Trends in Natural Product Research

PSE Young Scientists' Meeting

on Biochemistry, Molecular Aspects and
Pharmacology of Bioactive Natural Products

BUDAPEST, June 19-22, 2019

BOOK OF ABSTRACTS

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Trends in Natural Product Research

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Book of abstracts

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Leicester (UK), Szeged (HU)
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Welcome to PSE-YSM 2019 Budapest!

On behalf of Phytochemical Society of Europe (PSE), and the Organising and Scientific Committee of the PSE-YSM 2019 Budapest, we are delighted to welcome you to Budapest and the Phytochemical Society of Europe's Young Scientists' Meeting! This year's conference focuses on Trends in Natural Product Research - Biochemistry, Molecular Aspects and Pharmacology of Bioactive Natural Products, and promises to be an outstanding platform for scientists working on the field of natural product research, including phytochemistry, molecular biology, phytochemical analysis, bioactivity of natural products, phytotherapy. The conference takes place in Hotel Benczúr (Budapest), which is located in the heart of the city centre.

The aim of the conference is to serve as a forum for discussions on trends, most current topics and latest results of natural product research, and bringing together senior scientists, young researchers, and PhD students from all over the world. The scientific program includes 15 plenary lectures by leading scientists, 34 short lectures and 37 poster presentations. Moreover, the winner of the Pierre Fabre Research and Development Innovation Prize will present his results. Young scientists will have the opportunity to win Harborne and OlChemIm awards, honouring with them the best oral and poster presentations, respectively, in addition with the traditional PSE travel bursaries and PCA/Wiley Grant.

During your stay in Budapest, we hope that you take the opportunity to explore the beautiful metropolis with a history dating back over 2000 years. Budapest situating on both sides of the Danube River and having a vibrant cultural life and friendly atmosphere provided opportunity for the attendees to become acquainted with the monuments of the historical past of the city and discover its present with contemporary museums, spas and restaurants.

We hope that you will find the conference stimulating and rewarding, and we look forward to your contribution to make this an exciting and fruitful meeting.
Welcome to Budapest!

The organizers
Judit Hohmann, Dezső Csupor

Summary

SCIENTIFIC PROGRAMME

Venue: Hotel Benczúr (Benczúr utca 35, H-1068 Budapest, Hungary)
Lectures: Budapest Room
Poster session: Lobby

Wednesday June 19th, 2019

10:00-18:00	**Registration**	
12:00-13:30	**Lunch**	
Welcome and Opening Lecture		
13:30-14:00	Inauguration	Welcome and Announcements: Prof. Judit Hohmann Welcome: Prof. Éva Szökő, President of Pharmaceutical Committee of Hungarian Academy of Sciences PSE update: President of the PSE, Prof. Satyajit D Sarker
14:00-14:30	Satyajit D Sarker	**PL-1:** Libyan medicinal plants and their cytotoxic compounds
Session 1 Chaired by Satyajit D. Sarker		
14:30-15:00	Virginia Lanzotti	**PL-2:** NMR spectroscopy and mass spectrometry in the discovery of bioactive natural products
15:00-15:15	Odeta Celaj	**SL-1:** *In vitro* antioxidant and enzyme inhibitory properties, metabolomic profile and computational studies *Cistanche phelypaea* (L.)
15:15-15:30	Lina Yousef	**SL-2:** Metabolomics and *in vitro* cytotoxicity of extracts obtained from a desert plant and its soil
15:30-15:45	Aleksandra Burdziej	**SL-3:** Metabolomic alterations in elicitor-treated grapevine *Vitis vinifera* leaves monitored by ^{1}H NMR
15:45-16:00	Laura Grauso	**SL-4:** Metabolomics of the alimurgic plants *Taraxacum officinale, Papaver rhoeas* and *Urtica dioica* by combined NMR and GC-MS analysis
16:00-16:30	**Coffee break**	
Session 2 Chaired by Virginia Lanzotti		
16:30-17:00	Matthias Hamburger	**PL-3:** Searching for the needle in the haystack – targeted identification of pharmacologically active natural products
17:00-17:30	Anders Backlund	**PL-4:** Applications of chemography in natural products
17:30-17:45	Didem Şöhretoğlu	**SL-5:** Investigations on secondary metabolites of a relict oak: *Quercus pontica*
17:45-18:00	Gokay Albayrak	**SL-6:** Coumarins and polyacetylenes from *Prangos uechtritzii* Boiss&Hauskn roots
18:00-21:00	**Welcome reception**	Hotel Benczúr

Thursday June 20th, 2019

Session 3 Chaired by Luc Pieters		
8:30-9:00	Veronika Butterweck	**PL-5:** Polyphenols as biogenic additives and value added products
9:00-9:30	Rudolf Bauer	**PL-6:** The important role of gut microbiota for the therapeutic activity of herbal extracts
9:30-9:45	Kenneth J. Ritchie	**SL-7:** The conundrum of phytochemicals and cancer
9:45-10:00	Petr Voňka	**SL-8:** Molecular mechanisms of action of selected steroids in breast cancer cells
10:00-10:15	Wee Sim Choo	**SL-9:** Inhibitory activity of a betacyanin formulation from red pitahaya *(Hylocereus polyrhizus)* and red spinach *(Amaranthus dubius)* against polymicrobial biofilms of *Staphylococcus aureus* and *Pseudomonas aeruginosa*
10:15-10:30	Sushmita Nath	**SL-10:** Effects of major secondary metabolites of *Ricinus communis* on porcine uterine contractility
10:30-11:00	**Coffee break**	
Session 4 Chaired by Maria Jose U. Ferreira		
11:00-11:30	Giovanni Appendino	**PL-7**: Electrophilic natural products: friends or foes in natural products drug discovery?
11:30-11:45	Mayuri Napagoda	**SL-11:** *Plectranthus zeylanicus* Benth: A potent source of secondary metabolites with antimicrobial, disinfectant and anti-inflammatory activities
11:45-12:00	Karel Šmejkal	**SL-12:** Prenylated phenolics with anti-inflammatory effects
12:00-12:15	Hiba A Jasim	**SL-13:** Bioactivity of synthetic chalcones in MRC-5 SV2 cells
12:15-12:30	Nóra Gampe	**SL-14:** *Ononis* isoflavonoids aiming the CNS
12:30-14:00	**Lunch**	
Session 5 Chaired by Kenneth J. Ritchie		
14:00-14:30	Fang-Rong Chang	**PL-8:** Development of traditional complex formulas as therapeutic agents
14:30-15:00	Attila Hunyadi	**PL-9:** ROS scavenging by small-molecule antioxidants: key to a neglected treasury of bioactive compounds
15:00-15:15	Katalin Patonay	**SL-15:** Main phenolic constituents of *Mentha longifolia* (L.) L. samples from Northern Hungary – extractability, variability and contribution to some in vitro antioxidant properties of the plant
15:15-15:30	Kimel Katarzyna	**SL-16:** Comparative phytochemical analysis of active compounds from *Symphytum officinale* roots and leaves
15:30-15:45	Surat Laphookhieo	**SL-17:** Bioactive prenylated xanthones from the young fruits and flowers of *Garcinia cowa*
15:45-16:00	Marina Kritsanida	**SL-18:** Centrifugal Partition Chromatography method optimization for the isolation of antibacterial compounds from the fruits of *Pistacia lentiscus*

16:00-17:00	**Coffee + Posters**	**16:00-18:30 SCM**
Session 6 Chaired by Vassilios Roussis		
17:00-17:30	Jean-Luc Wolfender	**PL-10:** Do we still need to isolate Natural Products for their identification? – A paradigm shift in pharmacognosy
17:30-17:45	Anca Miron	**SL-19:** Plant-derived antimicrobials: combination strategies to mitigate antibiotic resistance
17:45-18:00	Aimond Axelle	**SL-20:** Anti-oxidant seasonal variation study of *Sideritis hyssopifolia* by untargeted metabolomics
18:00-18:15	Shaymaa Al-Majmaie	**SL-21:** Antimicrobial activity and mechanisms of action of selected flavonoids from the Rutaceae

19:30-22:00	**Gala dinner in Városliget Café & Restaurant anno 1895**

Friday June 21th, 2019

Session 7 Chaired by Karel Šmejkal		
8:30-9:00	Maria-José U. Ferreira	**PL-11:** Exploring plant metabolites to overcome multidrug resistance in cancer chemotherapy
9:00-9:30	Luc Pieters	**PL-12:** Biological activity of naturally occurring glycosides after gastrointestinal biotransformation
9:30-9:45	Afaf Gerushi	**SL-22:** *In vitro* cytotoxicity of *Asphodelus aestivus* against human cancer cell lines
9:45-10:00	Nancy A. ElNaker	**SL-23:** Antioxidant capacity and in vitro breast cancer cytotoxicity of aqueous extracts from *Arthrocnemum macrostachyum* are affected by drying method
10:00-10:15	Agata Rogowska	**SL-24:** Tracer method (^{14}C-labelling) for investigating the metabolic flux pattern in triterpenoid biosynthetic pathway in *Calendula officinalis* hairy roots after elicitation with jasmonic acid
10:15-10:30	Marie Pokorná	**SL-25:** Biological active compounds from *Morus alba* root bark
10:30-11:00	**Coffee break**	
Session 8 Chaired by Anca Miron		
11:00-11:30	Rudolf Brenneisen	**PL-13:** Medical Cannabis – An Update
11:30-11:45	Claudio Ferrante	**SL-26:** Phytochemical and pharmacological approach for the evaluation of water flower extract activity of four commercial Italian hemp cultivars
11:45-12:00	Misaki Ono	**SL-27:** Anti-tumour activity of four soy isoflavone components against Src-activated human adenocarcinoma cells
12:00-12:30		**AGM**
12:30-14:00	**Lunch**	
Session 9 Chaired by Krystyna Skalicka-Woźniak		
14:00-14:30	**Pierre Fabre Awards**	**PF Award Winner:** Marc Diederich: Natural compound inducers of immunogenic cell death
14:30-15:00	Bruno David	**PL-14:** Pharma industry and plant natural products: today and tomorrow
15:00-15:15	Johanna Gasser	**SL-28:** Polyphenols from waste streams of industrial marzipan production
15:15-15:30	Aidillla Mubarak	**SL-29:** Edible film incorporated with ternary blend cinnamon oil: a natural source for fruit preservation
15:30-15:45	Fatma Sezer Senol Deniz	**SL-30:** Evaluation of possible cosmeceutical effects of Turkish plants
15:45-16:00	Emil Jivishov	**SL-31:** Aromatic sulphur compounds from *Allium* species induce antioxidant signalling in human bladder cancer cells

Session 10 Chaired by Bruno David		
16:00-16:30	Gábor Vasas	**PL-15:** Nonribosomal peptides from cyanobacteria
16:30-16:45	Nellie Francezon	**SL-32**: Marennine-like pigments: microalgae blue mystery
16:45-17:00	Ahmed Latif	**SL-33:** *In vitro* antitumor activity of protoflavone-based hybrid compounds on human gynecological cancer cell lines
17:00-17:15	Marta Oliveira	**SL-34**: A first insight into the nutritional value, phenolic content and biological activities of the halophyte *Cladium mariscus* L. Pohl
17:15-17:30	**PSE Award Ceremony**	
17:30	**Closing Ceremony**	

Plenary Lectures

Satyajit D Sarker
Liverpool John Moores University
Liverpool, United Kingdom

Prof Satyajit D Sarker is the Director of School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, and a Professor of Pharmacy. He obtained his BPharm (Hons) and MPharm degrees from Dhaka University, and a PhD in Phytochemistry from Strathclyde University. His research focuses on prevention and cure of human ailments, particularly, cancers, microbial infections, malaria and inflammation, using phytochemicals. He is the author of >500 publications, and one of the most cited authors in phytochemistry and phytotherapy, with >12,160 citations (*h*-index 51 and *i*-10 index 304).

Prof Sarker is the Editor-in-Chief of *Phytochemical Analysis* (a Wiley journal), in the editorial board of 30 journals, and a regular reviewer for >70 journals. He co-authored *Chemistry for Pharmacy Students* (Wiley & Sons, 2007), which was subsequently translated in Portuguese (2009), Japanese (2012) and Greek (2015) languages; the 2nd edition is coming soon. His other books include, *Magnolia* (Taylor & Francos, 2002), *Steorid Dimers* (Wiley & Sons, 2012), the 2nd and 3rd editons of *Natural Products Isolation* (Humana Press-Springer-Verlag, 2005 and 2012) and *Computational Phytochemistry* (Elsevier, 2018). He has been a *Member* of the Phytochemical Society of Europe since 1991, served as the *Treasurer* (2008-13), the *Vice-President* (2016-18), and has become the President in July 2018. His scientific profile has been published in every volume of the *Marquis Who's Who in the World* since 2010.

PL-1

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Libyan medicinal plants and their cytotoxic compounds

Afaf Al Groshi, Lutfun Nahar, Andrew R Evans, Fyaz M D Ismail and Satyajit D Sarker*

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Libya is a vast country from North Africa. It comprises mainly huge Sahara Desert, the Mediterranean Coast extending over 2,000 km, sea grass meadows covering 1,500 km between Gulf of Sirte in Libya and the Gulf of Gabes in Tunisia, and the Green Mountains (the height can be up to 800 m) including dense forests. Plants from the coastal zone are generally grasses and herbs, the Green Mountains have grasses and trees like junipers, figs and olives as forests, and the desert produces palm, figs and dates [1,2]. There are over 130 vascular plants species that can be considered endemic to the Libyan flora [1]. Many of these plants have been used in the Libyan folk medicine over centuries, even for the treatment of cancers and tumours [3], and *Arbutus pavarii*, *Asphodelus aestivus*, *Juniperus phoenicea* and *Ruta chalepensis* are four of such medicinal plants [2]. Various extracts of these plants were screened for their cytotoxicity against five human cancer cell lines: urinary bladder cancer (EJ-138), liver hepatocellular carcinoma (HEPG2), lung cancer (A549), breast cancer (MCF7) and prostate cancer (PC3) cell lines. A bioassay-guided approach [4] was adopted to isolate and identify cytotoxic secondary metabolites from active extracts and fractions. The cytotoxic potential of the isolated compounds was assessed. This talk will present an overview of the key findings covering distribution, traditional uses, reports on previous studies, isolation and structure elucidation of active compounds, and will provide some scientific rationale behind traditional uses of these plants for the treatment of cancers and tumours.

References

[1] Gawhari AMH et al. *Phytotaxa* 2018; 338:1-16.
[2] Louhaichi M et al. *Advances in Environmental Biology* 2011; 5:359-370.
[3] Elmezogi J et al. *Indonesian Journal of Pharmacy* 2013; 24:127-130.
[4] Sarker SD and Nahar L (2012) *Natural Products Isolation*, 3rd Edition, Humana Press – Springer-Verlag, New Jersey, USA.

Virginia Lanzotti
University of Naples Federico II /Portici
Naples, Italy

Virginia Lanzotti is professor of Organic Chemistry at the University of Naples Federico II, Italy, where she got the degree in Chemistry cum laude on 1982. After a post-doctoral fellowship at the University of Bonn, joining the prof. Breitmaier group, on 1985 she was appointed as researcher at the National Council of Research (CNR), working on the isolation of membrane lipids from archaebacteria. From 1988 to 2009 she was first researcher and then professor of Organic Chemistry at the University of Molise, Italy, working on the discovery of new plant metabolites. On 1989, 1994, 1996 and 1997 she was visiting professor at the University of Leiden, The Netherlands, joining the prof. Altona group, working on conformational studies of DNA oligomers. On 2009 she moved to the University of Naples Federico II, Department of Agricultural Sciences, where she is ERASMUS and International Relationships Delegate. Her research interests are focused on the stereostructure of natural compounds, drug discovery, food chemistry and soil organic matter phytotoxicity. Winner of the 2003 Phytochemical Society of Europe – Pierre Fabre Award for excellence in Phytochemistry, she is in charge as Vice-President of the Phytochemical Society of Europe.

PL-2

doi: 10.14232/tnpr.2019.pl2

NMR spectroscopy and mass spectrometry in the discovery of bioactive natural products

Virginia Lanzotti

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Over the past years there was an increasing attention to the "omics" approaches opening new perspectives to study biological systems. This was mainly due to the development of analytical instrumentation, data processing and chemometric tools that simplified the study of complex systems on a large-scale. Metabolomics is the '-omics' studying the whole metabolome in a cell, tissue or organism from both qualitative and quantitative point of view. The interest in using metabolomics for nutrition, agricultural and food sciences, human health and drug discovery has seen an exponential increase reaching a peak in the last years. This because this approach allows the determination of the metabolite profile of the analysed material without time-consuming and expensive purification steps. Metabolomics is also able to define the biochemical phenotype of a cell or tissue because the chemical complexity of their metabolites, in term of chemical structure and properties, are regulated both by gene expression and environmental conditions. NMR spectroscopy and mass spectrometry are both used in metabolomics studies offering advantages and disadvantages at the same time [1]. We used both approaches for studying the metabolite profile of several plants. Liquid NMR were used to study the chemical composition of food plants of economic interest such as artichokes, tomatoes, and chia seeds [2,3]. Furthermore, these methods have been also used to support a completely new approach in drug development based on the use of nucleic acids searching for more accurate target-specific effects [4].

References

[1] de Falco B, Lanzotti V. *Phytochem. Rev.* 2018; 17: 951-972.
[2] de Falco B et al. *Phytochem. Anal.* 2016; 27:304-314.
[3] de Falco B et al. *Food Chem* 2018; 254:137-143.
[4] Mazzoleni S et al. *Phytochem. Rev.* 2014; 13:937-946.

Matthias Hamburger
University of Basel
Basel, Switzerland

Prof. Matthias Hamburger obtained a degree in Pharmacy from the ETH Zürich (Switzerland) in 1980, and a PhD in Phytochemistry (with Prof. Kurt Hostettmann) from the University of Lausanne (Switzerland) in 1985. He was Postdoctoral Fellow at the University of Illinois at Chicago (with Prof. Geoffrey Cordell), and a Senior Researcher and Privatdocent at the University of Lausanne. From 1993-1996, he was involved with establishing the Center for Natural Products Research (CNPR) in Singapore, a natural products based high-throughput screening and discovery joint-venture of Glaxo (now GlaxoSmithKline) and the Singapore Science and Technology Board. He was Professor and Chair of Pharmaceutical Biology, University of Jena (Germany) from 1997-2004. Since 2004 he is Professor of Pharmaceutical Biology at the University of Basel (Switzerland), and served as Head of the Department of Pharmaceutical Sciences from 2009-2012.

He has published over 300 research and review articles in peer reviewed journals. He served as Editor-in-Chief of Planta Medica, and as President of the Society for Medicinal Plant and Natural Product Research (GA). His main research interests are in natural product based lead discovery and development, in the validation of herbal drugs and phytopharmaceuticals, and in biopharmaceutical evaluation of natural products.

PL-3

doi: 10.14232/tnpr.2019.pl3

Searching for the needle in the haystack – targeted identification of pharmacologically active natural products

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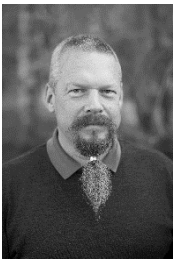
Natural product-derived or -inspired drug discovery continues to be relevant for the development of innovative medicines. However, screening of extracts and identification of bioactive compounds remain major challenges in natural product-based drug discovery. In recent years a wide range of new technologies and tools have been established in the biosciences and in analytical chemistry that enable new approaches. These new possibilities can be summarized with a few keywords such as: miniaturization, on-line analysis of complex samples, chemometric data analysis, functional assays, high-content screening, study of molecular modes of action, and systems oriented approaches towards the characterization of drug effects *in vitro* and *in vivo*.

Over the past years we explored some of these methodologies in our lab and, as a consequence, established a technology platform for miniaturized natural products-based lead discovery. This platform includes 2D-barcoded liquid extract libraries in 96-well format, HPLC-based micro-fractionation for off-line bioactivity assessment, simultaneous on-line spectroscopy (PDA, HRMS, and MS/MS), and off-line microprobe NMR spectroscopy. The platform is generically applicable with mechanism-based and functional assays in the 96-well MTP format and serves as a core for collaborative projects in various therapeutic areas.

Use of the technology platform will be illustrated with selected examples, including the discovery of new allosteric $GABA_A$ receptor modulators and image-based high content screening for compounds targeting key signaling pathways in melanoma. The power of miniaturization will be discussed with the identification of a selectively anti-proliferative cucurbitane derivative from just few mg of a plant extract, and the value of activity profiling data for subsequent structural optimization will be highlighted with the example of the $GABA_A$ receptor modulating lead compound SCT-66. We are currently also using our HPLC profiling approach for the assessment of potential cardiac toxicity of herbal drugs. Dehydroevodiamine and hortiamine, two alkaloids from the traditional Chinese herbal drug *Evodia rutaecarpa*, were identified as potent I_{Kr} blockers with proarrhythmic effects *in vitro*, and *in vivo* in rodent and dog models.



Anders Backlund
Uppsala University
Uppsala, Sweden

Prof. Anders Backlund was born in 1965 in Uppsala started his training at Uppsala University 1986 in the fields of social anthropology and biology, the latter in which he obtained a BSc in 1989 followed by a MSc in systematic botany 1990. The same year he was admitted to a PhD program under supervision by Prof. Kåre Bremer.

After successful defence of his thesis 'Phylogeny of the Dipsacales' in 1996, Backlund received a postdoctoral grant from Swedish National Research Foundation and moved to Trinity College Dublin pursuing a bioinformatics project on chloroplast evolution.

Returning to Uppsala in 1998 and a repatriation grant on structural biochemistry and evolution of RuBisCO with Prof. Inger Andersson at the Swedish University for Agricultural Studies.

In 1999 Backlund was recruited back to Uppsala University to fill a position as lecturer in pharmacognosy working with Prof. Lars Bohlin. Here he has remained and is today, together with Prof. Ulf Göransson, one of the two professors in pharmacognosy at Uppsala University. He also upholds an honorary professorship in natural products research at Kaohsiung Medical University.

At present Backlund is appointed to two administrative assignments, apart from still teaching and performing research in pharmacognosy. Since 2017 Backlund is holding the seat as Vice-Dean for research training at the scientific domain of medicine and pharmacy with a formal responsibility for ca950 PhD-students. Last year he was also appointed Special Advisor to the Vice-Chancellor of Uppsala University in the area of internationalization.

PL-4

doi: 10.14232/tnpr.2019.pl4

Applications of chemography in natural products

Anders Backlund

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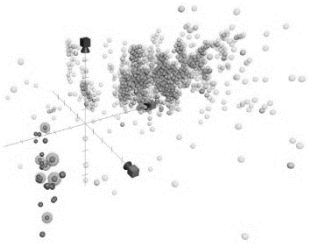
The concept of chemography, navigating chemical space, have over the last decade been applied to a number of studies of natural products.
It has been demonstrated that the concept of proximity in the ChemGPS-NP eight-dimensional chemical property space can be interpreted as a molecular similarity [2], and hence a proxy for the expected biological activity of a particular compound [1].
Combined with methods to define volumes from asymmetric 'clouds' of compound representations, and estimating if a specific compound representation is included in that volume, this provide us with a way of predicting biological activity for a compound – or indicating that an observed activity might be a result of a novel mode of action [3,4].
The basis of an efficient exploration of these possibilities, will be the definition of high-quality reference sets for different biological activities, effectively acting as placeholders.
In this study examples of these applications are demonstrated and discussed.



ChemGPS-NP-based analysis for a series of briarane-type diterpenoids active in an inhibition assay of COX-2, as well as previously studied 2,592 COX-2 (light green) inhibitors from the ChEMBL database.

References

[1] Buonfiglio R et al. *J Chem Inf Mod.* 2015; 55:2375-2390.
[2] Rosén J et al. *J Med Chem* 2009; 52:1953-1962.
[3] Xu J-H et al. *Marine Drugs* 2018; 16:75-83.
[4] Yang L et al. *Molecules* 2017; 22:1392-1408.

Veronika Butterweck

Max Zeller Söhne AG
Romanshorn, Switzerland

Personal Data

Date of Birth: April 16th, 1968

Positions Held

Since 10/2018: Medical Director (Head of Preclinical and Clinical Research), Max Zeller & Söhne AG, Romanshorn, Switzerland
01/2012 – 09/2018: Professor for Pharmacology and Pharmacokinetics, Institute for Pharma Technology, School of Life Sciences, University of Applied Sciences, Muttenz/Basel, Switzerland
07/2009 – 12/2011: Associate Professor of Pharmaceutics, College of Pharmacy, Department of Pharmaceutics, University of Florida, Gainesville, USA
09/2003 – 06/2009: Assistant Professor of Pharmaceutics, College of Pharmacy, Department of Pharmaceutics, University of Florida, Gainesville, USA
08/1997 – 08/2003: wissenschaftliche Mitarbeiterin am Institut für Pharmakologie und Toxikologie, Universitätsklinikum (Researcher, Postdoc level), Westfälische Wilhelms-Universität Münster, Germany

Education

27.07.2003: Venia Legendi for Pharmacology (Habilitation), Mathematisch-Naturwissenschaftliche Fakultät, Westfälische Wilhelms-Universität Münster, Germany
01.07.1997: PhD degree, Mathematisch-Naturwissenschaftliche Fakultät, Westfälische Wilhelms-Universität Münster, Germany
01.02.1994: Board Exam, Licensed Pharmacists
Fall 1988 - Summer 1992: Pharmacy Education, Westfälische Wilhelms-Universität Münster, Germany

Postdoctoral Fellowship

05/1999 – 12/1999 and 01/2001 – 07/2001: Post-Doctoral Fellow, National Institute of Mental Health, and Section on Functional Neuroanatomy, Bethesda, USA

Awards & Honors

1998: Rudolf Fritz Weiss Award, Germany Societyof Phytotherapy, Germany
2002: Phoenix Pharmazie Wissenschaftspreis, Germany
2008: Sebastian Kneipp Award, Germany
2011: Bionorica Phytoneering Award, Germany

Editorial Board

2016 – 2018: Editor in Chief of Planta Medica
2004 – 2015: Editor Planta Medica
2008 – present: Member of the Editorial Board "Phytotherapy Research"
2015 – 2018: Member of the Editorial Advisory Board of the "Journal of Natural Products"
2006 – present: Member of the Advisory Board of the American Botanical Council

Professional Associations

Society for Medicinal Plant & Natural Product Research (GA)
Deutsche Pharmazeutische Gesellschaft (DPhG) (German Pharmaceutical Association)
Deutsche Gesellschaft für experimentelle und klinische
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PL-5

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Polyphenols as biogenic additives and value added products

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Poor aqueous solubility is a common obstacle to delivering bioactive compounds. Numerous examples are known for influencing the absorption by natural adjuvant compounds. Bioavailability of compounds in a plant extract might be influenced by other components in the mixture which are not active themselves but can act to improve the stability, solubility, or the absorption of active compounds. Hypericin, a major active ingredient in St. John's wort, is a compound which is practically insoluble in water. Our search for natural solubilizers revealed that quercitrin and isoquercitrin, but not hyperoside, quercetin or rutin increased the uptake of hypericin in Caco-2 cells. Higher amounts of hypericin were recovered after cell extraction when hypericin was given in combination with various flavonoids [1]. Biogenic additives based on flavonoid structures may therefore provide an interesting strategy to address formulation problems of biopharmaceutically challenging drugs. From a toxicological standpoint flavonoids are ideal excipients since they are biodegradable. In addition, flavonoids are moderately water soluble and cannot cross lipid membranes in the intestine. Thus, their bioavailability is very low. Further, flavonoids are extensively metabolized by gut bacteria in the colon [2]. Many health benefits of flavonoids have been reported, however, the active compounds may not be the native polyphenols found in food, they are more likely to be metabolites [3]. These considerations make the development of a value added polyphenol based dietary supplement for oral intake difficult. To circumvent issues related to the low oral bioavailability of polyphenols a topical application seems to be the preferential form of treatment. However, the industrial development and utilization of flavonoids for medicinal uses are limited because their chemical synthesis is extremely complex and expensive. Using the example of rose oil distillation waste water a promising biotechnology approach will be presented for the recovery and biological activity of high value added flavonoid based 'bioproducts' [4,5].

References

[1] Verjee S et al. *Planta Med* 2015; 81:1111-1120.
[2] Mosele JI et al. *Molecules* 2015; 20:17429-17468.
[3] Dall'Asta M et al. *Nutrition* 2012; 28:197-203.
[4] Solimine J et al. *Fitoterapia* 2016; 108:13-19
[5] Walgren RA et al. *J Pharmacol Exp Ther* 2000; 294:837-843.

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Professor Dr. Rudolf Bauer studied pharmacy at University of Munich from 1976-1980; 1984 graduation as Ph.D. at the Institute of Pharmaceutical Biology, University of Munich, under the supervision of Prof. Dr. Dr.h.c. mult. H. Wagner; 1993-2002 appointment as Associate Professor at the Institute of Pharmaceutical Biology, University of Düsseldorf; since 2002 he is full professor of pharmacognosy at University of Graz, Austria, and since 2004 he acts as Head of the Institute of Pharmaceutical Sciences. He has long experience in natural product chemistry, analysis and the bioassay-guided isolation of constituents from medicinal plants. He has published ca. 360 research papers. From 2002-2007 he has been president of the Society for Medicinal Plant and Natural Product Research (GA), 2012–2014 the founding president of the Good Practice in TCM Research Association, and from 2015-2017 president of the International Society of Ethnopharmacology. He has been Editor of Planta Medica, and currently he is Associate Editor in Chief of the Chinese Journal of Natural Medicines, and Associate Editor of the Ethnopharmacology Section of Frontiers in Pharmacology. Prof Bauer has been doing research in phytochemistry and in the development of methods for quality control of medicinal plants for more than 35 years. He is member of the expert group 13A and chair of the working group on TCM of the European Pharmacopoeia Commission, and actively involved in the development of monographs for the European Pharmacopoeia. Together with Prof. Christine Moissl-Eichinger (Medical University of Graz) and Prof. Gabriele Berg (Technical University of Graz), he has established the "Microbiome and Health Initiative Graz", which is studying the interaction of plant extracts and intestinal bacteria and their impact on human health. He has participated in the Austrian National Research Network "Drugs from Nature Targeting Inflammation" and he is coordinating the TCM Research Cluster Austria within the Herbal Medicinal Products Platform Austria (HMPPA). He has received numerous awards, like Egon-Stahl-Award of the Society for Medicinal Plant Research (1990), the International Award of the Belgian Society of Pharmaceutical Sciences (1996), the Norman R. Farnsworth Excellence in Botanical Research Award of the American Botanical Council (2010), the Distinguished Achievement Award of the International Conference on the Science of Botanicals, Oxford, MS (2016), the Qihuang International Prize of China Association of Chinese (2017), and the Outstanding International Scientist Award (Pranab Banerji Memorial Award) of the Society for Ethnopharmacology India (2018).

PL-6

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The important role of gut microbiota for the therapeutic activity of herbal extracts

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Gut bacteria are processing food, but also herbal medicinal products, and produce signalling molecules that regulate appetite, satiety, and digestion, but also other body functions. Dysbiosis of gut microbiota can contribute to systemic inflammation, it can lead to obesity, asthma, diabetes, autoimmune diseases, and even to certain forms of cancer. Therefore, herbal extracts certainly modulate our health by influencing the gut ecosystem [1,2].

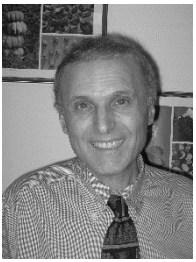
In our research platform, predigestion is conducted in a static *in-vitro* model, according to the InfoGest consensus method. Subsequently extracts are incubated with human fecal suspension under anaerobic physiological conditions. Samples are taken at time points 0.5 h, 4 h, and 24 h. Changes in the composition of plant extracts are monitored by LC-HRMS. Microbiome shifts are tracked by 16S RNA sequencing.

Microbial degradation of many classes of compounds has been observed during incubation of various herbal extracts with human fecal suspension. Flavonoid glycosides and aglycones, procyanidins, salicylic alcohol derivatives, caffeic acid derivatives, and triterpene glycosides, are rapidly and intensively metabolized. Numerous newly formed compounds could be assigned to putative microbial metabolites [3].

In conclusion, the combined LC-HRMS and next-generation sequencing approach allows straightforward detection of relevant microbiome shifts and metabolites. The role of the metabolites as active principles urgently needs to be investigated.

References

[1] Li H et al. *Phytother Res*. 2009; 23:1332-35.
[2] David LA et al. *Nature* 2014; 505:559-63.
[3] Pferschy-Wenzig EM et al. *Front Pharmacol*. 2017; 8:893.



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Born in 1955 (Carmagnola, Italy), Laurea Degree at the University of Torino (Italy) in 1979. Post-Laurea work at the Laboratory of Organic Synthesis, University of Gent (Belgium) with Prof. Pierre De Clercq. Full Professor of Organic Chemistry at the Università del Piemonte Orientale, Department of Pharmaceutical Sciences, Novara (Italy), since 2000.
Research activity in his laboratories takes inspiration from plant natural products to address problems in various realms of biomedical investigation, from pharmacology and nutrition (new drug leads and health-promoting dietary ingredients) to organic/medicinal chemistry (new synthetic methodologies and optimization of natural product drug leads) and cell biology (novel mechanisms of activity). Author of over 350 peer-reviewed articles and 15 book chapters on the chemistry and bioactivity of plant natural products. Editor-in-Chief of *Fitoterapia* and member of the Advisory Board of the *PharmaNutrition*, *Natural Products Reports, Acta Pharmaceutica Sinica b,* and *Progress in the Chemistry of Organic Natural Products*. Recipient of the Rhône-Poulenc Rorer Award of the Phytochemical Society of Europe (1991), of the Medaglia Quilico of the Società Chimica Italiana (2009), and the Bruker Prize of the Phytochemical Society of Europe in 2014 for his studies on bioactive natural products. Member of the Italian Academy of Sciences (Accademia dei XL).

PL-7

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Electrophilic natural products: friends or foes in natural products drug discovery?

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Over the past years, the clinical relevance of covalent modification of druggable proteins by small molecules has been extensively debated within the medicinal chemistry community [1]. Covalent modification underlies the activity of successful drugs, as exemplified by aspirin, penicillin, and modern blockbusters like Pravacid, Nexium and Plavix. Nevertheless, there is still a rooted bias against covalent drugs, dismissed as "library polluters", irrespective of the mechanism by which they ultimately bind to biomolecules. Because of concerns over non-specific toxicity and lack of selectivity, the Michael acceptor motif is rarely introduced in drug leads by design. Paradoxically, our diet is instead rife with Michael acceptors, and food plants provide countless leads to investigate the biological role of Michael reactivity in a molecular context substantially devoid of toxicity, at least at dietary dosages, and therefore of potential pharmaceutical relevance. To capitalize on this opportunity, we have developed an NMR assay (the cysteamine assay) that can identify the reactive sites in electrophilic natural products, rank them in terms of reactivity, and distinguish between transient and non-transient thiol trapping properties [2]. The application of the cysteamine assay to various classes of bioactive natural products will be presented, critically evaluating the information provided by the assay.

References

[1] Newman DJ, Cragg GM. *J Nat Prod*. 2007; 70:461-77.
[2] Avonto C et al. *Angew. Chem. Int. Ed*. 2011; 50:467-471.

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His main research field is including natural products chemistry, medicinal chemistry, transgenic plant (Arabidopsis) reporter assay, epigenetic modulation for microbial secondary metabolites, functional food, traditional Chinese (herbal) medicine, and new drug development. He has more than 380 research articles in SCI refereed journals, more than 500 oral or poster presentation, reviewer of more than 110 different international journals, editorial board members of 8 international journals, authorship of several book chapters; more than 20 patents issued or in application, more than 10 industry-academic cooperation, and more than 5 patent/tech transfer experiences (including one new drug R&D tech transfer).

PL-8

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Development of traditional complex formulas as therapeutic agents

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Traditional Chinese medicine (TCM), a traditional complex formula, has gradually been accepted with the accumulation of practices and experiences. Liu Wei Di Huang Wan (LWDH), Ma-Xing-Shi-Gan-Tang (MXSGT) and San-Huang-Xie-Xin-Tang (SHXXT) are three cases we would like to share in the concept of evidence-based developments on traditional complex formulas. On the basis of our observations, MXSGT would prevent lung fibrosis through the inhibitory effect on nitric oxide generation in bleomycin-induced lung-fibrosis rats. LWDH was proved to improve neurodegenerative disorders. The *in vitro* and *in vivo* evidences of enhanced antioxidant defence and decreased apoptotic death suggested its potential benefits for ameliorating Parkinson's disease. LWDH can also be regarded as a candidate for spinal motor neurons (SMN) deficiency-related diseases. Additionally, we also revealed that LWDH possessed the protection on diabetic muscle atrophy. Both of the LWDH and MXSGT HPLC fingerprints and their quality control parameters were established. However, different qualities and origins of the composed materials are always the most annoying concerns when using TCMs. We focused on comparing 10 commercial SHXXT products from eight TCM companies. Different chemical profiles were found and indicated that each product with the same name might be regarded as a sole medicine and need to be investigated individually. It is never too much to emphasize the importance of quality control in TCM development.

Acknowledgements
Ministry of Science and Technology, Taiwan. Ministry of Health and Welfare, Taiwan.

References

[1] Chang CW et al. *J Food Drug Anal*. 2011; 19:139-145.
[2] Tseng YT et al. *Phytomedicine*. 2014; 21:724-33.
[3] Tseng YT et al. *Phytomedicine*. 2017; 34:97-105.
[4] Tseng YT et al. *Phytomedicine*. 2019; 53:96-106.

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Dr. Attila Hunyadi obtained the PhD degree in 2007 in pharmacognosy from the University of Szeged, Szeged, Hungary. In 2008-2009, he was a postdoc at the Kaohsiung Medical University in Kaohsiung, Taiwan. He is now associate professor at the Institute of Pharmacognosy, University of Szeged.

His main research interest lies in the isolation, characterization, and semi-synthetic modification of bioactive natural products. Until now he published 66 SCI papers (cumulated IF > 180) in the field, more than half of them in the last 5 years. He is academic editor of the journal Evidence-Based Complementary and Alternative Medicine.

He has been the recipient of several prestigious awards, including the 2017 Egon Stahl Award-in-Silver awarded for outstanding achievements in pharmacognosy and phytochemistry. He is the first Hungarian researcher recognized with this distinguished Award.

Above other memberships in national and international scientific societies, he is member of the Board of Directors of the Society for Medicinal Plant and Natural Product Research (GA). For over 8 years he has been actively networking within the frameworks of several European COST Actions.

His current studies focus on biomimetic oxidative chemistry to prepare natural product metabolites, aiming at an antioxidant-inspired extension of chemical space to discover new lead compounds against drug resistance in cancer.

PL-9

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ROS scavenging by small-molecule antioxidants: key to a neglected treasury of bioactive compounds

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Small molecule antioxidants are well-known for their broad range of bioactivities. Most, if not all these bioactivities are connected to the ability of such compounds to interfere with redox biochemical processes. It is now well known that antioxidants modulate oxidative stress mostly through enzymatic processes, and their direct effect on the levels of reactive oxygen and nitrogen species (RONS) through free radical scavenging is rather negligible *in vivo*. Nevertheless, the oxidizable nature of such compounds assures that RONS scavenging does take place when they face a chemical environment provided by oxidative stress. Therefore, locally emerging metabolites of antioxidants oxidized through ROS scavenging must also be considered when evaluating their complex bioactivity [1].

In the lecture, several examples are presented that support the above notion. Biomimetic oxidation of various small-molecule antioxidants can lead to the formation of chemically stable oxidized species with dramatically altered bioactivity profiles as compared to their parent compounds. In our most recent proof-of-concept study we found that the potent antitumor agent graviquinone can be formed *in situ* upon ROS scavenging by methyl-*p*-coumarate, an abundant dietary antioxidant [2].

The above perspective suggests that chemically oxidized metabolites of antioxidants represent a rich segment of chemical space with a particularly high drug discovery potential.

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References

[1] Hunyadi A. *Med Res Rev*. 2019; doi: 10.1002/med.21592.
[2] Fási L et al. *J Med Chem*, 2019; 62:1657-1668.

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Jean-Luc Wolfender is a chemist, who completed a PhD in pharmacognosy with Prof. Kurt Hostettmann (University of Lausanne, Switzerland, 1993). After being responsible of the analytical services of this laboratory, he performed his postdoc with Prof. Al Burlingame on Conus venom profiling (UCSF, San Francisco). He is now full Professor at the Phytochemistry and Bioactive Natural Product research unit of the School of Pharmaceutical Sciences of the University of Geneva (Switzerland), where he was the president of the School and is presently vice-dean of the Faculty of Sciences. He has been strongly involved in the 90s in the introduction of LC-MS and LC- NMR for the profiling of crude plants extracts for dereplication purposes in natural product based drug discovery research programs. He is currently developing innovative MS- and NMR- based metabolomics strategies in the frame of projects related to phytochemistry, microbial interactions and phytotherapy. He is specialised in the de novo structure identification of biomarkers at the microgram scale and is using a miniaturised approach that combines activity-based HPLC profiling and high content information bioassays such as those involving zebrafish. His main research interests are focused on the search of novel inducible bioactive natural products in response to various biotic and abiotic stimuli as well for the study of the mode of action of phytopharmaceuticals from a systems biology perspective. He has many collaborations with South America and Asia mainly in relation with bioactivity guided isolation studies for the discovery of novel natural products of therapeutic interest and his involved in the organisation of workshops for the promoting metabolomics with the natural product community.

PL-10

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Do we still need to isolate Natural Products for their identification? - A paradigm shift in pharmacognosy.

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The recent rapid innovations made in metabolite profiling and bioassays may lead to a change of paradigm in NP research. Indeed having at hand full or partial of structure of possibly all metabolites in given natural extract open the possibility to perform pharmacognosy studies from a more holistic perspective. A question thus arise: *do we still need to isolate Natural Products for their identification*?

The increasing amount of accurate metabolome data that can be acquired from massive sample sets, including high-resolution mass spectrometry analyses (data dependent HRMS/MS), allows natural extracts to be mapped to an unprecedented level of accuracy [1]. To this end, the creation of integrated databases linking the valuable published knowledge provided by pharmacognosy with recent metabolite profiling data through appropriate computer tools could be extremely useful for future development in NP research [2].

In this context we push forward our applications and further development of UHPLC-HRMS/MS molecular network (MN) approaches [3,4] to provide enhanced annotation confidence level though multiple scores, notably taxonomy and MN structural consistency, and we are benchmarking this. We will discuss how far we are from the unambiguous identification of NPs by these approaches and how such advances could significantly accelerate NP research in future. Various recent applications of our research in metabolomics and phytochemistry will illustrate these aspects.

Acknowledgements

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References

[1] Wolfender JL et al. *Anal. Chem.* 2019; 91:704-742.
[2] Allard PM et al. *Curr. Opin. Biotechnol.* 2018; 54:57-64.
[3] Allard PM et al. *Anal. Chem. 2016*; 88:3317-23.
[4] Allard PM et al. *Curr. Opin. Chem. Biol.* 2017; 36:40-49.

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Maria José Umbelino Ferreira obtained her PhD in 1990. She is a Professor of Medicinal and Organic Chemistry at Faculty of Pharmacy, University of Lisbon and the President of the Pharmaceutical and Medicinal Chemistry Department. She is the Coordinator of the Master Course in Pharmaceutical and Medicinal Chemistry at this University.

She leads the research group of Natural Products Chemistry at Research Institute for Medicines (IMed.ULisboa), Faculty of Pharmacy, University of Lisbon.

She is a Regional representative for Portugal and Spain of the Phytochemical Society of Europe (PSE).

MJU Ferreira main research interest is the isolation of new bioactive chemical scaffolds from plant sources and molecular derivatization of selected compounds, using hemi-synthetic methodologies. She is focused on two research areas: cancer and infectious diseases. Particularly, her main goal is to discover anticancer compounds, with emphasis on targeting multidrug-resistant cancer cells, namely ABC-transporter modulators. The development of anti-infective molecules from African medicinal plants, used in traditional medicine, is also one of her goals.

PL-11

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Exploring plant metabolites to overcome multidrug resistance in cancer chemotherapy

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Cancer multidrug resistance (MDR) has been considered as one of the major obstacles for a successful chemotherapy. The most significant mechanism is due to the overexpression of transmembrane transporter proteins of the ATP-binding cassette (ABC) superfamily, which act as extrusion pumps for chemotherapeutic agents, decreasing their intracellular concentration. The most important ACB transporters associated with MDR are P-glycoprotein (P-gp), multidrug resistance protein (MRP1) and breast cancer resistance protein (BCRP). Aiming at obtaining plant-derived metabolites with improved MDR-reversing activity, we have evaluated as P-gp modulators a large number of natural compounds and derivatives, with different scaffolds, using both functional and chemosensitivity assays. Several compounds, namely alkaloid derivatives and nitrogen-containing flavonoids were also evaluated, using MRP1 and BCRP-overexpressing cancer cells as models. The anti-MDR potential of compounds was also assessed by evaluating their ability as collateral sensitivity agents, in resistant cancer cells [1-4].

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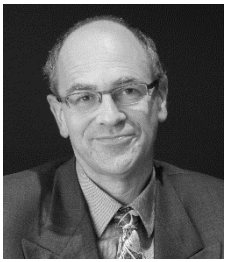
References

[1] Reis MA et al. *J Nat Prod*. 2017; 80:1411-20.
[2] Paterna A et al. *Eur J Med Chem*. 2017; 128:247-57.
[3] Paterna A et al. *Bioorg Med Chem*. 2018; 26:421-34.
[4] Ferreira RJ et al. *Future Med Chem.* 2018; 10:725-41.



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PL-12

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Biological activity of naturally occurring glycosides after gastrointestinal biotransformation

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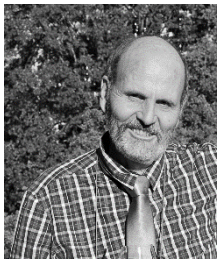
Natural products are often prodrugs, e.g. glycosides, which must undergo *in vivo* metabolic conversion (activation). A *Gloriosa superba* seed extract containing colchicine, a well-known cytotoxic compound, 3-*O*-demethylcolchicine and its glycoside colchicoside, was found to be active in a murine pancreatic tumor model. A colchicoside-rich/colchicine-poor extract with the same total level of colchicine and derivatives showed a similar activity, indicating that colchicoside can be considered as a prodrug [1]. The activity of the anticancer drug gemcitabine could be improved by combining it with a *Gloriosa superba* seed extract [2].
Extracts of the herb *Herniaria hirsuta* are traditionally used in Morocco against kidney and gallstones. Prolonged use of a *H. hirsuta* extract resulted in a cholesterol-lowering effect in the bile of dogs, a pharmacological effect that can prevent the formation of gallstones and can contribute to dissolving existing gallstones [3]. Saponins (medicagenic acid glycosides) have been hypothesized as active principles, but before absorption they need to be deglycosylated. The aglycones (or metabolites thereof) can be absorbed, and may further be metabolized to the ultimate active molecules. Therefore, an *in vitro* gastro-intestinal dialysis model (GIDM) was developed, including microbial fermentation in the colon, to mimic human biotransformation processes. The saponin hederacoside C is discussed as an example, and a novel data analysis approach is presented [4].

References

[1] Capistrano IR et al. *Cancer Biother Radiopharml* 2016**;** 31:99-100.
[2] Capistrano IR et al. *Phytomed* 2016; 23:1434-1440.
[3] Van Dooren I et al. *J Ethnopharmacol* 2015; 169:69-75.
[4] Peeters L et al. *J Chromat A* 2019; 1595:240-247.



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Between 1994-1996 he was appointed to Head of the Analytical Toxicology Unit, Institute of Pharmaceutical Sciences at UniBE; and subsequently to the Head of the Laboratory for Phytopharmacology, Bioanalytics and Pharmacokinetics, Dept. of Clinical Research, UNIBE (1997-2014).

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PL-13

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Medical Cannabis – An Update

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With more than 500 identified constituents *Cannabis sativa* L. (hemp, Cannabaceae) is one of the chemically most elucidated plant. Delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are the cannabinoids in focus whereas mainly terpenoids are part of the non-cannabinoid fraction. Most of the pharmacological effects of cannabis are due to interference with the endocannabinoid system. Despite a plethora of therapeutic effects cannabis and cannabinoids should not be classified as panacea. The still existing discrepancy between empirical (what patients claim from self-treatment) and evidence-based knowledge (what doctors and pharmacists know by education and experience in practice) requires a better interdisciplinary scientific bridging and clinical trials targeting the most promising indications. However, research and use of cannabis and cannabinoid-based medications pose different challenges, such as its complex pharmacokinetics, ideal formulation, safe application mode, and supply. Controversially debated are pros and cons of the two therapeutic options, i.e. «full spectrum» (e.g. cannabis flower extracts) and «single compound» (isolated or synthesized pure THC, CBD). Pharmacopoeia monographs to define quality and industry standards, and appropriate regulatory and legal measure are needed to facilitate the controlled access to medical cannabis, a powerful therapeutic tool still discriminated and ignored by too many countries and medical professionals.

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Bruno joined Pierre Fabre Pharmaceutical Group in 1990 to lead the phytochemistry group. Between 1998 and 2007, he was in charge of the Natural Products Drug Discovery joint team (Pierre Fabre Research Institute/CNRS/IRD) involved in High Throughput Screening. Since 2007, he has been the Director of Natural Products, R&D Sourcing & Botany. Member of the French National Academy of Pharmacy and of many scientific associations, he has coauthored more than 60 publications, books and patents. He also obtained the University Professor Habilitation in 2000.
He is also active in the field of Biodiversity and legal certainty (Member of the Strategic Orientation Council of the Foundation for Research on Biodiversity) and of many professional federations and groups dealing with biodiversity Access and Benefit Sharing (ABS) issues (LEEM, FEBEA, Cosmetics Europe, UNITIS…). He acts also an ABS expert for the French Ministry of Research and the European Commission.

PL-14

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Pharma industry and plant natural products: today and tomorrow

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Vegetal natural products (VNPs) have been the most successful sources of drugs in history. The development of High Throughput Screening (HTS) in the 80s generated a substantial shift towards plants extracts and VNPs in the Pharma Industry. This "Green Rush" terminated in the early 2000s when the Pharma companies stopped their HTS and bioprospecting programmes due to the intrinsic difficulties of this approach plus increasing costs and legal uncertainty to access genetic resources.

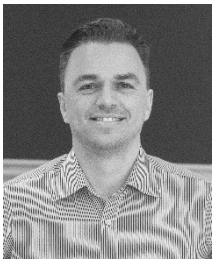
Current drug discovery avenues include the bioprospection of marine organisms and microorganisms (which still have more "low hanging fruits" than VNPs), mining databases like DNP® with biochemoinformatics and artificial intelligence tools, repositioning "old" drugs from vegetal origin, as well as extensive pharmacological profiling of pure compounds. The development of Natural Fragment Libraries such as the NFL® developed at Pierre Fabre is also rather promising.

Plants still have a bright future as Medicines despite the complexity of the recent Access and Benefit Sharing regulations. The use of standardized, purified extracts can bring effective public health solutions notably in developing country for a large part of pathologies. Their use in cosmetology is ever increasing.

These aspects of the future of VNPs will be discussed from the perspective of our 30-year industrial experience at Pierre Fabre (an international medium size Pharma and Dermocosmetics company, 13,000 employees worldwide which derives 40% of its turnover from plants).

References

[1] David B, Ausseil F. High throughput screening of vegetal natural substances. In *Handbook of Chemical and Biologycal Plant Analytical Methods*, First Edition, K. Hostettmann Editor-in Chief, John Wiley & Sons Ltd.
[2] David B et al. *Phytochem Rev.* 2015; 14:299–315.
[3] David B et al (2019) Renewed interest in natural products with a natural fragment library, a new and disruptive approach for innovative drug discovery. Submitted to *Phytochem Rev.*
[4] Chassagne F et al. *Phytochem Rev.* 2019; doi: 10.1007/s11101-019-09606-2



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Gábor Vasas (Hungary) is a full professor in the University of Debrecen, he is the head of the Department of Botany and Division of Pharmacognosy. He is interested in natural product research and chemical ecology of cyanobacteria, microalgae and plants. His department focuses mainly on the identification and quantification of bioactive products, metabolom and microbiome interactions in plants. He is also interested in the potentially toxic cyanobacteria and their toxins, bioactive products and also interested in the cyanobacterial toxin –plant interactions with molecular methods. The Lab's early work on the toxins of cyanobacterial toxicity led to the discovery of the cyanobacterial blooms specificity in Hungarian waters with the grant financed by Hungarian Scientific Research Fund (OTKA) with the project titled "Analyses of the toxin content of cyanobacterial and algal mass production in Hungarian water bodies. Physiological and bioanalytical measurement of the effect of environmental factors on toxin production in isolated cyanobacterial and algal strains". Nowadays They started a new project in this topic with the help of a national grant (NKFIH 119647), titled "Metabolite diversity and function of toxic cyanobacteria". This project focuses mainly on the cyanobacterial oligopeptides produced by the freshwater Microcystis and Nostoc species which form extended layers mass on alkali grasslands in Hungary. The aim is to characterize and identify these peptides, as well as try to improve the understanding of the role of these metabolites in community and their potential use in industrial applications.

PL-15

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Nonribosomal peptides from cyanobacteria

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Cyanobacteria are a diverse and unique photoautotrophic group of prokaryotic microorganisms, thriving in various habitats, such as in aquatic ecosystems, soils and air, and can cope successfully with extreme conditions typical for example in hot springs and polar frosty environments. Most of the cyanobacterial species can produce a wide variety of secondary metabolites with diverse biological activities. The unique cyanobacterium-specific secondary metabolites originated from variable biosynthetic pathways have a great chemical diversity and are widespread across cyanobacterial taxa. Many of these compounds have been isolated and partly or fully characterized from strains cultured under controlled conditions and from field samples, respectively.
The discovery of cyanobacterial natural products has been focusing mainly on their potential pharmacological applications, toxic effects on human and animal health, the physiological roles in the producers or their potentials to serve as allelochemicals. A major family of cyanobacterial secondary metabolites are the oligopeptides synthesized by non-ribosomal pathways, a highly diverse group of low molecular weight peptides built from proteinogenic and non-proteinogenic amino acids. By the most widely accepted classification seven major peptide classes are the follows: aeruginosins, cyanopeptolins, anabaenopeptins, microginins, microviridins, cyclamides, and the well-studied and notorious microcystins.
The aim of this presentation to provide a complete overview of the diversity, distribution and the possible application of these secondary metabolites.

Recipient of the PSE – Pierre Fabre Prize

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Prof Marc Diederich earned his PhD in molecular pharmacology in 1994 from the University Henri Poincaré Nancy 1, France. After training at the University of Cincinnati, USA, he focused his research on cancer and leukaemia cell signalling pathways and gene expression mechanisms triggered by natural compounds with epigenetic-, anti-inflammatory and cell death-inducing potential. He directs the Laboratory for molecular and cellular biology of cancer (LBMCC) at Kirchberg Hospital in Luxemburg. He was appointed Professor of Biochemistry at the College of Pharmacy of Seoul National University in 2012. Since 1998, he is the organizer of the "Signal Transduction" meetings in Luxembourg.

Prof Diederich's research focuses on the development of novel anticancer drugs. As an example, natural marine compounds represent an interesting source of novel leads with potent chemotherapeutic or chemo-preventive activities. In the last decades, structure-activity relationship studies have led to the development of naturally-derived or semi-synthetic analogues with improved bioactivity, a simplified synthetic target or less toxicity. He and his collaborators investigated for example chalcones that are aromatic ketones, known to exhibit anti-microbial, anti-inflammatory and anti-cancer activities. Organic sulphur compounds (OSCs), cardiac glycosides and epigenetically active molecules derived from plants, fungi or bacteria can also serve as chemopreventive and/or chemotherapeutic agents and attracted Prof Diederich's interest as a promising source for novel anti-cancer agents.

PFP

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Natural compound inducers of immunogenic cell death

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Accumulating evidence documents the anticancer potential of the immune response that can be re-established by modulating the immunogenicity of dying cancer cells. This regulated cell death process is called immunogenic cell death (ICD) and constitutes a new innovating anti-cancer strategy with immune-modulatory potential thanks to the release of damage-associated molecular patterns (DAMPs). Some conventional clinically-used chemotherapeutic drugs as well as preclinically-investigated compounds of natural origins such as anthracyclines, microtubule-destabilizing agents, cardiac glycosides or hypericin derivatives possess such an immune-stimulatory function by triggering ICD. In this review, we summarize the effects of ICD inducers on DAMP signaling leading to immune recognition. We will discuss potential strategies allowing to overcome resistance mechanisms associated with this treatment approach as well as co-treatment strategies to overcome the immunosuppressive microenvironment. We will highlight the potential role of metronomic immune modulation as well as targeted delivery of ICD-inducing compounds with nanoparticles or liposomal formulations to improving immunogenicity of ICD inducers aiming at long-term clinical benefits.

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References

[1] Cerella C et al. *Leukemia.* 2017; 31:755-759.
[2] Diederich M., and Cerella C. *Semin Cancer Biol.* 2016; 40-41:4-34.
[3] Mazumder A et al. *Biotechnol Adv.* 2018; 36:1563-1585.
[4] Radogna F et al. *Oncogene.* 2016; 35:3839-3853.

Short Lectures

SL-1

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In vitro antioxidant and enzyme inhibitory properties, metabolomic profile and computational studies *Cistanche phelypaea* (L.)

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Cistanche phelypaea L. is a chlorophyll-free obligate parasitic plant distributed in some arid and semi-arid regions. It is also an edible plant like other species of *Cistanche* genus composed by a variety of phenylethanoid glycosides (PhGs), iridoids, and lignans. These bioactive ingredients are used for treatment of a wide range of human disease [1-3], therefore in this study, ethyl acetate, acetone, ethanol and water extracts from flowers, stems and roots of *C. phelypaea* were appraise for *in vitro* antioxidant activity. Therefore, since the water extracts had the highest antioxidant capacity, they were further evaluated for enzymatic inhibition related with the onset of acetylcholinesterase and butyrylcholinesterase, type 2 diabetes mellitus and skin hyperpigmentation (tyrosinase).
The structural characterization of water extracts was performed by NMR (1D and 2D) analyses. The secondary metabolites present in *C. phelypaea* water extracts showed differences in each sections studied of this plant: in stems, PhGs and iridoids were detected, especially acteoside; in roots were detected essentially PhGs, mainly echinacoside and tubuloside A.
Finally, docking studies were performed on the identified compounds, and indicated this compound as a possible competitive inhibitor of glucosidase and tyrosinase.
Our results suggest that *C. phelypaea* is a promising source of biologically active compounds with health promoting properties for pharmaceutical applications.

References

[1] Zhao S et al. *Recent Progress in Medicinal Plants* 2016; 43:427-456.
[2] Ma Z et al. *Analytical Letters* 2014; 47:2783-2794.
[3] Bougandoura A et al. *Fitoterapia* 2016; 109:248-253.

SL-2

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Metabolomics and *in vitro* cytotoxicity of extracts obtained from a desert plant and its soil

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The use of metabolomics in phytochemical research and drug discovery is becoming more widespread and has been particularly useful for studying changes in biological systems. The metabolomics approach can also be a powerful forensic tool to characterize environments by developing chemical fingerprints for a given environment and detecting environmental changes that are ecologically relevant. This study comparatively evaluates the metabolomics and *in vitro* cytotoxicity (MDA-MB231 breast cancer cells) of aqueous extracts obtained from an arid desert shrub (*Tetraena qatarensis*) and the soil surrounding it (rhizosphere and bulk soil). Metabolites present in extracts were separated and characterized using UHPLC coupled to a quadrupole time-of-flight mass spectrometer (Q-ToF-MS). *In vitro* cytotoxicity was carried out using MTT assays. Preliminary analysis of metabolomic profiles suggest that the plant extract and its soil are remarkably similar and appear well-clustered using principal component analysis. The most abundant secondary metabolites detected in both plant and soil extracts were oleamide, hispidulin and scutellarein-7-glucuronide. Interestingly, only the soil extract exhibited *in vitro* cytotoxicity (LD_{50}=4.57 µg/mL) suggesting the presence of toxins in the soil extract that are not directly of plant origin. Results from this study also suggest that a plant and its soil have a similar metabolomics fingerprint which maybe unique to each plant-soil environment.

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SL-3

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Metabolomic alterations in elicitor-treated grapevine *Vitis vinifera* leaves monitored by ^{1}H NMR

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Pest control represents a predominant issue in viticulture and it is currently achieved by intensive use of fungicides threatening environment and human health. Stimulation of defense responses by elicitors has become a promising alternative strategy of plant protection [1]. In this context, knowledge on impact of such compounds on primary metabolism is fundamental. The aim of this study was a metabolic characterization of grapevine leaves elicited by different molecules triggering jasmonic acid- and/or salicylic acid-dependent responses. Greenhouse *Vitis vinifera* cv. Cabernet Sauvignon cuttings were treated with methyl jasmonate, benzothiadiazole and potassium phosphonates. The changes in metabolism under each condition in regard to untreated leaves were evaluated using proton nuclear magnetic resonance spectroscopy (^{1}H NMR) followed by multivariate statistics. The extensive reprogramming of primary metabolic pathways was demonstrated. The highest concentration of the majority of the identified metabolites, particularly sugars (*myo*-inositol, fructose, sucrose, α- and β-glucose), some organic acids (malic, pyruvic, tartaric, ascorbic and fumaric acids), and phenolics (quercetin-3-*O*-glucoside, syringic, gallic and shikimic acids) was detected in control leaves. Some specific and/or common modifications according to the type of applied elicitor was noticed. A redirection of carbon and energy flow from primary to secondary metabolism in stress mimicked leaves was suggested.

Acknowledgements
The study was performed owing to the financial support of the French Government and the French Embassy in Poland.

Reference
[1] Delaunois B et al. *Environ Sci Pollut R*. 2014; 21:4837-46.

SL-4

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Metabolomics of the alimurgic plants *Taraxacum officinale, Papaver rhoeas* and *Urtica dioica* by combined NMR and GC-MS analysis

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Phytoalimurgy is a term that derives from Greek and Latin and is a combination of the words φυτόν (phytón), which means plant, and alimenta urgentia, which indicates food that one can resort to in case of urgency and necessity, referring to the edible flora that can be used in cases of famine or wars. Nowadays, the lack of produce from agriculture is fortunately no longer a problem, but phytoalimurgy is still a valid part of the applied botany. In fact, today people are becoming more and more interested in foraging for wild plants. This trend is driven by many factors, such as: i) the desire to enrich our diet with healthy food, avoiding pesticides and pollution; ii) the desire to combine outdoor activity, with picking edible plants; iii) the preservation of ancient knowledge and traditions. Furthermore, nourishing our bodies with these plants can provide a wide variety of phytochemicals, ranging from important nutrients our modern diet is often lacking to numerous active constituents that can act on different ailments.

This metabolomic study aimed at evaluating the chemical composition of three cosmopolitan and spontaneous herbaceous plants, namely common dandelion (*Taraxacum officinale*), corn poppy (*Papaver rhoeas*) and stinging nettle (*Urtica dioica*). By involving both NMR and GC-MS techniques, it was possible to detect a wide variety of both primary and secondary metabolites, which possess different nutritional and health benefits.

SL-5

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Investigations on secondary metabolites of a relict oak: *Quercus pontica*

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The genus *Quercus* L. (Fagaceae) has been the subject of intense research due to its important role in the maturation of wines in oak barrels, durability and protection against fungal decay and its application as a food. Some of the *Quercus* (oak) species are used as antifungal, antidiarrheic, astringent, for the treatment of hemorrhoid, tonsillitis, and diabetes [1]. In our previous studies we found that different *Quercus* species exhibited antimicrobial, antioxidant, tyrosinase and α-glycosidase inhibitory properties [2-4]. The genus *Quercus* is known to contain various classes of compounds such as saponins, flavonoids, and tannins. As a part of our ongoing investigations on the *Quercus* species [1-4], we have investigated leaves of *Quercus pontica* C. Koch. A phenolic acid (rosmarinic acid), four flavonol glycosides (kaempferol 3-*O*-β-glucopyranoside, kaempferol 3-*O*-(6''-*O*-galloyl)-β-glucopyranoside, kaempferol 3-*O*-(6''-*O*-coumaroyl)-β-glucopyranoside, quercetin 3-*O*-β-glucopyranoside), a dihydrochalcone (phlorizin) and a flavanol (catechin) were isolated from the ethyl acetate subfraction of the methanol extract of *Q. pontica*. The structure of isolated compounds were elucidated by spectroscopic methods (^{1}H, ^{13}C, and 2D-NMR). To the best of our knowledge, the occurrence of a chalcone is being reported for the first time from the genus *Quercus*. Our investigations on DNA binding properties and inhibitory effects on topoisomerase I and II of isolated compounds is currently ongoing.

References

[1] Şöhretoğlu D, Sakar, MK. *Ankara Univ. J. Fac. Pharm*. 2004; 33:183-215.
[2] Şöhretoğlu D et al. *Food Chem. Toxicol*. 2012; 50:141-146.
[3] Şöhretoğlu D et al. *Rec. Nat. Prod.* 2014; 8:323-329.
[4] Sari S et al. *Bioorg Chem.* 2019; 86:296-304.

SL-6

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Coumarins and polyacetylenes from *Prangos uechtritzii* Boiss&Hauskn roots

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Prangos sp. is an Iran-Turan element, consist of 17 species, is a member of Apiaceae family [1]. There are 30 species around the world mostly distributed in Turkey, Iran, Pakistan and India [2]. The aerial parts of the genus are commonly used as stimulant and carminative whereas roots of the plant are benefitted as aphrodisiac and wound healing agent in Anatolia. *Prangos uechtritzii* is an endemic plant to Turkey, traditionally used in various diseases including stimulant, carminative, wound healing agent and aphrodisiac in Anatolian folk medicine [3]. The purpose of this study is to isolate and elucidate the compounds from *Prangos uechtritzii* root extracts.

The plant material was collected from Taskent/Konya province, 1350 m, on June 3, 2016. Voucher specimens have been deposited in the Ege University Herbarium, Faculty of Pharmacy, Izmir, Turkey (IZEF no: 6050). Air dried roots were extracted with *n*-hexane, chloroform and methanol for 24 h, then filtered. The combined extracts were evaporated with a rotary evaporator to dryness at 40 ˚C. Fractionation and isolation studies of the extracts were carried out with column chromatography, preparative TLC and precipitation methods. Structural elucidation of the compounds was based on spectroscopic evidences (1D, 2D NMR (400 MHz) and MS) and reference data comparison.

13 molecules were isolated which of two are poliacetylenic compounds. Rest of them are coumarin and furanocoumarin derivatives. Suberosin, 7-demethyl suberosin, psoralen, umbelliferone, imperatorin, oxypeucedanin, oxypeucedanin hydrate, oxypeucedanin methanolate, prantschimgin, ulopterol, marmesin, falcarindiol, panaxynol were isolated for the first time from *P. uechtritzii*. Suberosin was found as major one among others in accordance with HPLC results. 7-demethyl suberosin, falcarindiol and panaxynol were isolated and elucidated for the first time from *Prangos* genus.

Through our ongoing study on *Prangos uechtritzii*, 13 compounds have been isolated and identified so far. Pyhtochemical experiments are going on with methanol extract of *Prangos uechtritzii*.

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References

[1] Güner A. *Türkiye bitkileri listesi (Damarlı bitkiler):* ANG Vakfı. Istanbul, Turkey, 2012.
[2] Tada Y et al. *Phytochemistry* 2002; 59:649–654.
[3] Bulut G et al. *J Fac Pharm, Istanbul Univ*. 2014; 44:163–179.

SL-7

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The conundrum of phytochemicals and cancer

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Phytochemicals occupy a unique position in cancer research as they represent the largest class of chemicals that are currently being investigated for the ability to treat cancer (chemotherapy) and the ability to prevent cancer (chemoprevention). Notably this level of investigation into finding new cytotoxics is not without justification as demonstrated by the continued extensive use for cancer treatment of vinca alkaloids (*Catharanthus roseus*), taxanes (*Taxus baccata*), etoposide (*Mandragora officinarum*) and camptothecins (*Camptotheca acuminate*). The relationship between phytochemicals and cancer with regards to chemoprevention is however not as clearly defined as many chemopreventive phytochemicals which can activate important cellular defence pathways are the same chemicals that activate pathways which lead to the development of cancer drug resistance. At the cellular level this seemingly divergent consequence of phytochemical stimulation can be distilled down to the effects of one transcription factor, NF-E2 p45-related factor-2 (Nrf2) which binds to the antioxidant response element (ARE) found in the regulatory regions of over 200 genes involved in both cellular protection and cancer drug resistance [1]. To investigate the potential of phytochemicals to induce this pathway we have utilised a unique cell-based reporter assay [2]. In this presentation our recent efforts to investigate the delicate balance that phytochemicals play in cancer will be considered.

References

[1] Hayes JD et al. *Antioxid Redox Signal*. 2010, 13:1713-1748.
[2] Basar N et al. *Phytochem Anal*. 2016; 27:233-238.

SL-8

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Molecular mechanisms of action of selected steroids in breast cancer cells

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Oestrogen receptors (ERs) represent key biomarker for breast cancer, and their status significantly influences disease prognosis and treatment regimens. Unique library consisting of approximately 8000 steroids derived from natural compounds, e.g. brassinosteroids, with described synthetic pathways was used to find potential ligands for ERs in order to predict compounds that may block their activity.

Two compounds, MU-5562 and MU-5611 showing similar structure motives to estrone have been selected as the most promising candidates showing ER inhibitory activity comparable to routinely used ER inhibitors tamoxifen and fulvestrant. These compounds stabilize ERs similarly to tamoxifen. Determination of luciferase activity showed reduced signals comparable to commercial inhibitors. However, immunochemical analysis revealed decreased AGR2 expression indicating different mechanism of action compared to tamoxifen.

Inhibitory effect of these compounds on ER is probably caused by presence of double bond in their D ring, which protects activation of ERs by decreasing of electron density on keto group. This configuration blocks development of hydrogen bonds network, which is responsible for conformational changes of α-helix H12.

Selected combination of computational and experimental methods represents rational and fast way to determine the activity of given compounds towards ERs. We believe that these data would be used not only in research field, but also in clinical practice.

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SL-9

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Inhibitory activity of a betacyanin formulation from red pitahaya (*Hylocereus polyrhizus*) and red spinach (*Amaranthus dubius*) against polymicrobial biofilms of *Staphylococcus aureus* and *Pseudomonas aeruginosa*

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Staphylococcus aureus (Gram-positive bacteria) and *Pseudomonas aeruginosa* (Gram-negative bacteria) are common biofilm forming bacterial species in many resistant infections. This study investigated the effect of a combination of betacyanin fractions from red pitahaya and red spinach on inhibition of polymicrobial biofilm formation by *S. aureus* and *P. aeruginosa.* Betacyanin fractions were obtained from the pulp of red pitahaya and the leaves of red spinach. Screening of formulations containing various concentrations of the betacyanin fractions showed that the formulation combining 0.625 mg mL^{-1} of each betacyanin fraction inhibited 30.3–45.6% of biofilm formation by five *S. aureus* strains and 32.5–49.8% of biofilm formation by four *P. aeruginosa* strains on polystyrene surfaces. This formulation was 7–9% more effective in inhibiting polymicrobial biofilm of *S. aureus* ATCC 6538P and *P. aeruginosa* ATCC 27853 on polystyrene surfaces compared to using a single fraction. The betacyanin fraction formulation also significantly inhibited polymicrobial biofilms (62.8–78.0%) and reduced bacterial attachment (0.98–1.30 log CFU cm^{-2}) on various other polymer surfaces (polypropylene, polyethylene, polyvinyl chloride and silicone rubber). The betacyanin fraction formulation improved anti-biofilm activity against co-culture of *S. aureus* and *P. aeruginosa* biofilm as compared to individual fractions.

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SL-10

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Effects of major secondary metabolites of *Ricinus communis* on porcine uterine contractility

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Uterine contractility is essential for maintaining reproductive function and fertility. Some medicinal plants are reputed for their effects on fertility and reproduction [1]. *Ricinus communis* L. (Euphorbiaceae), commonly known as 'castor oil plant', is one of those plants well known for its ethnopharmacological usage in controlling reproductive functions and fertility [2,3]. Except for the triglyceride isolated from the beans of this plant, the mechanisms underlying fertility related pharmacological effects of its secondary metabolites remain elusive. Previously, it was shown that the stem bark extracts of castor oil plant could interfere with ovarian cell functions and secretory activity [2]. In continuation of that work, the current *ex vivo* study was undertaken to evaluate the effect of an alkaloid and a triterpene obtained from the stem bark of *R. communis* on porcine uterine contractility. The results indicated the involvement of these tested secondary metabolites in the excitement and depolarisation of the uterine smooth muscle cells.

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References

[1] Das B et al. *Int J Pharm Pharm Sci.* 2014; 6:47-53.
[2] Nath S et al. *Int J Impot Res.* 2015; 27:215-220.
[3] Nath S et al. *J Ethnopharmacol.* 2013; 149:328-334.

SL-11

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Plectranthus zeylanicus Benth: A potent source of secondary metabolites with antimicrobial, disinfectant and anti-inflammatory activities

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Plectranthus zeylanicus Benth is widely used in Sri Lankan folk medicine as a remedy for inflammatory and microbial diseases. In continuation of our previous work on anti-inflammatory activity in lipophilic extracts of this plant, the present investigation was undertaken to evaluate the antimicrobial and disinfectant potency in different organic extracts of *P. zeylanicus* and to isolate bioactive secondary metabolites. The activity-guided fractionation of the most potent dichloromethane extract resulted in the isolation of a pure compound which was extensively studied for its antimicrobial activity by broth microdilution method. Further, its disinfectant potency was evaluated by surface disinfectant assay, while the anti-inflammatory activity was determined by investigating its ability to inhibit the pro-inflammatory enzymes 5-lipoxygenase (5-LO) and microsomal prostaglandin E_2 synthase (mPGES)-1. The spectral data revealed the identity of this compound as 7α-acetoxy-6β-hydroxyroyleanone. It displayed strong antibacterial activity against clinical isolates of methicillin-resistant *Staphylococcus aureus* along with an extremely potent disinfectant capacity, which is comparable to the potency of a commercial disinfectant. Interestingly, it effectively inhibited 5-LO with IC_{50} of 1.3 and 5.1 µg/mL in cell-free and cell-based assay, respectively. Thus, the observed bioactivities of 7α-acetoxy-6β-hydroxyroyleanone rationalize the ethnomedicinal significance of *P. zeylanicus*.

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SL-12

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Prenylated phenolics with anti-inflammatory effects

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The biological activity of phenolics is often modified and enhanced by prenylation by prenyl and geranyl; higher terpenoid chains are rare. The type of the prenyl connection and modification affects their biological activity. The lecture shortly summarizes the effects of prenylated phenolics *in vitro* in cellular or biochemical systems on the production and release of inflammation-related cytokines; their effects on the inhibition of cyclooxygenases and lipoxygenases; the effects on the production of nitric oxide, an antiradical and antioxidant activity, and the effect on the inhibition of the release of enzymes and mediators from neutrophils, mast cells and macrophages. We would show some of our confirmations of selected prenylated flavonoids, 2-arylbenzofurans, and stilbenes as potential antiphlogistic substances. The information about the antiphlogistic potential of prenylated phenolics gives the idea that a big pool of natural prenylated phenols represents a source of inspiration for synthesis, and that prenylated phenols are active principles of various medicinal plants used to combat inflammation.

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SL-13

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Bioactivity of synthetic chalcones in MRC-5 SV2 cells

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Recently researchers have shown an increased interest in chemoprevention using natural products to prevent cancer occurrence and to slow its progression. Chalcones belong to the flavonoid family of phytochemicals and have been extensively investigated for their chemopreventive capacity, and found to induce a battery of cellular detoxification enzymes through activation of the transcription factor NF-E2 p45-related factor-2 (Nrf2) [1,2]. Additionally, chalcones are known to inhibit DNA synthesis consequently inducing cell cycle arrest [3].
In this study, we have investigated the ability of a library of novel synthetic chalcones to induce the classical Nrf2 stimulated gene NAD(P)H: quinone oxidoreductase-1 (NQO1) in MRC-5 SV2 cells (human lung epithelial cancer). NQO1 protein induction was assessed by western blotting and the results showed that five chalcones induced NQO1 protein at 24 h. Interestingly, it was also noted however that chalcones (at non-toxic concentrations) decreased cellular viability in presence of malondialdehyde.

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References
[1] Suwito H et al. *J Chem and Pharm Res* 2014; 1076-1088.
[2] Zhou B and Xing C. *Med Chem* 2015; 5:388–404.
[3] Watson R et al. *Polyphenols in Human Health and Disease*, 1st Edition, Academic Press, Amsterdam, Netherlands, 2014.

SL-14

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Ononis isoflavonoids aiming the CNS

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Based on our previous results, *Ononis spinosa* L. contains a wide variety of isoflavonoids [1,2], of which formononetin showed favourable results in the treatment of Alzheimer-disease *in vivo* and *in vitro* [3], maackiain could inhibit selectively the MAO-B enzyme [4]. Regarding these outcomes, *Ononis* species could be rich sources of compounds affecting the CNS.

Since with biotechnology secondary metabolite production can be multiplied, the investigation of the isoflavonoid production of *in vitro* cultures was aimed beside the qualitative and quantitative characterization of free-range *Ononis* species. Moreover, we intended to study the CNS permeability of these isoflavonoids.

The main technique of the qualitative investigation was UHPL-HR-MS/MS supplemented with NMR experiments. For the quantitative measurements, HPLC-DAD and HPLC-ESI-MS/MS methods were developed. The isolation of the compounds was executed using flash-chromatography and preparative HPLC. The permeability through the blood-brain barrier was estimated by PAMPA-BBB model.

Based on the results of the quantitative analysis both *Ononis* species are very rich in isoflavonoids, but the hairy root cultures of *O. spinosa* exceeded all samples with outstandingly high total-isoflavonoid content. However, we found remarkable differences between the isoflavonoid profile of the *in vitro* and the free-range samples. According to the PAMPA-BBB measurements, all investigated isoflavonoid could pass the brain-blood barrier.

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References

[1] Gampe N et al. *J Pharm Biomed Anal* 2016; 123:74–81.
[2] Gampe N et al. *J Chromatogr B* 2018; 1091:21–28.
[3] Fei HX et al. *Biosci Biotechnol Biochem* 2018; 82:57–64.
[4] Lee HW et al. *Bioorg Med Chem Lett* 2016; 26:4714–4719.

SL-15

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Main phenolic constituents of *Mentha longifolia* (L.) L. samples from Northern Hungary – extractability, variability and contribution to some *in vitro* antioxidant properties of the plant

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Mentha longifolia (L.) is a less studied wild-growing species. The aim of experiments is to define effective extraction of its polyphenolic antioxidants, and to observe the variability of them. The present work is the first phytochemical screening of the plant in Europe. Thirty-six accessions were sampled in flowering state. Soxhlet and ultrasonic (US) extraction, both with methanol (MeOH) and ethanol-water 7:3 (WA) were applied. HPLC-DAD measurements were performed on extracts. Dominant phenolics were rosmarinic acid (7043-38667 mg/kg drug, lower than determined in Israeli populations of the plant [1], similar to peppermint [2]) and hesperidin (from 1985 mg/kg to 20000< mg/kg), accompanied by diosmin (398.3-7987 mg/kg, similar to peppermint[2]), and cynaroside (318-2553 mg/kg). For cynaroside and rosmarinic acid, WA methods were more efficient than MeOH extractions. In case of the other two flavonoids, MeOH extraction were the more efficient compared with the WA and there was no significant difference between US and MeOH Soxhlet. Rosmarinic acid was in significant, medium correlation with the DPPH and FRAP values of extracts (R=0.49-0.55 depending on extract type; $p<0.01$ in all cases). Cynaroside did not show significant correlation with these activities contrary of its strong antioxidant capacity.
Other major constituents were observed in all of the chromatograms at ca. t_R=13.7' and t_R=19.7'. Their identification needs further examinations.

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References
[1] Dudai N et al. *Acta Hortic* 2006; 709:69-78.
[2] Guédon DJ, Pasquier BP. *J Agric Food Chem* 1994; 42:679-684.

SL-16

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Comparative phytochemical analysis of active compounds from *Symphytum officinale* roots and leaves

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Comfrey (*Symphytum officinale*) has been used as a herbal medicine for >2000 years, mostly as a promoter of wound healing, analgesic and anti-inflammatory agent in musculoskeletal problems [1,2]. Although its molecular mechanism of action remains unclear, the efficacy of comfrey remedies has been confirmed in several clinical trials [3]. The aim of the research was to analyze and compare chemical composition of biologically active compounds, especially allantoin and phenolic compounds – simple phenols and flavonoids in comfrey roots and leaves obtained from different sources. Therefore, the TLC-densitometric method of allantoin determination was optimized. The analysis was carried out on TLC Si60 and TLC $Si60_{F254}$ plates with the mobile phase: butanol-50 % methanol 2:1+0.16 mL HCOOH/60 mL of solvents mixture. The determined allantoin content varied from 0.35 to 2.17% in roots and was below the quantification limit in leaves. Moreover, the chemical profiles of analysed samples were compared with HPLC methods. As the result, quantification of phenolic acids was carried out (rosmarinic acid – in range of 0.59-1.84% in roots and 1.91-2.41% in leaves and caffeic acid – respectively 0.11-0.14% and 0.13-0.19%) and new glycosylated flavonoids in comfrey leaves were identified by the HPLC-DAD-MS. Antioxidant activity of both plant materials was compared with spectrophotometric assays (DPPH, ABTS and FRAP) and TLC-bioautography methods (DPPH, XO inhibition, riboflavin-light-NBT).

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References

[1] Rode D. *Trends Pharmacol Sci*. 2002; 23:497-499.
[2] Frost R et al. *Complement Ther Clin Pract.* 2014; 20:347-355.
[3] Staiger C. *Phytother Res.* 2012; 26:1441-1448.

SL-17

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Bioactive prenylated xanthones from the young fruits and flowers of *Garcinia cowa*

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The phytochemical investigation of *Garcinia cowa* (fruit, flower, and stem bark extracts) resulted in the isolation and identification of nine compounds including six xanthones, two benzophenones, and one symmetrical dimeric dihydrobenzopyran together with 25 known compounds. The structures of these new compounds were determined on the basis of their spectroscopic data. Most of the isolated compounds were evaluated for their antibacterial activities and α-glucosidase inhibitory activity. Some compounds showed good antibacterial activity against the Gram-positive bacteria, *Bacillus subtilis* TISTR 688, *B. subtilis* TISTR 008, *Staphylococcus aureus* TISTR 1466, and methicillin-resistant *S. aureus* (MRSA) SK1 with MIC values ranging from 2-8 μg/mL. α-Mangostin and β-mangostin isolated from the flower extract showed good α-glucosidase inhibitory activity.

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SL-18

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Centrifugal Partition Chromatography method optimization for the isolation of antibacterial compounds from the fruits of *Pistacia lentiscus*

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Herbal preparations from several parts of *Pistacia lentiscus* L. (Anacardiaceae) such as resin (mastic gum), fruits, leaves, oil have been traditionally used in the Mediterranean basin for more than 2,500 years for their medicinal properties [1]. Mastic gum of this species harvested from Chios Island (Greece) contains antibacterial triterpenes (24-*Z*-masticadienonic acid derivatives MAD) [2] but their isolation is tedious, due to the presence of a myrcene polymer. The chemical composition of the fruits, considered as a waste of mastic production, was never extensively studied. Thus, we focused on this part of the plant as a potential source of bioactive metabolites.

In a preliminary step, small amounts of MAD and salicylic acid derivatives (SAD) isolated from a fruit extract using silica gel chromatography have strongly inhibited the growth of *Gram+* aerobic and aerotolerant bacterial strains.

Centrifugal Partition Chromatography is a fast technique with feasible scale-up, based on the partition between two immiscible liquid phases. However, because of close polarity, SAD partially co-elute with triterpenes. A solvents combination including some percent of ammonia solution was then optimized in order to provide a better retention of the salicylates and an efficient separation of all of the targeted compounds in only one run with a good yield.

These results could lead to the valorisation of fruits and of their constituents as natural preservatives for food and cosmetic industry.

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References

[1] Assessment report on *Pistacia lentiscus* L., resin (mastix). EMA/HMPC/46756/2015 Committee on Herbal Medicinal Products (HMPC).
[2] Rodriguez-Garcia A et al. *Mini-Reviews in Organic Chemistry* 2017; 14:272-279.

SL-19

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Plant-derived antimicrobials: combination strategies to mitigate antibiotic resistance

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Infectious diseases (lower respiratory infections, diarrhoeal diseases, tuberculosis) are among the top 10 global causes of death. The high mortality rate of infectious diseases is primarily due to antibiotic resistance. Synergistic combinations of natural products with conventional antibiotics represent a promising strategy in overcoming antibiotic resistance. Due to a multitarget activity, synergistic combinations might reverse antibiotic resistance. In our studies, we investigated both volatile and non-volatile plant extractives but also pure phytochemicals regarding their potential to act synergistically with antibiotics and reverse antibiotic resistance. Checkerboard and time kill assays allowed us to identify plant extracts (white mulberry leaf extract, coriander essential oil) and phytochemicals (morusin, kuwanon G, xanthohumol, 8-prenylnaringenin) having the ability to reverse oxacillin resistance of methicillin-resistant *Staphylococcus aureus* and tetracycline resistance of *Staphylococcus epidermidis* [1]. Synergistic interactions between plant extractives/phytochemicals and conventional antibiotics are also described [1-3]. The findings are promising for the development of novel strategies in the treatment of bacterial infections.

References

[1] Aelenei P et al. *Lett Appl Microbiol*. 2018; 68:156-164.
[2] Gradinaru AC et al. *Lett Appl Microbiol*. 2018; 67:449-457.
[3] Gradinaru AC et al. *Nat Prod Res*. 2014; 28:2076-2080.

SL-20

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Anti-oxidant seasonal variation study of *Sideritis hyssopifolia* by untargeted metabolomics

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Untargeted metabolomics can be a useful approach to follow the metabolome variation of a plant in term of composition and biological activity. In this study we used this approach to follow the metabolomics variations occurring during the seasons in the species *Sideritis hyssopifolia*. 10 samples of the plant were collected at four different periods of the year. After an ethanolic extraction, the extracts were analysed by DDA LC-MS/MS. The pre-processing of the data was managed on MZmine2 with using .mzXML converted files. The resulting aligned peak intentisties was uploaded on the MetaboAnalyst 3.0 website for the statistical analysis. All extracts were tested for anti-oxidant activity.
From a metabolome perspective, the data showed a good separation of the 4 groups with a seasonal trend and the same pattern was observed using a biological mapping of the data. In order to annotate the features of interest, molecular networking was undertaken using both MetGem and MetWork (for the *in silico* metabolization). Eventually, isolation of the compounds was realized for the pure compound activity testing.

SL-21

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Antimicrobial activity and mechanisms of action of selected flavonoids from the Rutaceae

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Flavonoids are phenolic compounds widely distributed in plants, some of which are pigments and provide protection against ultraviolet radiation, pathogens and herbivores. They are often used as nutritional supplements to promote health and well being. Flavonoids are also added to pharmaceutical and cosmetic products. They possess antioxidant, antifungal, antibacterial, antimutagenic and anticancer proprieties. In the current study, thirteen flavonoids isolated from *Citrus sinensis* and *C. grandis* of the family Rutaceca using Soxhlet extraction (*n*-hexane, dichloromethane and methanol) [1], and the extracts were screened for antimicrobial activity using the resazurin assay [2]. The active extracts were fractionated by vacuum liquid chromatography or solid-phase-extraction, and subjected to antimicrobial tests. The active fractions were analysed by preparative high performance liquid chromatography (HPLC). Finally, the antimicrobial activity of the isolated flavonoids were determined against two strains of Gram negative (*Escherichia coli, Pseudomonas aeruginosa*) and two strains of Gram positive (*Micrococcus luteus*, *Staphylococcus aureus*) bacteria. In addition, the flavonoids were screened for antifungal activity against *Candida albicans*. The possible mechanisms of action of these compounds were also evaluated.

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References
[1] Sarker SD, Nahar L. *Natural Products Isolation*, 3rd Edition. Humana Press – Springer-Verlag, New Jersey, USA, 2012.
[2] Sarker SD et al. *Method*. 2007; 42:321-324.

SL-22

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In vitro cytotoxicity of *Asphodelus aestivus* against human cancer cell lines

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Asphodelus aestivus Brot. (Asphodelaceae) (AA) is a Libyan medicinal plant used traditionally to treat haemorrhoids, burns and some skin diseases. Previous studies on AA identified the presence of anthranoids, flavonoids and triterpenes. In this study, the cytotoxicity of *n*-hexane, dichloromethane (DCM) and methanol (MeOH) extracts of the leaves and tubers of AA were studied against EJ138 (human bladder carcinoma), HepG2 (human liver hepatocellular carcinoma), A549 (human lung carcinoma), MCF7 (human breast adenocarcinoma) and PC3 (human prostate carcinoma) cell lines using the MTT assay. The DCM tuber extract showed high cytotoxicity against both A549 and PC3 cell lines with IC_{50} values 16 and 19 µg/mL, respectively, while the DCM extract of the leaves displayed cytotoxicity against both HepG2 and A549 cell lines with IC_{50} values of 70 and 90 µg/mL, respectively. Six compounds were isolated from different extracts of AA including: luteolin (**1**), *p*-hydroxy-phenethyl *trans*-ferulate (**2**), chrysophanol anthrone (**3**), chrysophanol-10,10'-bianthrone (**4**), aloe-emodin (**5**) and C-α-rhamnopyranosyl bianthracene-9, 9'-trione glycoside (**6**). The isolated compounds **1, 3**, **4** and **6** were tested for their cytotoxicity against the prostate cancer (PC3) cell lines. Compound **6** revealed good cytotoxicity with an IC_{50} value of 62 µM, while luteolin (**1**) showed moderate cytotoxicity with an IC_{50} value of 201 µM.

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SL-23

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Antioxidant capacity and *in vitro* breast cancer cytotoxicity of aqueous extracts from *Arthrocnemum macrostachyum* are affected by drying method

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Arthrocnemum macrostachyum is a halophytic perennial shrub that is widespread across coastal zones in the Mediterranean basin, Middle East, and Asia. This plant can survive in arid desert climates where temperatures can sometimes exceed 60 °C in mid-summer days. In this study, we examine how drying method (oven vs. lyophilization) and drying temperature (40 and 60 °C) of macerated extracts (water and 50% aq. ethanol) from *A. macrostachyum* are affected in terms of antioxidant capacity and bioactivity (cytotoxicity towards MDA-MB231 cancer cells). Oven drying caused a 1.5-2 fold reduction in antioxidant capacity for both extracts (water and 50% ethanol) compared to lyophilization. The lyophilized 50% ethanol extract had the highest antioxidant capacity (DPPH IC_{50}=35.84 µg/mL) compared to all other treatments. Oven drying of extracts also resulted in a reduction in *in vitro* anti-cancer activity as measured using MTT assay on MDA-MB231 breast cancer cells. Lyophilized water extract showed the highest *in vitro* cytotoxic activity (LD_{50}=0.671 mg/mL) compared to all other treatments. These findings indicate that drying conditions impact bioactivity and suggest that *A. macrostachyum* is a potential source of anti-cancer agents.

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SL-24

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Tracer method (^{14}C-labelling) for investigating the metabolic flux pattern in triterpenoid biosynthetic pathway in *Calendula officinalis* hairy roots after elicitation with jasmonic acid

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Triterpenoids are plant metabolites derived from the C30 linear precursor squalene. Their functions are ascribed both to primary metabolism (e.g. participation of sterols in the structure and fluidity regulation of cellular membranes) and secondary (specialized) metabolism, particularly involved in diverse strategies of plant chemical defence. Therefore, the biosynthetic step of 2,3-oxidosqualene cyclization is often regarded as a branch point between primary and secondary triterpenoid metabolism [1], which can be switched in response to various stress factors. The aim of the present study was to investigate the possible modifications in metabolic flux pattern in biosynthetic pathway of triterpenoids in marigold *Calendula officinalis* hairy root culture after elicitation with jasmonic acid with the use of radioactive precursor: ^{14}C-labelled mevalonic acid. Labelling dynamics evaluated during 3 weeks after elicitation revealed that pentacyclic triterpene acid – oleanolic acid was approx. 100-times better labelled that in the untreated control, whereas sterols were labelled by 30% better in the control as compared to elicited samples. The obtained results confirmed that jasmonic acid induces the redirection of the carbon flow between the two competing pathways following 2,3-oxidosqualene cyclization, and it favours the biosynthesis of defence compounds over metabolites involved in basic metabolism.

Reference

[1] Moses T et al. *New Phytologist* 2013; 200: 27-43.

SL-25

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Biological active compounds from *Morus alba* root bark

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In vitro biological screening of 26 mulberry constituents identified promising candidate drugs for further biological research. Antiviral, antibacterial, anti-inflammatory, and antiplasmodial activities were evaluated. Five prenylated compounds, together with a phenolic ester, proved to possess inhibitory activity against the replication of HSV-1 or HSV-2 with IC_{50} (EC_{50}) values of 0.64–1.93 μg/mL. Molecular docking studies for HSV were performed for active compounds. Several compounds exhibited significant growth inhibition of all bacterial strains tested with MICs values 1–16 μg/mL. Furthermore, one compound was found to inhibit COX-2 with a greater activity than positive control indomethacin.

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SL-26

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Phytochemical and pharmacological approach for the evaluation of water flower extract activity of four commercial Italian hemp cultivars

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One of the most promising economic perspectives of hemp production chain is female inflorescence valorization. By contrast, scientific literature lacks on chemical composition or biological activity data from aqueous fraction obtained from industrial hemp flowers, which have long been considered as waste products. In this context, the main focus of the following study is the evaluation of protective effects related to water flower extracts from four commercial hemp cultivars (Futura 75, Kc virtus, Carmagnola Cs and Villanova). We evaluated the phytochemical profile of the extract. Then we studied the water extracts both *in vitro* and *ex vivo* in order to assay protective effects in an experimental model of ulcerative colitis, constituted by isolated LPS-stimulated colon. All cultivar extracts displayed similar total phenol and flavonoid content. On the other hand, Futura 75 cultivar extract displayed a better antioxidant and anti-inflammatory profile. Considering this, Futura 75 extract has been subsequently assayed to evaluate its effect on pathogen bacterial and fungal species involved in ulcerative colitis, finding a significant inhibition on the growth of *C. albicans* and selected Gram positive and negative bacterial strains.
Taken together, our results support the potential efficacy of Futura 75 water extracts in managing the clinical symptoms related to ulcerative colitis.

SL-27

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Anti-tumour activity of four soy isoflavone components against Src-activated human adenocarcinoma cells

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Src oncogene has been strongly implicated in the development, growth, progression, and metastasis of a variety of human cancers [1]. Genistein (GEN), a natural isoflavonoid phytoestrogen, is a strong inhibitor of Src [2]. Although daidzein, glycitein and equol, a metabolite of daidzein, are also major soy Isoflavone components, their functional role in Src activity remains unknown. Using HAG-1 human adenocarcinoma cells transfected with v-src (HAG/src), we investigated the anti-tumour activity of four isoflavone components by measuring proliferation, apoptosis, cell cycle perturbation, and signal proteins with WST-1 assay, FACS analyses, and Western blot, respectively. Activation of Src conferred resistance to either daidzein, glycitein or equol, but rendered the cells more sensitive to GEN. GEN arrested HAG/src cells at G2/M phase, while other isoflavones could not arrest HAG/src cells at any phase of the cell cycle. The sub-G0/G1 apoptotic cell populations were not increased over 72h exposure with either isoflavone components. GEN increased the expression levels of p53 and p21 with decreased phosphorylated p21. The levels of other main cell cycle-related proteins were not affected. These data suggest that GEN would be the only isoflavone component that may potentially suppress oncogenic activity driven by Src through increasing p53 and p21 levels.

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References
[1] Yeatman TJ. *Nature Reviews Cancer.* 2004; 4:470-480.
[2] Akiyama T et al. *The Journal of Biological Chemistry*. 1987; 262:5592-5595.

SL-28

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Polyphenols from waste streams of industrial marzipan production

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The valorisation of waste streams from industrial marzipan production is to be realised by the recovery of bioactive components. Almond skins as well as blanch water contain a crude mixture of polyphenols and procyanidins with high structural variety [1]. New sources for polyphenols are in demand due to their antioxidant potential and their suggested ability to prevent chronic diseases [2]. Here we report the isolation and structural characterisation of polyphenols yielded from the waste streams. The selected extraction methods allow application in a recycling concept by providing the substances in a transportable and storable form. Polyphenols from the blanch water were enriched by a factor of 3.4 using Amberlite XAD-7HP adsorption [3]. After ultrafiltration of the eluate, preparative C18-HPLC separation yielded corresponding fractions of polyphenols. Total phenolic content was measured with Folin Ciocalteu assay, while oxygen radical capacity assay was used to determine the antioxidant activity of the fractions. Active fractions were characterized by HPLC-ESI-ion trap MS identifying known compounds. Also not yet described compounds like dimeric *B*-linked propelargonidin-hexoside as $[M-H]^-$-ion at *m/z* 723 were detected by LC-MS. These results should lead to a scale up of the described methods for polyphenol recovery in food industry.

Acknowledgements
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References
[1] Hughey CA et al. *Food Chemistry* 2012; 131:1165–1173.
[2] Bolling BW. *Comprehensive Reviews in Food Science and Food Safety* 2017; 16:346–368.
[3] Buran TJ et al. *Journal of Food Engineering* 2014; 128:167–173.

SL-29

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Edible film incorporated with ternary blend cinnamon oil: a natural source for fruit preservation

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Perishability of fruits has continued to be a challenge in extension of shelf life in the effort to reduce extensive postharvest losses. Among various treatments to delay deterioration of fruits, interest in research of edible films is sustained due to its potential as a natural source substitute to the use of synthetic coatings [1]. Edible film has the ability to be a carrier for other substances containing rich amount of phytochemicals such as essential oil [2], which can provide additive protection on the fruits. Cinnamon oil has been utilized for centuries as medicinal plant as well as food preservatives largely due to its various bioactive phytochemical constituents [3]. The efficacy of an edible film with combination of essential oil depends largely on the production method and the ability of the film to adhere to the fruit surface. Combination of oil and water through the ternary blend strategy has enabled the development of edible films with unique and riveting properties. In this study, gelatin-based edible films containing different ratios of cinnamon oil:Tween 80:water was prepared through solvent-casting method to evaluate the effectiveness on retaining quality and freshness of wax apples (*Syzygium samarangense* L.). An increase in the cinnamon oil content shows reduction in the water solubility and water vapour permeability of films which are the key parameters to maintain freshness of food. Quality factors of the wax apples which include weight loss, ascorbic acid content and antioxidant activity were improved significantly ($p<0.05$) in wax apple wrapped with the cinnamon oil-incorporated films when compared to control wax apples (unwrapped) as well as wax apple wrapped with gelatin film only. These findings suggest that edible film incorporated with cinnamon oil using the ternary blend is a promising natural source alternative that can replace the use of synthetic materials in retaining quality, as well as enhancing safety and nutritional trait of the fruit.

Acknowledgements

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References

[1] Rojas-Graü MA et al. *Trends Food Sci Technol*. 2009; 20: 438-447.
[2] Raybaudi-Massilia RM et al. *Int J Food Microbiol*. 2008; 121: 313-327.
[3] Rao PV, Gan SH. *Evid Based Complement Alternat Med*. 2014; 2014:1-12.

SL-30

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Evaluation of possible cosmeceutical effects of Turkish plants

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Cosmeceuticals contain synthetic, plant-, and animal-derived materials. However, use of herbal ingredients in cosmetic formulations are on increase mostly due to side effects of synthetic compounds. Dermis, which is the middle layer of the skin consisting of connective tissue components, provides flexibility and resistance to skin. Elastin and collagen, two important proteins being the main components of the connective tissue, are responsible for resistance and elasticity of the skin. Hydrolysis of them through elastase and collagenase triggered by free oxygen radicals cause wrinkle formation accompanied by skin aging. Reactive oxygen species are not stable and cause a huge level of physiological damage, while they are associated with cell damage in various tissues in addition to many diseases. Antioxidant compounds are the substances that may scavenge harmful free radicals produced in the body by different reasons. Tyrosinase is a copper-containing melanogenic enzyme that is present in microorganisms, plant, and animal tissues. Recently, search on reliable and potent tyrosinase inhibitors have gained importance for skin-bleaching purpose in hyperpigmentation therapy. In the light of this information, approximately 99 herbal extracts and propolis were investigated for their elastase, collagenase, and tyrosinase inhibitory effects using ELISA microtiter assays in a large screening, while their antioxidant effect was determined using various *in vitro* methods. Based on our results we selected *Cotinus coggyria* Scop. (Anacardiaceae) and *Maclura pomifera* (Raf.) C. K. Schneid. (Moraceae) for future studies.

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SL-31

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Aromatic sulphur compounds from *Allium* species induce antioxidant signaling in human bladder cancer cells

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In this study, anticancer effect of ethyl acetate extracts from bulbs and flowers of 68 *Allium* species originated from Southwest Asia to the high mountains of Central Asia were analysed, with many of them being evaluated for the first time. The extracts were analysed dose dependently and compared to two pure known *Allium* compounds namely, 2,2'-dipyridyl disulphide and dipyrithione. Doxorubicin drug was used as a reference. Human bladder cancer cell lines T24 and UMUC3 were tested in comparison to non-cancer primary human foreskin fibroblasts (HFF). The most cytotoxic species were *A. stipitatum* (Afghanistan), and *A. aflatunense* with the LD_{50} values comparable to the doxorubicin's LD_{50} value. Toxicity of the *Allium* extracts against human foreskin fibroblasts (HFF) cells was considerably higher than the toxicity of the doxorubicin. The extracts of *A. stipitatum, A. aflatunense,* and of other species were analysed for effects on cell death and cell cycle. The extracts caused a significant increase of the sub G1 events. Additionally, cyclin dependent kinase inhibitor (CDKN1A) was induced. Using bioassay guided fractionation, aromatic sulphur compounds from *A. stipitatum* and *A. aflatunense* extracts, were identified as active compounds acting as oxidative stress inducers. This suggestion was supported by the observation that the treated cells displayed enhanced antioxidant signaling pathway mediated by Nrf2 as indicated by enhanced HO-1 levels.

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Marennine-like pigments: microalgae blue mystery

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Microalgae represent new sources of proteins, lipids, carbohydrates and molecules with high added value. Among them, blue diatoms of the genus *Haslea* stand out for their ability to produce water-soluble blue-green pigments, released in the so-called "blue water" [1]. In particular, the species *Haslea ostrearia* has long been known to synthesize marennine, which is responsible for the greening of oysters in refining oyster-ponds of western France ("fines de claires vertes"). This compound could be regarded as a new natural blue dye for the cosmetic and food industries, as the demand is growing increasingly, however, the chemical structure of this complex biopolymer still remains unknown. Moreover, new species of blue *Haslea* producing marennine-like pigments have been discovered recently [1, 2]. The Bluedimary project (Blue diatoms and marennine-like pigments for biorefinery) seeks to elucidate the structure of these pigments and to bring information on the other biomolecules produced by *Haslea* species, in complement with the H2020 GHaNA programme, which main objective is to study the biodiversity of the genus. Recent progress on the purification steps and the structural characterization of marennine-like pigments will be presented, especially on the polymer backbone and the chromophore nature. Further results on the different compounds in the "blue water" will be discussed, for the overall valorisation of this natural extract.

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References
[1] Gastineau R et al. *Mar Drugs*. 2014; 12:3161-3189.
[2] Pouvreau JB et al. *J Appl Phycol.* 2006; 18:757-767.

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SL-33

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In vitro antitumor activity of protoflavone-based hybrid compounds on human gynecological cancer cell lines

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Protoflavones are rare and unusual flavonoid derivatives having a non-aromatic B-ring; in nature, they can most typically be found in certain genera of fern species. Protoflavones are promising, natural anticancer agents, and their *in vitro* and in *vivo* activity inspired the synthesis of many semi- and total synthetic analogs [1]. In the current study, our aim was to evaluate the antitumor potential of a set of new hybrid compounds, each containing a protoflavone and a chalchone or ferrocene fragment.
Four new compounds were prepared and studied for their *in vitro* antitumor activity against four gynecological human cancer cell lines including HeLa and SiHa (cervical), and MCF-7 and MDA-MB-231 (breast) cancer cells, with cisplatin as a positive control. When testing by MTT assay, the compounds showed strong antiproliferative activities with IC_{50} values in the low-medium nanomolar range. To quantitatively evaluate pharmacological benefit gained by the coupling, bioactivity of each compound was further analyzed in a virtual combination study, i.e. considering it as an interaction of a 1:1 ratio mixture of the corresponding protoflavone and chalchone building block. The most potent compound demonstrated an IC_{50} value of 153 nM against SiHa cells, representing a combination index value of 0.10 (i.e. very strong synergism) for the two separate fragments. This compound was found to induce apoptosis in MDA-MB-231 and SiHa cells through the significant increase in the hypodiploid (sub G1) population as evidenced by cell cycle analysis and induced the activation of caspase-3.
Our study highlights the pharmacological potential of protoflavone-based hybrid compounds and demonstrates that these hybrids are much more than a simple addition of their chemical elements.

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Reference
[1] Hunyadi A et al. *Phytochem Rev.* 2014; 13:69-77.

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A first insight into the nutritional value, phenolic content and biological activities of the halophyte *Cladium mariscus* L. Pohl

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Cladium mariscus (L.) Pohl, also known as swamp sawgrass, is a halophyte plant common in the Mediterranean area. Swamp sawgrass is traditionally used for the treatment of colds, renal pain and gastrointestinal disorders, has a high polyphenolic contents and displays in vitro radical scavenging capacity [1]. In our ongoing studies to identify halophytes species with biotechnological uses, including for veterinarian applications, we explored the proximate composition, phenolic profile and *in vitro* antioxidant, anti-inflammatory and anthelmintic properties of 80% acetone extracts from swamp sawgrass aerial organs collected along the year (spring, summer, autumn and winter). The total phenolics content was appraised by spectrophotometric assays and the detailed phenolic profile was established by HPLC-DAD. The extracts displayed a high antioxidant and anthelmintic activity and moderate anti-inflammatory properties. Biomass has an interesting nutritional profile, and high polyphenolic content, especially condensed tannins. These results encourage further investigations on the potential use of *C. mariscus* as veterinary nutraceutical and/or phytotherapeutical drugs for small ruminants.

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Reference
[1] Lopes A et al. *Ind Crops Prod.* 2016; 94:299-307.

Poster Presentations

PO-1

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Evaluation of bioactive compounds in leaves of *Moringa concanensis* accessions

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Moringa concanensis Nimmo is a medicinal tree belonging to the family Moringaceae. It occurs in tropical dry forest from south eastern Pakistan to the southern tip of India. Leaves, flowers and seeds are used for curing various ailments in humans. Leaves are used to reduce cholesterol and body weight, to increase fertility in women, to reduce fatigue, for constipation and to treat jaundice. Even though its medicinal properties has been known, there is not much work has been done on the quantitative determination of bioactive compounds in this species. In this study bioactive compound in different accessions of *M. concanensis* was analysed. Results revealed that ascorbic acid, total carotenoids, total polyphenol, chlorophyll a, b and total chlorophyll content was highest in accession MC-16 (442.30 mg/100g), MC-19 (70.64 mg/100g), MC-10 (35.80 mg/g), MC-25 (1.812 mg/g), MC-19 (0.273 mg/g), MC-25 (2.409 mg/g) respectively. This study shows that *M. concanensis* is very good source of bioactive compounds which are beneficial to human health. So *M. concanensis* leaf can be used as functional ingredients in therapeutic food and for the development of nutraceuticals.

PO-2

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Targeted HPLC-MS analysis of sesame (*Sesamum indicum* L.) seeds, roots and hairy roots

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The metabolic profiles of sesame seeds, roots and hairy roots of twenty-five sesame cultivars that were collected from different parts of the world were analyzed using high-performance liquid chromatography-mass spectrometry (HPLC-MS). The results showed significant differences in metabolome among the sesame cultivars and four differential metabolites namely pinoresinol, sesamin, sesaminol and sesamolin were identified in the seeds while one metabolite-sesamin was identified in the roots and hairy roots respectively. Quantification of these compounds by HPLC-MS showed that sesamin was the major compound in both the seeds, roots and hairy roots. The results of this study exhibited useful lignan information of the different sesame cultivars collected across different regions and identified potential cultivars having high sesamin and other related lignans for functional food, pharmaceutics and cosmetic industries.

PO-3

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Nootkatone elicits hepatoprotective and anti-fibrotic actions in a murine model of liver fibrosis by suppressing oxidative stress, inflammation, and apoptosis

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In this study, the hepatoprotective and anti-fibrotic actions of nootkatone (NTK) were investigated using carbon tetrachloride (CCl_4)-induced liver fibrosis in mice. CCl_4 administration elevated serum aspartate and alanine transaminases levels, respectively. In addition, CCl_4 produced hepatic oxidative and nitrative stress, characterized by diminished hemeoxygenase-1 expression, antioxidant defenses, and accumulation of 4-hydroxynonenal and 3-nitrotyrosine. Furthermore, CCl_4 administration evoked profound expression of pro-inflammatory cytokine expressions such as tumor necrosis factor-α (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and interleukin-1β (IL-1β) in hepatic tissues, which corroborated with nuclear factor-κB (NF-κB) activation. Additionally, CCl_4-treated animals exhibited higher apoptosis, characterized by increased caspase 3 activity, DNA fragmentation, and poly (ADP-ribose) polymerase [PARP] activation. Moreover, histological and biochemical investigations revealed marked fibrosis in the livers of CCl_4-administered animals. However, NTK treatment mitigated CCl_4 -induced phenotypic changes. In conclusion, our findings suggest that NTK exerts hepatoprotective and anti-fibrotic actions by suppressing oxidative stress, inflammation, and apoptosis.

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PO-4

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Isolation and characterization of bioactive compounds from *Broussonetia papyrifera* (L.) L'Hér. ex Vent.

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Broussonetia papyrifera (L.) L'Hér. ex Vent. (Moraceae), known as paper mulberry, is a deciduous tree naturally occurring in Southeast Asia. Like other plants of the Moraceae family, *B. papyrifera* can be characterized by the presence of prenylated substances that possess various pharmacological effects. Extracts of *B. papyrifera* exhibit antioxidant, anti-inflammatory, antidiabetic and antimicrobial properties.
In the present work, chromatographic separation of chloroform part of ethanolic extract of *B. papyrifera* wood led to the isolation of several phenolic compounds from the group of flavonoids, coumarins, lignans and stilbenoids. The structures of the substances were determined by HRMS, and by 1D and 2D NMR. Currently, the biological activity of isolated compounds is evaluated in *in vitro* assays.

PO-5

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The beneficial effect of extracts from *Eucalyptus globulus* leaves on modulation of antioxidant enzymatic defense system

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Phenolics are the main compounds in *Eucalyptus globulus* leaves responsible for antioxidant activity. Oxidative stress has been proposed as major factor in the pathogenesis of neurodegenerative diseases. The upregulation of antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD), glutathione reductase (GR) and glutathione peroxidase (GPx) constitute a target protective mechanisms against oxidative stress.

The aim of the present work is to evaluate the effect of different varying polarity extracts from *Eucalyptus* leaves on modulation of antioxidant enzymatic defense system. We have employed an *in vitro* cellular model of human neuroblastoma SH-SY5Y cells under hydrogen peroxide-induced oxidative stress conditions. Cells were pretreated with different concentrations of acetone, ethanol and methanol extracts for 24 h previous to the exposure to hydrogen peroxide (0.1 mM, 30 min). The activities of the antioxidant enzymes CAT, SOD, GR and GPx were significantly reduced after H_2O_2 treatment. Pretreatments with acetone, ethanol and methanol extracts increased antioxidants enzymes activities compared to H_2O_2-treated cells. Particularly highlights the protective effect of acetone extract at the concentration of 50 µg/mL and ethanol and methanol extracts at the concentration of 10 µg/mL. These results suggest that extracts from *E. globulus* leaves exert a neuroprotective effect through modulation of antioxidant enzymatic defense system, positively impacting in health properties.

PO-6

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α-Bisabolol mitigates rotenone-induced dopaminergic neurodegeneration by suppressing oxidative stress, neuroinflammation and apoptosis in rat model of Parkinson's disease

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Parkinson's disease (PD), a chronic age related neurodegenerative disease is characterized by progressive loss of nigrostriatal dopaminergic neurons. Convincing number of studies showed that oxidative stress, neuroinflammation, impaired apoptosis and autophagy leads loss of dopaminergic neurons and accumulation of α-synuclein, a characteristic of Lewy's bodies in PD. There is scarcity of agents to cure, delay, or prevent the onset and progression of the diseases. In recent years, numerous dietary phytochemicals gained interest for their neuroprotective property and among these, α-bisabolol (BSB), a sesquiterpenes from essential oil of *Matricaria chamomilla* (chamomile) and *Salvia runcinata* (sage) generated interest for evaluation in neurodegeneration. In the present study, rotenone (2.5 mg/kg/day for 4 weeks)-induced rat model of PD was used to investigate the neuroprotective potential of BSB that was administered daily for 4 weeks 30 minutes prior to rotenone. Rotenone induced loss of dopaminergic neurons in the substantia nigra, activated microglia and astrocytes and reduced striatal expression of tyrosine hydrolase, a rate-limiting enzyme in the dopamine metabolism. Rotenone also decreased antioxidants, enhanced α-synuclein and induced proinflammatory cytokines. However, BSB treatment attenuated oxidative stress, cytokines, enzymes and apoptosis along with preserving dopaminergic neurons. BSB also reduced activation of microglia and astrocytes as evidenced by Iba-1 and GFAP and α-synuclein accumulation. The findings demonstrate that BSB exert neuroprotective effects against dopaminergic neurodegeneration induced by rotenone and has potential for further development as a therapeutic candidate for PD.

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PO-7

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Hypolipidemic effect of autumn olive berry in mice fed a high-fat, high-sucrose diet

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Autumn olive (*Elaeagnus umbellata* Thunb.) is a good source of phytochemicals including lycopene [1,2]. It was reported that lycopene exerted antihyperlipidemic effect in atherosclerosis-induced rats [3]. The aim of this study was to investigate the hypolipidemic effect of autumn olive berry (AOB) in mice fed a high-fat, high-sucrose (HFHS) diet. Seven-week-old male C57BL/6J mice were fed a basal diet, a HFHS diet, or the HFHS diet containing 0.4% AOB extract (low AOB, LAOB) or 0.8% AOB extract (high AOB, HAOB) for 12 weeks. After sacrifice, serum triglyceride, cholesterol, LDL-cholesterol, and HDL-cholesterol were measured. Serum triglyceride, cholesterol, and LDL-cholesterol levels of HFHS group were significantly elevated compared with the control group ($p<0.05$). Consumption of LAOB or HAOB significantly reduced serum triglyceride levels compared with the HFHS group ($p<0.05$). Serum cholesterol and LDL-cholesterol levels were significantly lower in the HAOB group than in the HFHS group. Serum cholesterol and LDL-cholesterol levels of the LAOB groups were not significantly different from those of the HAOB and HFHS groups. Serum HDL-cholesterol levels of the four groups were not significantly different. These results suggest that AOB could have hypolipidemic effect in mice fed a HFHS diet.

Acknowledgements

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References

[1] Fordham IM et al. *HortScience*. 2001; 36:1136-1137.
[2] Guo X et al. *J Agric Food Chem*. 2009; 57:5334–5339.
[3] Kumar R et al. *Pharmacognosy Res*. 2017; 9:161–167.

PO-8

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Gene expression profiles of MCF-7 cells treated with oxyresveratrol

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Oxyresveratrol (OXY) is a naturally occurring polyphenol belonging to the group of stilbenoids [1]. The aim of this study was to elucidate, using micro-array analysis, the biological pathways altered in the breast cancer cell line MCF-7, following treatment with OXY. The gene-level expression of more than 20,000 human well-annotated genes was determined using Clariom Affymetrix microarray under two different OXY treatments (50 μM (IC_{50}) and 100 μM) for 24 h. A total of 686 genes were found to have altered mRNA expression levels of two-fold or more in the 50 μM OXY-treated group (262 upregulated and 424 downregulated genes). Total 2,338 genes were differentially expressed in the 100 μM-treated group (907 upregulated and 1,431 downregulated genes). The relevant visualise global expression patterns of genes and pathways were generated; genes involved in cell cycle control, DNA repair, and apoptosis, as well autophagy, showed the greatest differences in expression relative to controls. Gene expression was validated by quantitative PCR. Protein-level expression was investigated using western blot and flow cytometry analysis. We continue to elucidate the cellular consequences of OXY treatment.

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Reference
[1] Mongolsuk S et al. *Journal of the Chemical Society (Resumed)*. 1957; 0:2231-2233.

PO-9

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Calpurnia aurea ethanol extract reduces *Pseudomonas aeruginosa* quorum sensing- dependent virulence factors

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Pseudomonas aeruginosa is the causative agent of several life-threatening human infections like urinary tract infections, lung infections and skin infections among many. *P. aeruginosa*, like many other pathogens exhibits quorum sensing controlled virulence factors such as biofilm during disease progression, complicating the treatment with conventional antibiotics. Thus, impeding with the pathogen's QS circuit appears as promising new strategy to overcome pseudomonad infections. In the present study, *Calpurnia aurea* ethanol extract, along with other extracts (acetone, ethyl acetate, water) of *Leonotis ocymifolia* and *Moringa oleifera* were evaluated for anti-quorum sensing/ anti-virulence potential against *Pseudomonas aeruginosa*. *Calpurnia aurea* extracts demonstrated effective antimicrobial activities with MIC value between 1.5-3.5 mg/mL. *Calpurnia aurea* ethanol extracts demonstrated effective anti-QS and anti-virulence (biofilm formation, motility, pyocyanin and pyoverdine production). The quantitative violacein inhibition of *Calpurnia aurea* ethanol extracts showed ≥ 51 % at 1 mg/mL. *P. aeruginosa* was significantly inhibited by ≥ 50% with same plant extract at 1 mg/mL, whereas observation of dead/live cells with confocal laser microscopy showed a significant reduction of biofilm formation. While extracts altered swimming motility, swarming motility was not significantly altered. Ethanolic *Calpurnia aurea* extracts reduced pseudomonad virulence, albeit in a strain- and extract-specific manner. *Calpurnia aurea* extracts may be suitable for identification of lead compounds with QS inhibitory potential for control of *P. aeruginosa* infections.

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PO-10

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Anti-quorum sensing and antibiofilm activities of South African medicinal plants against uropathogens

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Urinary tract infections (UTIs) primarily affect women and have increasingly become a serious health problem globally. These infections are largely attributed to the quorum sensing (QS)-dependent ability of pathogens to form biofilms in the urinary tract. Microbial pathogenicity can be attenuated by disturbing the QS system of bacteria. The aim of the study was to document the antibacterial and anti-quorum sensing (AQS) potential of medicinal plants that are used as traditional medicine in South Africa to treat UTIs. Plant extracts were prepared from six medicinal plants using solvents of different polarities. When plant extracts were screened for their ability to inhibit the QS-controlled violacein production by *Chromobacterium violaceum*, only two species (*H. africana* and *C. latifolia*) exhibited AQS activity in the qualitative agar well diffusion assay. However, eight extracts inhibited violacein production by 57-71% in the quantitative dilution assay. The ability of uropathogens to form biofilms upon exposure to the plant extracts was subsequently investigated using the crystal violet assay. It was found that the polar extracts of *Cenchrus ciliaris* and *Eucomis autumnalis*, *Cryptocarya latifolia, Hydnora africana* and *Rhoicissus tridentata,* as well as non-polar extract of *Hypoxis hemerocallidea* were able to reduce initial cell attachment of *S. aureus*, *P. mirabilis* and *S. marcescens* by approximately 50%. However, the preformed biofilm was inhibited less than 30% by the extracts. The study revealed that several South African medicinal plants have antibacterial and AQS properties, validating their use in traditional medicines to treat UTIs to some degree, and indicating that they may be a suitable source of anti-pathogenic drugs to treat urinary infections.

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PO-11

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Neorogioltriol and related diterpenes from the red alga *Laurencia* inhibit inflammatory bowel disease in mice by suppressing M1 and promoting M2-like macrophage responses

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Macrophages, central mediators of inflammation, obtain pro inflammatory (M1) and anti-inflammatory (M2) phenotypes, which can be modulated by soluble factors, including natural products. Despite the crucial protective role of inflammation, chronic or deregulated inflammation can lead to pathological states, such as autoimmune diseases, metabolic disorders, cardiovascular diseases and cancer. In the present study we evaluated in depth the anti-inflammatory activity of the brominated diterpene neorogioltriol and identified two structurally related diterpenes, neorogioldiol and *O*[11],15-cyclo-14-bromo-14,15-dihydrorogiol-3,11-diol, with equally potent activity. We investigated the mechanism of action of the three metabolites and found that all three suppressed macrophage activation and promoted an M2-like anti-inflammatory phenotype by inducing expression of Arginase1, MRC1, IRAK-M, the transcription factor C/EBPβ and the miRNA miR-146a. In addition, they suppressed iNOS induction and nitric oxide production. Importantly, treatment of mice with the bioactive compounds suppressed DSS-induced colitis by reducing tissue damage and pro-inflammatory cytokine production. Thus, all these three diterpenes are promising lead molecules for the development of anti-inflammatory agents targeting macrophage polarization mechanisms.

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PO-12

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Anti-inflammatory activity of steroids from *Hypholoma lateritium*

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Hypholoma lateritium (Schaeff.) P. Kumm., brick cap by its vernacular name, is a basidiomycetes species, member of the Strophariaceae family. It is a saprobic macrofungus native to Europe, North America and the Far East, occurring usually in small tufts or occasionally singly on hardwood stumps. Previous mycochemical studies reported the presence of sesquiterpenoids, ergostane and lanostane triterpenes with cytotoxic activity.

In this study we aimed to investigate the anti-inflammatory properties of *H. lateritium* extracts, as well as to identify the characteristic secondary metabolites which may contribute to the beneficial pharmacological properties of this mushroom. In this view organic (n-hexan, chloroform and 50% methanol) and water extracts of *H. lateritium* and six fasciculol type steroids isolated from this species were subjected to 3 different *in vitro* assays focusing on COX-2 inhibition, and production of cPGES and Nrf2, respectively. Significantly decreased expression of cyclooxygenase-2 (COX-2) and increased synthesis of PGE3 and Nrf2 were observed for exracts, as well as for the steroids of this species. The results obtained demonstrate that extracts of brick cap mushroom and its isolated steroids exert not only significant inhibitory activity on COX-2, but they are also capable to stimulate the Nrf2 pathway. Our study furnishes experimental evidence that *Hypholoma lateritium* has notable anti-inflammatory properties which can be explored in future studies in the view of potential medical application.

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PO-13

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A novel pyruvate dehydrogenase kinase inhibitor hemistepsin A increases mitochondria-dependent apoptosis of colorectal cancer

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Most cancer cells primarily produce their energy through a high rate of glycolysis followed by lactic acid fermentation even in the presence of abundant oxygen. This phenomenon is called Warburg effect, also known as aerobic glycolysis, was firstly reproted by Warburg in 1920s. Pyruvate dehydrogenase kinase (PDK) 1, a kinase which inactivates the enzyme pyruvate dehydrogenase (PDH), is commonly overexpressed in tumors and recognized as a novel therapeutic target in colon cancer. Suppression of PDH by PDK1 prevents the conversion of cytoplasmic pyruvate into acetyl-CoA and then cytoplasmic pyruvate is converted into lactate even in the presence of oxygen presenting an advatage for cancer growth. Here, we report hemistepsin A, as a novel PDK kinase inhibitor, decreases PDK activity by binding to the lipoamide-binding domain of PDK1 without affecting its expression. Hemistepsin A is a sesquiterpene lactone isolated from *Hemistepta lyrata* Bunge (Compositae). *H. lyrata* has been used for the treatment of colon disease, such as diarrhea, hemafecia, and anal fistula, in traditional medicine of Eastern Asia. We demonstrate that hemistepsin A has anti-cancer effect on several colorectal cancer cells. After treatment with hemistepsin A, lactate production was markedly decreased. In the meantime, intracellular reactive oxygen species (ROS) levels and mitochondrial damages were increased. In addition, apoptosis was promoted with enhanced activation of caspase-3 and -9, improved cleaved PARP, enhanced level of Bax expression, decreased Bcl-2 expression. In *in vivo* mice models inoculated with CT26 colon carcinoma, hemistepsin A effectively suppressed tumor growth as determined by the reduction of tumor volume and weight, inducing by inhibiting the PDK1 activity but not by its expression. Taken together, we suggest that hemistepsin A suppresses growth of colorectal cancer through inhibiting activity of PDK1.

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PO-14

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Paeoniflorin increases the adhesion of trophoblast to the endometrium by upregulating the expression of Integrin αVβ3 and αVβ5

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Successful implantation requires uterine receptivity which is determined by diverse biological factors such as adhesion molecules, cytokines, growth factors, and receptors. In our previous study, water extract of *Paeonia lactiflora* enhanced embryo implantation in vitro and in vivo via induction of the leukemia inhibitory factor (LIF)-dependent expression of Integrin αVβ3 and αVβ5. To investigate which one is the major component, we performed high-performance liquid chromatography (HPLC) analysis. Next, we tested these five compounds to confirm whether these single compounds enhance the adhesion of human trophectoderm-derived JAr cells to the endometrial Ishikawa cells. In addition, we checked the expression of adhesion molecules in mRNA and protein levels and performed *in vivo* study using the implantation failure model mice by treating RU-486. Paeoniflorin, the most abundant molecule among tested five major compounds of *P. lactiflora*, showed enhancing effect on cellular interaction between JAr and Ishikawa cells. Paeoniflorin increased the expression of Integrin αVβ3 and αVβ5 in LIF-dependent manner. Furthermore, *in vivo* study showed that paeoniflorin significantly improved the number of implantation embryos. Therefore, our results suggest that paeoniflorin, a major compound of *P. lactoflora*, is a potent agent for enhancing endometrial receptivity.

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PO-15

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Isolation and characterization of fungal secondary metabolites with anti-*Naegleria fowleri* (brain eating amoeba) activity

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Naegleria fowleri, commonly known as "brain eating amoeba" is a free-living amoeba, which is responsible for primary amoebic meningoencephalitis (PAM). This is a very rare but severe human disease that is rapidly fatal leading to death in approximately one week or less [1]. Due to the low number of infections, to date, there are no clinical trials addressing the efficacy of one treatment over another. The lack of effective treatments as well as the 95% mortality rate creates an urgent need for new and more effective therapeutics [2,3]. Our goals is to address this compelling need by exploring the vast untapped biodiversity in the fungal kingdom. We have screened over 4000 fungal extracts in a single point assay at 50 µg/mL concentration. For elimination of cytotoxic fractions, we tested the samples against four different human cancer cell lines including melanoma, breast, ovarian, and lung carcinoma cell lines. To exclude the already known compounds, the active samples were evaluated by using our in-house developed UPLC-PDA-HRMS-MS/MS dereplication method. Bioactivity directed isolation and structure elucidation of secondary metabolites, resulted in several compounds with notable activity against *Naegleria fowleri*. The characterization of additional fractions is currently ongoing. This study shows that the inherent structural diversity of fungal secondary metabolites indicates that fungi can be a promising source for new anti-*Naegleria* therapeutics.

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References

[1] Martinez-Castillo M et al. *Journal of Medical Microbiology* 2016; 65:885-896.
[2] Grace E et al. *Antimicrob Agents Chemother* 2015; 59:6677-6681.
[3] Visvesvara GS et al. *FEMS Immunol Med Microbiol* 2007; 50:1-26.

PO-16

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Inhibition of PTP1B of phenolic compounds from the root bark of *Morus alba*

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As part of our continuing research to obtain pharmacologically active compounds from *Morus alba* L. (Moraceae), four new Diels-Alder type adducts (DAs) [morusalbins A–D], one new isoprenylated flavonoid [albanin T], together with twenty-one known phenolic compounds were isolated from its root bark. The chemical structures were established using NMR, MS, and ECD spectra. The DAs including morusalbins A–D, albasin B, macrourin G, yunanensin A, mulberrofuran G and K, and albanol B exhibited strong inhibitory activities against protein tyrosine phosphatase 1B (PTP1B) (IC_{50}, 1.90–9.67 μM). In the kinetic study, morusalbin D, albasin B, and macrourin G showed non-competitive PTP1B inhibition, with K_i values of 0.33, 1.00, and 1.09 μM, respectively. Furthermore, molecular docking studies revealed that these active DAs have high affinity and tight binding capacity towards the active site of PTP1B.

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PO-17

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Polychlorinated pyrrolidinones from a Saudi Arabian Red Sea sponge of the genus *Lamellodysidea*

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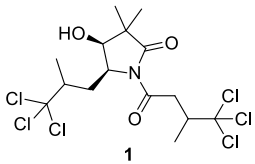
The Red Sea, the world's northernmost tropical sea, is a seawater inlet of the Indian Ocean, lying between Africa and Asia. The more than 2,000 km long stretch of coral reef system in the Red Sea ranks among the five most significant reefs in the world and hosts approximately 1,100 species of fish and more than high degree of endemism. Nonetheless, the Red Sea still remains one of the most understudied ecosystems on the planet. In the framework of a joint project aiming at the bioprospection of marine organisms from the Saudi Arabian Red Sea as a source of new bioactive secondary metabolites, a large number of invertebrates and algae were collected from various coral reefs surrounding Thuwal. Among them, the organic extract of a sponge of the genus *Lamellodysidea* was prioritized for phytochemical analysis on the basis of its interesting chemical profile, as analyzed by NMR and LC-MS. Fresh tissues of the organism were extracted with mixtures of CH_2Cl_2/MeOH and the resulting organic extract was subjected to a series of chromatographic separations that led to the isolation of a number of polychlorinated pyrrolidinones (eg. **1**). The structures of the isolated alkaloids, among which two are new natural products, were established mainly on the basis of extensive analysis of their 1D and 2D NMR and MS data.



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PO-18

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Mono- and diphenanthrenes with antiproliferative activity from *Juncus gerardii*

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Plants belong to family Juncaceae accumulate different types of secondary metabolites, e.g. phenanthrenes, flavonoids, coumarins, triterpenes, steroids and phenolic acid derivatives. The main bioactive components of *Juncus* genus, the largest genus of the family, are phenanthrenes; several of them possess interesting biological activities (e.g. antiproliferative, antimicrobial, anti-inflammatory, antioxidant, and spasmolytic effects) [1].

In continuation of our work dealing with the isolation of biologically active secondary metabolites from Juncaceae species, *Juncus gerardii* was investigated. 23 Phenanthrenes were isolated from the methanol extract of the plant using different chromatographic methods. The structure elucidation of the compounds was carried out by extensive NMR and HRMS experiments. 12 Compounds (gerardiin A-L) are new natural products (8 mono- and 4 diphenanthrenes), while 11 phenanthrenes (compressins A and B, effusol, juncusol, effususol A, jinflexin C, dehydroeffusol, 7-hydroxy-2-methoxy-1-methyl-5-vinyl-9,10-dihydrophenanthrene, 2-hydroxy-1-methyl-7-hydroxymethyl-5-vinyl-9,10-dihydrophenanthrene, 5-aldehyde-2,7-dihydroxy-1-methyl-9,10-dihydrophenanthrene, 2,7-dihydroxy-5-hydroxymethyl-1-methyl-9,10-dihydrophenanthrene) were isolated for the first time from the plant. The isolated phenanthrenes were tested for their antiproliferative effect against human tumour (HeLa, SiHa) cell lines. Several compounds possessed higher activity (IC_{50}s 1.31–10.66 μM) in case of HeLa than the positive control cisplatin (IC_{50} 12.43 μM).

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References

[1] Bús Cs et al. *Phytochem Rev.* 2018; 17:833–51.

PO-19

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Isolation and pharmacological investigation of compounds from *Euphorbia matabelensis*

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Members of the genus *Euphorbia* (family Euphorbiaceae) are characterized by the production of irritating milky latex [1]. Diterpene-containing plants of this genus are of considerable interest for natural product drug discovery programs because of the wide range of potentially valuable biological activities and broad structural diversity due to the different polycyclic and macrocyclic skeletons and various aliphatic and aromatic ester groups [2]. However, other compounds, e.g. triterpenes, steroids, and flavonoids can also contribute to their diverse pharmacological activities [3].

The present work deals with the isolation and phytochemical and pharmacological investigations of compounds of *Euphorbia matabelensis*. After multiple separation process, including TLC, vacuum liquid chromatography, preparative TLC, and HPLC, one diterpene (ingenol) and two flavonoids (naringenin and eriodictyol) were obtained from the methanol extracts prepared from the stems and roots of the plant. The structures of the isolated compounds were determined by 1D and 2D NMR (^{1}H-^{1}H COSY, HSQC, and HMBC) and MS measurements, and comparing them with literature data. All compounds were isolated for the first time from the plant. The compounds were tested for their antiproliferative (on HeLa, C33a, MCF-7, and MDA-MB-231 cell lines) and GIRK channel blocking activities. Marginal pharmacological activities were found for all compounds in both test systems.

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References

[1] Scholz A. Euphorbiaceae. In: *Syllabus der Planzenfamilien*. Vol. 2, Engler A. (Ed). Gebrüder Bornträger, Nikolassee, Berlin, 1964; 255-261.
[2] Vasas A, Hohmann J. *Chem Rev*. 2014; 114:8579-8612.
[3] Shi QW, Su XH, Kiyota H. *Chem Rev*. 2008; 108:4295-4327.

PO-20

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Isolation and pharmacological investigation of jacaranone derivatives from *Crepis pulchra*

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Members of the family Asteraceae are distributed worldwide and they are exceptionally rich in secondary metabolites. The rich chemistry of the family is the basis of their very widespread use as medicinal plants. Over the last few decades, different species from Asteraceae family have been studied from phytochemical and pharmacological points of view. Among them, terpenoids and flavonoids stand out because of their biological activities and potential health benefits.

The present work deals with the isolation and pharmacological investigation of compounds from *Crepis pulchra*. After multiple separation process, including TLC, vacuum liquid chromatography, preparative TLC, and HPLC, three cyclohexanones, namely jacaranone, 2,3-dihydro-3-hydroxyjacaranone methyl ester, and 2,3-dihydro-3-methoxyjacaranone methyl ester were isolated from the methanol extract prepared from the whole plant. The structures of the isolated compounds were determined by 1D and 2D NMR (^{1}H-^{1}H COSY, HSQC, and HMBC) and MS measurements, and by comparison with literature data. All compounds were isolated for the first time from the plant. The compounds were tested for their antiproliferative activity on four human tumour (MCF-7, A231, HeLa and C33a) cell lines. Among them, jacaranone proved to be the most active against all cell lines (IC_{50}s 6.27 μM – 14.61 μM). It can be stated that besides flavonoids and terpenoids, cyclohexanone derivatives can also contribute to the pharmacological potency of Asteraceae species.

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PO-21

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Isolation of sesquiterpene lactones from common ragweed (*Ambrosia artemisiifolia* L.)

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Common ragweed (*Ambrosia artemisiifolia* L., Asteraceae) is an invasive species in Europe with allergic pollens. Ragweed originates from North America, but it also occurs and is spreading in Europe, due to the plant's successful reproductive potential and a strong allelopathic effects against the native flora. Some of the plant's secondary metabolites, called sesquiterpene lactones possess allergic, allopathic, anti-inflammatory, antitumor, antimicrobial activity. In a phytochemical view the plant secondary metabolites have not explored completely. The aim of our study was to isolate the major phytochemicals from the aerial parts of *Ambrosia artemisiifolia*, especially focusing on the sesquiterpene lactone compounds, and elucidate their chemical structure. The methanolic extract of the plant was separated by several chromatographic techniques, including preparative TLC and HPLC analysis. One new and six known sesquiterpene lactones were isolated from the aerial parts of ragweed. Their structure was identified by ^{1}H NMR, ^{13}C NMR and mass spectroscopy. 1'-Noraltamisin, a seco-pseudoguaianolide was reported for the first time from this plant. Further investigation needed to identify the biological activities and molecular mechanisms of the isolated compounds, particularly the new seco-pseudoguaianolide.

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PO-22

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Isolation and structural elucidation of secondary metabolites from *Eremurus persicus*

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Eremurus persicus (Jaub. & Spach) Boiss., belonging to Xanthorrhoeaceae family is an endemic medicinal plant widely distributed in Iran. The leaves have been traditionally used as a remedy of constipation and diabetes, and to treat of different disorders of liver, stomach and the genitourinary system [1, 2], to cure of atherosclerosis, inflammation-related diseases, as well as against fungal skin diseases, and as diuretic [1, 3,4]. Regarding the widespread application of *E. persicus* in Iranian folk medicine, and the insignificant investigation of its phytochemicals, this study was aimed at the isolation and identification of the major secondary metabolites of this plant. Five pure compounds were isolated from EtOAC and $CHCl_3$ soluble-extracts. All the identified phytoconstituents were reported for the first time from *Eremurus* genus. By applying various chromatography techniques rare compounds corchoionoside A, and 4-amino-4-carboxychroman-2-one from EtOAc fraction; along with isoorientin, auraptene, and imperatorin from $CHCl_3$ extract were isolated. Structure elucidation of the pure compounds was performed by NMR spectroscopy. Due to the extensive utilization of *E. persicus* in folk medicine, more investigation is needed to study the phytochemicals of the plant.

References

[1] Shahrokhi SR et al. *Bull Env Pharmacol Life Sci*. 2014; 3:45–49.
[2] Vala MH et al. *Afr J Microbiol Res.* 2011; 5:2349–2352.
[3] Zare A et al. *Euro J Exp Bio.* 2014; 4:583–587.
[4] Hashemi SJ et al. *Res J Pharmacog*. 2014; 1:39–43.

PO-23

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Development of herbal sunscreen formulations from the flowers of *Osbeckia octandra* DC.

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The exposure to ultraviolet (UV) component of the solar radiation could lead to conditions like photoaging and photocarcinogenesis. Although synthetic sunscreens are introduced as protectants against harmful UV radiation, the adverse effects associated with these products demand the development of sunscreens of herbal origin. Thus, the present study focuses on the formulation of herbal sunscreens from flowers of *Osbeckia octandra* DC., a dermatological remedy in Sri Lankan folklore medicine. Initially, the UV filtering potential and subsequently the sun protection factor (SPF) was determined for the methanolic extract of *O. octandra*. Thereafter, this extract was incorporated into the aqueous cream base at different percentages (25%, 50% and 75%) and the SPF values and the photostability of the resulting formulations were evaluated against a commercial synthetic sunscreen (positive control) and the aqueous cream base (negative control). Interestingly, the crude extract displayed a SPF value of 39.91, which had hardly changed (SPF=37.38) even after incorporating this extract at 75% into the aqueous cream base. It surpassed the other two formulations as well as the commercial synthetic sunscreen in terms of SPF, photostability, and broader-spectrum of UV absorption. Therefore, this study clearly demonstrated the suitability of *O. octandra* to be developed into a commercial herbal sunscreen. Experiments are underway to enhance its bioavailability via nanotechnology approach.

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PO-24

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Green synthesis of silver nanoparticles using *Pinus nigra* bark aqueous extract and their potential applications

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This study aimed to develop an innovative, eco-friendly, cost-effective and rapid method for the synthesis of silver nanoparticles from a silver salt and *Pinus nigra* bark aqueous extract [1,2]. The extract had a total phenolic content of 1.26 mg/mL, procyanidins being major constituents as revealed by HPLC-DAD-ESI-Q-TOF-MS/MS analysis. The synthesis of silver nanoparticles was monitored by UV-VIS spectroscopy which showed a peak between 420 and 430 nm corresponding to the surface plasmon resonance of silver nanoparticles. Dynamic light scattering technique revealed uniform and stable silver nanoparticles indicated by a size range between 50 and 60 nm and a zeta potential of -16 mV. Electron transmission microscopy showed a uniformly distributed spherical shape, while the EDX analyse confirmed a crystalline elemental silver composition of the bio-synthesised silver nanoparticles. Moreover, the potential genotoxicity and antioxidant capacity of *Pinus nigra* bark aqueous extract before and after silver nanoparticles synthesis was screened using *Allium cepa* root apexes and DPPH assays, respectively. To conclude, we present herein a facile route for the synthesis of silver nanoparticles which could be further explored for their therapeutic applications due to promising antioxidant and cell cycle arrest potential.

References

[1] Karthika V et al. *J Photochem Photobiol B*. 2017; 167:189-199.
[2] Nasiriboroumand M et al. *J Photochem Photobiol* B. 2018 ; 179 :98-104.

PO-25

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Thymoquinone prevents neurodegeneration against MPTP *in vivo* model of Parkinson's disease and modulates α-synuclein aggregation *in vitro*

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Parkinson's disease (PD) is a common neurodegenerative disease, characterized by progressive dopaminergic neurodegeneration with concomitant increase in oxidative stress and subsequent neuroinflammation in the substantia nigra pars compacta (SNc) of the midbrain. Studies are currently focusing on targeting neuroinflammation and oxidative stress to effectively treat PD. This study evaluated the neuroprotective effect of TQ, one of the active compounds in the black seed, against 1-methyl-4-phenyl 1,2,3,6 tetrahydropyridine (MPTP)-induced PD mouse model. Here, TQ treatment for 1 week (dose, 10 mg/kg *b. wt.)* prior to MPTP (25 mg/kg *b. wt.*) was performed. MPTP administration caused decreased activities of superoxide dismutase, catalase and depletion of reduced glutathione, with a concomitant rise in the lipid peroxidation product. It significantly increased pro-inflammatory cytokines and elevated inflammatory mediators such as COX-2 and iNOS in the striatum. Immunohistochemical analysis revealed dopamine neuron loss in the SNc area and decreased dopamine transporters in the striatum following MPTP administration. However, TQ treatment significantly rescued dopaminergic neuronal loss and dopamine transporters. TQ treatment further prevented glutathione depletion, inhibited lipid peroxidation, and attenuated pro-inflammatory cytokines. TQ also reduced the increased levels of inflammatory mediators, such as COX-2 and iNOS. *In vitro* analysis found that TQ significantly inhibits α-synuclein aggregation and prevents cell death induced by pre-formed fibrils. Thus, TQ not only scavenges the MPTP-induced toxicity but also prevents α-synuclein-fibril formation and associated toxicity.

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PO-26

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Standardization of extracts from roots *P. ginseng* and *P. quinciphola* by the use of HPLC/MS

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Ginseng (*Panax* genus) is currently used as a dietary supplement, adaptogen and fortifying agent, which increases the body's resistance to physical, chemical and biological stress [1]. Ginsenoside biomarkers belong to the class of triterpene glycosides. The quality control of phytochemicals is an actual task of modern health care, since they do not go through all the stages of the compliance of the composition, unlike drugs [2]. In our work an approach of triterpene glycosides detection in ginseng extracts was developed on the basis of HPLC-MS. Enhanced selectivity compared to commonly employed HPLC-UV techniques with the use of sorbent modified with octadecyl groups as stationary phase allowed simultaneous determination of 23 major and minor ginsenosides. For this purpose, specially adjusted chromatographic conditions for separation on a sorbent modified with pentafluorophenyl groups together with selective MS detection of ginsenoside sodium adducts and sapogenin fragment ions were employed. Separately the influences of column temperature and mobile phase composition on selectivity for determined glycosides were investigated. For all investigated compounds, linearity ranges and calibration equations were established, and metrological characteristics such as detection limit and reproducibility were determined. The developed approach was tested during standardization of reference extracts from the roots of *P. ginseng* and *P. quinquefolius.*

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This work was supported by the Russian Science Foundation (Grant No. 17-13-01146).

References

[1] Kiefer D, Pantuso T. *Am. Family Phys.* 2003; 68:1539–1542.
[2] Dharmananda S. *HerbalGram*. 2002; 54:34–51.

PO-27

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Preparative isolation and structure determination of three steroidal saponins and their isomers from *Dioscorea deltoidea* based on an NMR and HRMS methods

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Dioscorea is a genus in the family Dioscoreaceae. Numerous pharmacological studies investigated the biological activity of compounds found in *Dioscorea*. These properties are attributed to the presence of biologically active compounds called saponins [1]. Traditionally, steroid saponins are extracted from intact plant. However, the isolation of saponins in an individual form from a plant requires time-consuming sample pretreatment. The development of a biotechnological method for isolating the necessary compounds by extracting them from cell cultures simplified this process [2]. However, secondary metabolism has a number of features specific to cultured cells, such as the synthesis of both stereoisomers. Thus, studying metabolites from cell culture is an important task especially since isomers oftentimes have different biological activities. In our work, we developed a method of preparative isolation of steroid saponins and their stereoisomers from the cell culture of *Dioscorea deltoidea*. The isolated compounds were further subjected to NMR and HRMS analysis. The optimization of the process included variation of the following chromatographic parameters: stationary and mobile phases, composition of the eluent, concentration of the modifier, column thermostat temperature, injection volume and flow rate. It was found that the best separation is achieved in the isocratic mode with the flow rate 0.25 mL/min, at a column thermostat temperature of 22°C and injection volume - 2 µl.

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References

[1] Sautour M et al. *J Nat Med.* 2007; 61:91–101.
[2] Khandya MT et al. *Prikladnaya Biokhimiya i Mikrobiologiya.* 2016; 52:614–620.

PO-28

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Maximizing plant's capacity to synthesize antimicrobial compounds

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The current era of increasing bacterial resistance along with consumers' negative perception on synthetic food preservatives and highly-processed foods have fuelled research on novel and natural alternatives of potent antibacterials. An attractive way to generate such antimicrobials is to make use of plants' weaponry. Plants generate such compounds as one of their defence responses. Legumes, specifically, are known to be excellent sources of antibacterials. Fungus-elicited soybeans seedlings, for example, synthesize a class of prenylated isoflavonoids*, glyceollins*, known to exert remarkable antibacterial properties [1]. The amount of generated antibacterials can be further enhanced when seedlings are primed prior to elicitation. Primed plants are shortly sensitized, being stimulated to respond more intensely towards subsequent fungal stress [2]. Priming before elicitation minimizes the fitness costs of the plants for resistance compared to direct elicitation [2]. Wounding, beneficial microbes or chemical compounds involved in plants' defence mechanism are mostly used as primers [3]. Reactive Oxygen Species (ROS), important key molecules in plants' defence, can be externally applied as an effective chemical primer. We found that priming of soybean seedlings with ROS prior to fungal elicitation significantly increases the glyceollin content compared to unprimed or wounding-primed seedlings. The effectiveness of ROS-priming was observed in two soybean cultivars with different genetic characteristics. ROS-priming provides opportunities for large-scale antimicrobial production due to its easiness of application and its increased robustness compared to solely fungus- or wounding-primed fungus-elicitation.

References

[1] Araya-Cloutier C at al. *Food chemistry*, 2017; 226:193-201.
[2] Conrath U et al. *Molecular Plant-Microbe Interactions*, 2016; 19:1062-1071.
[3] Balmer A et al. *Trends in Plant Science*, 2015; 20:443-452.

PO-29

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Examination of cannabinoid content of different extracts prepared from *Cannabis sativa* L.

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Cannabis has a controversial state nowadays, since in some countries it is used as a medicinal plant against pain, while in other countries, it is frequently consumed for abuse, and therefore prohibited. *Cannabis sativa* L. has different varieties with different cannabinoid content. The cultivation of those species, which has low THC content (<0.2%), is allowed in Hungary [1]. Our aim was to examine the cannabinoid content of different extracts, which can be prepared at home by laypersons from a KcZuzana variety of cannabis (nominal THC content <0.12%) [2].

An HPLC/DAD method was developed and used for the qualitative and quantitative determination of some major cannabinoids [Δ9-tetrahydrocannabinol (THC), THC acid (THCA), cannabidiol (CBD), and cannabinol (CBN)] in cannabis plant material and its different extracts with both direct analysis and after liquid-liquid extraction (internal standard: mefenamic acid). For our purpose, we modified the method recommended by UNODC [3].

We developed an HPLC/DAD method (column: C18 Kinetex® 150x2.1 mm; 2.6 µm + Phenomenex SecurityGuard™ cartridge for C18 HPLC; gradient elution with mixtures of 0.05% HCOOH/H_2O and 0.05% HCOOH/ACN; flow rate: 0.25 ml/min; detection: 220 and 240 nm) for detection of the main cannabinoids in different water/ethanol extracts.

Our future aims are to examine the cannabinoid content of further homemade extracts (prepared e.g. with olive oil).

References

[1] https://mkeh.gov.hu/kereskedelmi/mezogazdasag/hemp (01/03/2019)
[2] https://www.ihempfarms.com/DS_KcZuzana (01/03/2019)
[3] UNODC (United Nations Office on Drug and Crime): Recommended methods for the identification and analysis of cannabis and cannabis products. Manual for use by national drug analysis laboratories. New York, USA, 2009.

PO-30

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Quantitative and qualitative differences of phenolic compounds in apples grown in different geographical regions

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The objective of this study was to evaluate phenolic compounds quantitative composition in apple fruits grown in different geographical region. In the study were investigated biological replicates of apples (cv. 'Ligol') grown in Lithuania, Latvia, Poland and Estonia. There were performed 3 biological replicates, one of each contained 10 apples. Samples of lyophilised apple fruits were extracted with 70% ethanol (v/v) for 20 min at 40°C temperature using ultrasonic bath. The ethanol extracts of apple fruits were analyzed by the HPLC method [1].

The study found that the geographical location of apple-trees had an impact on the composition of phenolic compounds in apples. The amount of quercetin glycosides varied from 314.78±9.47 μg/g (Poland) to 648.17±5.61 μg/g (Estonia). The same trend was also observed with flavan-3-ols (from 829.56±47.17 μg/g to 2300.85±35.49 μg/g), phloridzin (from 55.29±1.7 μg/g to 208.78±0.35 μg/g), and chlorogenic acid (from 501.39±28.84 μg/g to 1704.35±22.65 μg/g). It was observed that the amount of investigated phenolic compounds tended to increase from apples grown in the southern location (Poland) (1701.02±75.38 μg/g) to apples grown northern location (Estonia) (4862.15±56.37 μg/g). Apples (cv. 'Ligol') grown in Estonia accumulated approx. 2.86 times higher amount of phenolic compounds than apples grown in Poland.

In conclusion, the geographic region has meaningful influence on variance of quantitative composition of phenolic compounds.

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References
[1] Liaudanskas M et al. *J Chem*. 2014; 2014.

PO-31

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Increase of phytosterols content in response to cytokinin kinetin treatment of marigold (*Calendula officinalis*) hairy roots

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Phytosterols are plant primary metabolites known for being cell membranes constituents and substrates of synthesis of phytohormones brassinosteroids [1]. Their bioactivities in humans include reduction of cholesterol levels in plasma, antidiabetic, antiinflammatory and antitumor which makes them valuable resource for production of pharmaceuticals, cosmetics and functional food [2]. Phytosterols have rarely been regarded as the target products in plant *in vitro* cultures, however, this interest appeared recently due to their beneficial effects on human health and other possible applications. Different strategies have been applied to increase the sterol accumulation, including elicitation and metabolic engineering. However, the majority of elicitors (e.g. jasmonates, pectins) caused a decrease in sterol biosynthesis. In this study we treated hairy roots of marigold with four different phytohormones, auxins: IAA (indole-3-acetic acid) and NAA (1-naphthaleneacetic acid), and cytokinins BAP (6-benzyloamino purine) and kinetin in concentration of 0.75 mg/L. From all four phytohormons only natural cytokinin – kinetin affected phytosterols' levels. The total sterol content in control culture was approximately 435 µg/g DW, and after treatment with kinetin it was increased by 27%. Particulary strong effect was observed in stigmasterol – 34% increase and isofucosterol up to 19 µg/g DW. Simultaneously, no remarkable effect of kinetin on hairy root culture growth was observed.

References

[1] Valitova JN et al. *Biochem (Mosc)*. 2016; 81:819-834.
[2] Miras-Moreno B et al. *J Agr Food Chem*. 2016; 64:7049-7058.

PO-32

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Metabolism of sterols and pentacyclic triterpenoids in grapevine *Vitis vinifera* leaves elicited with methyl jasmonate

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In the context of pesticide misuse, elicitor-triggered stimulation of natural resistance represents a promising sustainable disease control approach in vineyard. Applied elicitors should be tested not only for their ability to induce defense reactions but also for their impact on the overall plant vigor. Study on triterpenoid biosynthesis in elicitor treated plants allows to follow both primary and secondary metabolism. Sterols play essential role in formation of cell membranes and regulation of their fluidity. Defense function and accumulation of some pentacyclic triterpenoids in response to elicitation was reported [1,2]. In this study, greenhouse *Vitis vinifera* cv. Cabernet Sauvignon cuttings were sprayed with methyl jasmonate known for inducing a large number of defense responses in grapevine [3]. The young, medium, and old leaves were harvested after 7, 14, and 21 days post-treatment (d pt) and subjected to GC-MS/FID analysis of triterpenoids. Significative decrease of sterol content was observed in treated leaves, the most spectacular decline (4.93 times) was noted in old leaves 7 d pt. Elicitation triggered a slight accumulation of pentacyclic triterpenoids uniquely in old leaves at 14 d pt. The quantities of taraxerol, β-amyrin, α-amyrin/lupeol, α-amyrenon and lupeol acetate increased 1.60, 3.45, 3.07, 5.07, 1.24 times, respectively. After 21 d pt the amounts of sterols and pentacyclic triterpenoids were progressively pursuiting to the levels present in control leaves.

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References
[1] González-Coloma A et al. *Phytochem Rev*. 2011; 10:245-260.
[2] Lucini L et al. *Phytochemistry.* 2018; 156:1-8.
[3] Belhadj A et al. *J Agric Food Chem*, 2006; 54:9119-9125.

PO-33

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Exploring free and glycosidic forms of triterpenoids in cuticular waxes and tissues of chokeberry and blackberry leaves

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Various forms of triterpenoids (e.g., free, esters and glycosides) differ in polarity and solubility in water, and as a consequence in localization in cells, tissues and whole plant organs, as well as in their functions. The aim of the study was to investigate the occurrence of various forms of triterpenoids in cuticular waxes and remaining tissues of leaves of two plants from family Rosaceae: chokeberry and blackberry. It was confirmed that the chosen plants differ significantly in distribution of triterpenoids between cuticular waxes and internal tissues of leaves. In chokeberry triterpenoids occur mainly in the free form in the surface waxes, where they probably constitute the "first line of chemical defense". In blackberry the "second line of defense", i.e. accumulation of saponins in internal tissues, predominates. The total content of free forms of triterpenoids in chokeberry (the chloroform wax extract and diethyl ether extract of remaining tissues) accounted for approximately 3878 mg per one gram of fresh weight, while the glycosidic forms (methanol extract) for 454 mg. For blackberry leaves, the total content of free forms of triterpenoids was almost six times lower while the glycosidic forms was almost two times higher than in chokeberry. The obtained results provided the new data on triterpenoid profiles in both studied plants.

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PO-34

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Insights into epicuticular wax composition of fruits and leaves of Saskatoon (*Amelanchier alnifolia* Nutt. cv. Smoky and Northline)

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Amelanchier alnifolia Nutt. known as Saskatoon berry, Juneberry, or Western Serviceberry, is a deciduous shrub native to the Northern plains of North America [1]. The fruit is often reported as a berry, but it is actually a pome fruit (accessory fruit) typical in the pome fruit family Rosaceae [2]. The most common cultivars are Honeywood, Martin, Northline, Pembina, Smoky and Thiessen [3]. The aim of this study was GC-MS qualitative and quantitative determination of triterpenoids occurring in surface waxes of fruits and leaves of two cultivars of Saskatoon (*Amelanchier alnifolia* Nutt. Smoky and Northline). The chemical composition of plant waxes is highly variable among plant species, organs of the plant (e.g., fruits and leaves), and during organ ontogeny.

Nineteen triterpenoid compounds were identified in analyzed cultivars, including five triterpene acids (3-oxo-oleanolic, oleanolic, betulinic, ursolic and corosolic), eight steroids (mainly campesterol, stigmasterol, sitosterol and tremulone), and six neutral triterpenes (α- and β-amyrins, ursolic aldehyde, erythrodiol, uvaol, and taraxerol – only in leaf extracts). The results of the analyses showed that the leaf extracts had significantly higher content of triterpenoids in comparison to the fruit extracts. The content of triterpenoids in Smoky and Northline cultivars amounted to approximately 127.85 and 45.69 μg/mg of fruit wax extracts, and to 215.80 and 214.03 μg/mg of leaf wax extracts, respectively.

Acknowledgements

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References

[1] St-Pierre RG et al. *Can J Plant Sci*. 2005; 85:929-932.
[2] Pruski K et al. *Plant Cell Tissue Organ Cul.* 1990; 21:103-109.
[3] Zatylny AM et al. *Can J Plant Sci.* 2005; 85:933-938.

PO-35

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Isolation of phenanthrenes from the moss *Paraleucobryum longifolium*

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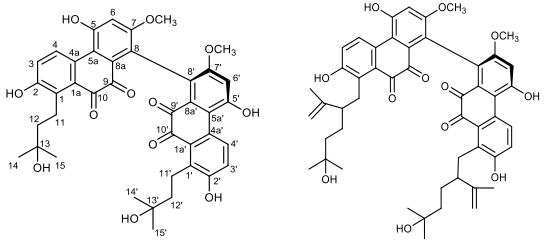
Paraleucobryum longifolium (Ehrh. ex Hedw.) Loeske (Dicranaceae) is distributed in Northern America, Asia and Europe. The plant has 4-8 mm long whitish or grayish green, glossy leaves, and it grows on cliffs, tree trunks, and rotten logs, in the moderate zone. In a screening experiment, different extracts of *P. longifolium* showed antibacterial and antiproliferative effects [1], so it was chosen for further preparative work to identify secondary metabolites.



From the methanolic extract of the moss, compounds **1**-**2** were isolated as amorphous compounds with dark violet color. The separation required the combination of chromatographic methods, including vacuum liquid chromatography on silica gel and on reversed phase silica gel, gel filtration and RP-HPLC. The structures were determined by spectroscopic methods, such as NMR, HRESIMS spectroscopy. The identified compounds are the first 9,10-phenanthrenequinone dimers, in which the monomers are connected through their C-8 atoms. The presence of these compound in this plant may explain the observed bioactivities, since monomeric 9,10-phenanthraquinones have been reported to have strong antibacterial effects.

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References

[1] M Vollár et al. *Molecules*, 2018; 23: E1520.

PO-36

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Chemical characterization of common ragweed (*Ambrosia artemisiifolia* L.) root

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Common ragweed (*Ambrosia artemisiifolia* L.), a North-American native species, is present as an invasive plant in Europe. Because of it purported allelopathic effect and since it does not have any natural pests on our continent, it spreads very quickly, and this is triggered by the change of the climate. It is one of the hundred worst invasive aliens, therefore the European Food Safety Authority promotes its eradication.
The aim of our work was to characterize the chemical profile of common ragweed in order to identify metabolites with potential medicinal use. In earlier studies we detected *in vitro* antitumor effects of ragweed extracts. The extract of the herb was effective on human breast adenocarcinoma cells (MCF-7, IC_{50}: 10.2 µg/ml) and human skin epidermoid carcinoma cells (A431, IC_{50}: 11.1 µg/ml) while the extract of the root showed activity on human skin epidermoid carcinoma cells (A431, IC_{50}: 8.5 µg/ml) [1].
Based on these results, we carried out chromatographic separation of the root extract by using different chromatography methods. From the non-polar fractions of the methanolic root extract we isolated five substances, a thiophene, a lignin, a triterpene sterol and a fatty acid. The structures of the isolated compounds were determined with 1D and 2D NMR spectroscopy. The pharmacological effects were tested on human cancer cell lines (using MTT-assay) and on human pathogen bacteria strains (using disc diffusion assay).

References

[1] Réthy B et al. *Phytother Res*. 2007; 21: 1200-1208.

PO-37

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Development and validation of a HPLC-UV method for the quantification of charantin in *Momordica charantia* products

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Momordica charantia L., also known as bitter melon, is widely cultivated as a vegetable crop in tropical and subtropical countries. It has been used in traditional medicine for various actions. Among them, the most studied is the hypoglycemic activity, attributed to different chemical compounds, like some triterpene glycosides and charatin. This work is part of a project which aims the comparison of chemical components of the greenhouse-grown plants in Romania and imported vegetable products (India). We measured the charantin content of 8 samples obtained from 3 different Romanian producers (fruits and leaves) and an import drug. In addition, we analyzed 2 tea products and 4 food supplements containing bitter gourd extracts. A HPLC-UV method was developed and validated for the determininationof charantin content. We found that greenhouse-grown plants of Romanian origin have similar charantin content (0.39-0.64 mg/g) to those from India (0.58 ± 0.01 mg/g). In food supplements, the charantin content was in expected range, except one product which had lower content (0.131 ± 0.008 mg/g) and in case of one of the teas, where the charantin content was below the LOD. The organoleptic analysis of this tea shown to contain only traces of bitter melon, and probably contains black tea. This assumption has been confirmed by TLC analysis.
This proposed method is suitable and practical for comparison of the charantin content of herbal products of different origin and could be of use for analysis of charantin in food supplements.

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References
[1] Habicht SD et al. *Curr Diabetes Rev*. 2014; 10: 48-60.
[2] Rédei D et al. *Gyógyszerészet*. 2011; 55: 463-71.

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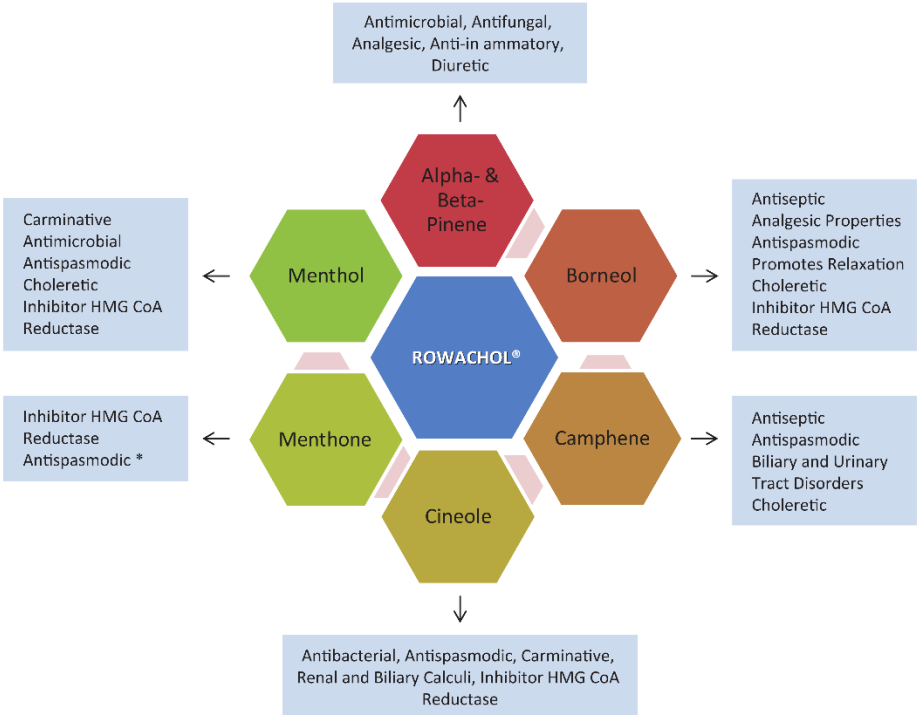

References: * EMA Assessment report on menta x piperita L. aetherolateum Sep 2008

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