoxidation of α-copaene afforded a-copaene epoxide (4), which underwent stereoselective ring opening to generate β-copaen-4α-ol (5). Potassium permanganate mediated oxidation resulted in the formation of copa-3-ol-4-one (6) and copa-3,4-diol (7). The stereochemistry of these oxidation products was unequivocally defined by 2D NMR experiments, which has addressed some confusions in literature. Fire ant assay of the oxidation products demonstrated a promising repellency potential. The repellency activity obtained was corroborated with molecular docking of the active compounds with pheromone-binding protein Gp-9 (Source: Solenopsis invicta x Solenopsis richteri). Site mapping predicted two putative binding sites. The screened compounds gave a docking score in the range of -5.828 to -8.869 Kcal/mol and -1.707 to -3.188 Kcal/mol, respectively in Sites 1 and 2. Overall, these findings highlight the potential role of α-copaene and its oxidation products in fire ant management.

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