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“NATURAL PRODUCTS IN COSMETICS, FOOD AND MEDICINE”

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Summary:

The 4th Annual CNPD (Centre for Natural Products Discovery) Conference was held on 19-22 June 2023 at the John Lennon Arts and Design Building (Liverpool John Moores University).

The Organisation Committee has kindly approved the publication of all communications presented to this event in this issue of the Journal of Natural Products Discovery.

This issue will replace the classic “Book of Abstracts” that was published in previous years. Therefore, authors will have a collective D.O.I. associated with their presentations instead of an ISSN.

We hope that in this way both the event and splendid work of the attendants will be more publicly accessible.

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Communication to Congress (Abstract)

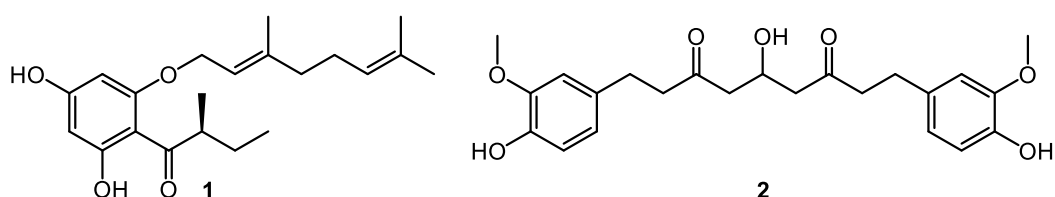
PHYTOCHEMISTRY: NOT JUST FOR DRUGS AND BUSTING BUGS

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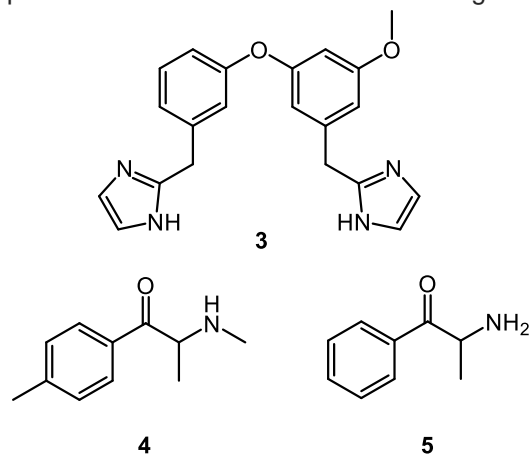
Abstract

This lecture will cover some highlights from research on new antibacterial natural products from plants. Examples will include those with activity against antibiotic-resistant strains of bacteria, such as olympicin A (**1**), a potent anti-Gram positive acylphloroglucinol from *Hypericum olympicum*, a beautiful Greek member of this taxon (Shiu *et al.*, 2012). I will then discuss phytochemicals that inhibit antibiotic efflux in bacteria, such as the unusual diarylnonanoid **2** from a South African *Dioscorea* species (Sibandze, Stapleton and Gibbons, 2020).



We also studied compounds such as the imidazole alkaloid **3**, which can inhibit the transfer of plasmids between bacteria (Kwapong, Stapleton and Gibbons, 2018). This approach has great potential as plasmids harbour antibiotic resistance genes and virulence factors and inhibition of the transfer can

reduce the spread of resistance and bacterial pathogenicity. Such materials could have topical utility in the preparation of soaps, lotions and in combination with antiseptic materials, particularly for travellers visiting areas of high antibiotic resistance. During my academic career I also advised the British Government on the scheduling and classification of drugs of abuse. This was at a time when Europe was under considerable threat from Novel Psychoactive Substances (NPS). This led to a fruitful area of research on the characterisation of some of these materials, a few of which are analogues of plant natural products. Examples of these include mephedrone (**4**), which is an analogue of cathinone (**5**), and a very brief overview of NPS will be given (Gibbons and Zloh, 2010).



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Communication to Congress (Abstract)

PLANT-DERIVED PRODUCTS IN RHEUMATOID ARTHRITIS: FROM TRADITIONAL MEDICINE TO EVIDENCE-BASED CLINICAL PRACTICE

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Abstract


Rheumatoid arthritis is a chronic autoimmune disease characterized by synovial inflammation, cartilage, tendon and bone destruction resulting in severe functional disability and decrease in patients' life quality. Various genetic and environmental factors trigger an exacerbated immune response (production of autoantibodies, TNF-alpha, IL-1, -4, -6, -17 and reactive oxygen species) that causes a chronic inflammatory condition affecting predominantly the small joints of hands and feet. The pharmacological treatment of rheumatoid arthritis includes nonsteroidal anti-inflammatory drugs, glucocorticoids, disease-modifying antirheumatic drugs and biological therapies. But all these treatment options are endowed with severe side effects. Therefore, in recent years, the interest in plant-derived products as alternative and/or adjuvant therapy in rheumatoid arthritis has significantly increased. Various phytochemicals (phenolic acids, flavonoids, diarylheptanoids, stilbenes, terpenes, alkaloids, benzenoids) and plant extracts have been reported to modulate the production and activity of inflammatory mediators involved in the pathogenesis of rheumatoid arthritis. In addition, the efficacy and safety of some plant-derived products supplementation in patients with rheumatoid arthritis has been investigated in clinical trials. This presentation, including also own studies, focuses on the plant-derived products having positive therapeutic effects in patients with active rheumatoid arthritis. Taken together, plant-derived products ameliorate both the clinical symptoms and inflammatory biomarkers, being promising for the development of adjuvant therapies in rheumatoid arthritis.

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Communication to Congress (Abstract)

PHYTOHORMONES FULL OF AMAZING BIOLOGICAL AND MEDICAL ACTIVITIES

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Abstract


Plant hormones (or phytohormones) are signalling molecules produced in plants that occur at very low femto – and picomolar levels. These hormones control all aspects of plant growth and development, from embryogenesis to full plant development, regulation of organ size and development, pathogen defence and stress tolerance. Unlike animals, where hormone production is limited to specialized glands, every plant cell is capable of producing phytohormones. In vitro and in vivo experiments have also demonstrated that they can also have diverse effects on animal cells and tissues. Of particular interest is their ability to protect cells against various forms of stress and prevent some of the harmful effects of cell aging. For example, human skin fibroblasts cultured in the presence of cytokinin kinetin or trans-zeatin retain some characteristics of cells of lower passage. Kinetin is even able to increase the lifespan of invertebrates. The anti-proliferative activity of cytokinin ribosides (through induction of cell cycle block or/and cell death) and bases (through induction of cell differentiation) has prompted studies into their potential utility for the therapy of proliferative diseases like leukaemia, cancer and psoriasis. Furthermore, inhibitors of cyclin-dependent kinases olomoucine, boheminine, roscovitine, indirubin, etc., were inspired also by cytokinins and auxins. Particularly CDK5 inhibitors, as antiangiogenic agents, indicated that structure-activity analyses of N6-substituted adenine derivatives could greatly facilitate the identification of potent new antiangiogenic compounds. In this presentation, the protective effects of phytohormones at molecular, cellular, tissue and organismal levels will be discussed. We would also like to discuss potential application of phytohormones for the treatment of age-related diseases, including neurodegenerations.

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Communication to Congress (Abstract)

TYROSINASE INHIBITORY PROPERTIES OF POLYPHENOLS: INSIGHTS INTO MECHANISM OF ACTION THROUGH INHIBITION KINETICS AND DOCKING SIMULATIONS

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Abstract


Tyrosinase plays key role in melanin biosynthesis in mammals, bacteria, plants, and fungi. It is well known that melanin protects the skin from UV damage but its excessive production causes freckles, melasma, skin cancer, and age spots. Moreover, studies reported that many melanogenesis disorders have been linked to the neurodegenerative diseases including Parkinson's, Alzheimer's, and Huntington's diseases. Tyrosinase oxidizes dopamine to form melanin in the brain. Dopaquinones trigger neuronal damage in the brain due to dopaminergic neurons deficiency in turn lead to neurodegenerative diseases. Furthermore, tyrosinase can lead to unfavorable enzymatic browning in vegetables and fruits and reduce their nutritional and market values in food industry. Consequently, tyrosinase inhibitors get attention of cosmetic, pharmaceutical and food industry. We tested tyrosinase inhibitory effects of different types of polyphenolic compounds, especially flavonoids to discover natural hits. In our investigations we found some compounds more potent than the positive control, kojic acid (Şöhretoğlu et al., 2018, Arroo et al., 2020). In this presentation, tyrosinase inhibition of different type of phenolics, their mechanisms of action and structure–activity relationships will be discussed. Moreover, enzyme kinetics of the tested compounds *in vitro* and their possible interactions with the enzyme predicted by structure-based molecular modelling approaches will be provided.

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Communication to Congress (Abstract)

PRENYLATED PHENOLS WITH POTENT ANTI-INFLAMMATORY EFFECTS

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Abstract

Natural substances often have a pleiotropic effect and can affect several cellular processes in parallel. They can have parallel anti-inflammatory and antibacterial effects, together with the current antiviral effect. Their mechanism of action is complex. However, the problem of natural substances is often their limited solubility and consequently also problematic bioavailability (Brezani, *et al.* 2018). Series of prenylated phenols were isolated from Paulowniaceae, Moraceae, and Euphorbiaceae plants (Lelakova *et al.*, 2019; Hanáková *et al.*, 2017; Malaník *et al.*, 2020; Čulenová *et al.*, 2020). As part of the lecture, we will introduce the isolation and identification of prenylated phenols with potential antiviral and anti-inflammatory effects, we will describe their bioactivity, their formulations to increase solubility, and will describe the possibilities of their further development. We described the effects of 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, and also some *in vivo* experiments confirming activity. At the end, an improvement of solubility by incorporating of tested substances into liposomes was presented.

Acknowledgements

The work was supported by the Czech Science Foundation grant no. GF21-38204L Complexes of selected transition metals with plant-derived compounds with anti-NF-kappa B and pro-PPAR dual activities.

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Communication to Congress (Abstract)

USE OF NATURAL PRODUCTS IN 3D PRINTING OF MEDICINAL TEDDY BEARS

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Abstract

Solid oral dosages, although widely accepted by society, are inconvenient for children, with 54% between the age of 6 and 11 years unable to swallow a tablet easily. The lack of will to swallow solid forms is also common in healthy adults. If a drug formulation, appropriate for paediatric use, is not commercially available, then tablets or capsules intended for adults are often converted into powder or liquid by hospital pharmacists. Normally, drug powder formulation and liquid have bitterness and cause noncompliance issues. 3D printing has proved to be a manufacturing technique with great potential. Since it allows the creation of three-dimensional objects, layer by layer leading to total freedom of form and design. 3D printed medicines have been produced in pharmaceutical factories, but it can be produced in medical institutions such as hospitals because the printers are small. 3D printing of drug formulations can be useful for treating paediatric patients. 3D printed medicines mask the bitterness of drugs and thus are attractive alternatives. 3D printing has been employed to produce gummies attractive to children. However, 3D printed gummy bears have not produced for antibiotics with bitter taste such as ciprofloxacin.

We have applied gel 3D printing to produce ciprofloxacin gummy bears using gelatine or pectin as the main gelling agents. Gummy bears of ciprofloxacin were produced with desired details using both gelling agents, however, pectin gummy bears showed better appearance. The gummy bears showed excellent antimicrobial activity, indicating that the formulation did not affect the antimicrobial activity. In conclusion, natural products can be used in 3D printed gummy bears of ciprofloxacin with excellent visual appearance and antimicrobial activity.

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Communication to Congress (Abstract)

COMPOSITION EFFICACY WITHIN *P. DULCE* PLANT TO NEUTRALISE VENOMS OF THREE CLINICALLY IMPORTANT SNAKE SPECIES

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Abstract

Envenoming by snakes frequently results in life-threatening or life-altering pathologies and is one of the most neglected global public health issues, as evidenced by the substantial morbidity and mortality rates observed in many tropical and subtropical countries. Despite the routine use of polyclonal antibody-based antivenom therapies to manage the onset of systemic envenoming, the clinical consensus is that these interventions are ineffective against the local venom effects (such as painful progressive swelling, blistering, and tissue necrosis, resulting in loss of limb function and amputations) because of their inability to penetrate the blood-tissue barrier.

We have screened the *P. dulce* plant leaf for active components using different approaches to cross-neutralising activity against toxins responsible for local tissue damage induced by three clinically important snake species, *B. jararaca*, *C. atrox*, and *E. carinatus*. The phytochemical characterisation showed that the active fractions (consisting mainly of secondary metabolites such as tannins and polyphenols) were found to be promising in neutralising local haemorrhage caused by the three clinically important snake species using different assays such as ex vivo (using chicken egg embryos) assays including the use of animal (WKY-rat) model. The animal responded very well, and results were found to be encouraging, i.e., were matched by the successful elimination of venom-induced haemorrhage, which we believe will span the early development of the first cost-effective localised snakebite therapy through preclinical validation and be ready for future clinical evaluation. This study aligns with the core objectives of the WHO's roadmap to reduce snakebite envenoming by 50% by 2030 via the delivery of effective therapies.

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Communication to Congress (Abstract)

ANTIANGIOGENIC PTEROCARPAN AND FLAVONOID CONSTITUENTS OF *ERYTHRINA LYSISTEMON*

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Abstract


The roots of *Erythrina lysistemon*, growing in Egypt, yielded 24 flavonoid compounds, including 17 pterocarpan, two isoflavanones, one flavanone, two isoflavans, one 2-arylbenzofuran and an isoflavan-3-ene. Nine pterocarpan have not been reported previously (7-9, 11-14, 19 and 20) and 11 are reported here for the first time from this species. Structures were established using HRESIMS, NMR and circular dichroism techniques. Selected compounds were tested for their ability to block the growth of human retinal endothelial cells and antiangiogenic activity in vitro. The isoflavonoids 5 and 6, and the pterocarpan 1, 2, 4, 20 and 22 demonstrated selective antiproliferative activities on endothelial cells compared to a non-endothelial cell type, with concentration-dependent antiangiogenic effects in vitro against HRECs, a cell type relevant to neovascular eye diseases.

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Communication to Congress (Abstract)

ANTIPROLIFERATIVE HIGH-VALUE PHYTOCHEMICALS FROM THE UNDER-EXPLORED CROP, *PIPER COLUBRINUM*

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Abstract

Plants can be regarded as chemical libraries of structurally diverse compounds with tremendous ethno-medical importance with fewer side effects, therefore constituting a promising approach in drug discovery. However, a myriad of plants with immense pharmacological and therapeutic potential are still in the “under-explored” category. The present study was carried out to discover the anticancer phytochemicals from the under-utilized plant *Piper colubrinum*. Matured and dried fruits of *P. colubrinum* were sequentially extracted with hexane, chloroform, methanol and water. The chloroform extract exhibited a very good cytotoxicity (IC₅₀ - 65.94 µg/mL) on cervical cancer cells, CaSki. Nine compounds were separated from the chloroform extract using preparative TLC and two among them (C-1 and C-2) were screened for high cytotoxicity against CaSki cells. The cytotoxic potential of these two compounds were further validated in a concentration-dependent manner by PI live dead flowcytometry assay. The underlying mechanisms of their cytotoxicity on CaSki cells were further elucidated by measuring mitochondrial membrane potential loss, reactive oxygen species (ROS) production, apoptosis in terms of externalization of phosphatidylserine to the outer membrane using annexin VFITC/PI and cell cycle arrest. C-1 and C-2 caused mitochondrial membrane aberration and thus exerts the cytotoxic effect on CaSki cells by inducing mitochondrial-mediated apoptosis. The findings have further demonstrated that C-1 and C-2 triggered oxidative stress and ROS production which leads to oxidative stress mediated cell death. C-1 and C-2 also showed cytotoxic potential by inducing apoptosis in a concentration-dependent manner as observed by annexin VFITC/PI staining. The noteworthy observation on cell cycle analysis was the increasing sub-G1 peak, which indicated the occurrence of apoptosis brought about by the treatment with C-1 and C-2 at their IC₅₀ concentration. Further, these compounds successfully prevented metastasis, which was tested using Scratch wound assay. C-1 and C-2 phytochemicals were identified by Gas Chromatography/Mass Spectrometry as fatty acids. Further purification of C-1 and C-2 will be performed, and structural elucidation of individual compounds will be established further. To the best of our knowledge, this study is first of its kind to target the anticancer drugs from *P. colubrinum* against cervical cancer. The findings mark *P. colubrinum* as a potential source for the discovery of natural anticancer drugs.

Acknowledgements

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Communication to Congress (Abstract)

RECENT PROGRESS IN THE ISOLATION OF PRENYLATED FLAVONOIDS FROM *BROUSSONETIA PAPHYRIFERA* WITH POTENTIAL ANTI-INFLAMMATORY PROPERTIES

Milan Malaník¹,* and Karel Šmejkal¹

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Abstract

Broussonetia papyrifera (Moraceae) is a rich source of prenylated flavonoids and the reports of isolation and identification of new compounds increase at a rapid pace. Recently, we described a novel 5,11-dioxabenzob[*b*]fluoren-10-one derivative named brousofluorenone C and together with further thirteen known compounds, their anti-inflammatory activities were evaluated in the LPS-stimulated THP-1 cells as well as their cellular antioxidant effects. Since then, our ongoing work with different parts of *B. papyrifera* revealed that stem bark is rich in prenylated flavonoids while wooden parts of branches are rich in lignans. Subsequent extraction and chromatographic separation led to the isolation of further eight prenylated flavonoids that have never been described in *B. papyrifera* of which three compounds have been isolated from the plant material for the first time. We also suggested the structural revision of 3,4-dihydroxyisolonchocarpin that was isolated from *B. papyrifera*, previously. Based on the structures of isolated compounds, it can be postulated their anti-inflammatory and antioxidant potential.

Acknowledgement

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Communication to Congress (Abstract)

BIOACTIVE COMPONENTS FROM CHINESE MEDICINAL FOOD WITH GOOD ANTI-DIABETES AND ANTI-OBESITY POTENTIAL EXPLORED BY BIOAFFINITY ULTRAFILTRATION LC-MS

Ming-Quan Guo ^{1,✉} and Meng-jia Xu ¹

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Abstract

Many traditional medicinal herb and vegetable plant in China have long been reported to treat obesity, diabetes, and other diseases. However, the mechanisms of action regarding their anti-diabetes and anti-obesity effects and correlated functional chemical components still remain elusive. In the present study, our aim is to explore the underlying mechanisms of anti-diabetes and anti-obesity effects and the potentially responsible chemical components these plants such as *Nelumbo nucifera Gaertn Lam.* (also called lotus), *Morus alba L.* (Mulberry). To evaluate the in vitro hypoglycemic and hypolipidemic activities, their extracts were tested using Hep G2 cells, and in vitro inhibition on α -glucosidase and pancreatic lipase was also conducted as well as their effects on both glucose consumption and lipid levels. Then, their chemical profiles were characterized and identified by using LC/Q-Tof-MS, and it was found that some bioactive components (Lotus alkaloids, and Mulberry polyphenols) might be their major functional phytochemicals. To further reveal the functional components, affinity ultrafiltration LC-MS (UF-LC/MS) with α -glucosidase and pancreatic lipase was thus conducted, and some key components displaying certain binding affinity to α -glucosidase and pancreatic lipase, were screened out and identified. Furthermore, molecular docking simulations revealed competitive binding effects of the number of hydrogen bonds and binding energies, which were in good agreement with the enrichment factors between the bioactive components and these target enzymes. Further animal studies were also conducted to verify these key compounds aiming to push forward to the clinical applications. To conclude, this study suggested lotus and mulberry leaves would be a promising natural source for the prevention and treatment of obesity and diabetes and could be further explored as the functional foods or other products for health care in the near future.

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Communication to Congress (Abstract)

HIGH PERFORMANCE THIN LAYER CHROMATOGRAPHY – A USEFUL TOOL FOR RANDD AS WELL AS QUALITY, SAFETY AND EFFICACY OF NATURAL HEALTH PRODUCT

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Abstract

In recent years, the instrumental advances in Phytochemical Analysis have facilitated and accelerated the examination of natural products, their complex mixtures when derived from natural sources and the quantitation and structure elucidation of individual compounds. Liquid-Column and Gas Chromatography hyphenated with MS as well as NMR are the most common methods from secondary metabolic analysis and quantitation of standardization markers. Nevertheless, the simplest form of chromatography – planar chromatography - is in its modern and automated form as High-Performance Thin Layer Chromatography (HPTLC) still an important part of pharmaceutical quality control – especially in Ph Eur monographs it is used for plant material authentication.

But HPTLC can be the basis of much more: it basically is a planar solid phase extraction and fractionation tool in one step. It can be hyphenated with MS or bioassays (bioautography). The latter is also called “effect-directed analysis” and has a huge potential in complementing the common phytochemical analysis methodologies for quality assessment and functioning as a pre-screening tool for safety and efficacy testing.

The lecture gives insights into HPTLC as a tool for phytochemical and bioactivity research, mutagenicity assessment and anti-fungal efficacy screening.

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Communication to Congress (Abstract)

ANTIMICROBIAL ACTIVITIES OF THE BORNEAN SPECIES *CANTHIUM DIDYMIUM*

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Abstract

Antimicrobial resistance, particularly to multiple drugs, is a growing problem worldwide severely limiting therapeutic options. Current issues include the spread of Methicillin-Resistant *Staphylococcus aureus* (MRSA), some Gram-negative bacteria that produce β -lactamases and other resistance determinants. Novel strategies and approaches are necessary to tackle these issues. Natural products, especially from plants, continue to provide new chemical structures with high levels of antibacterial activity. Borneo rainforest, in Malaysia, is considered one of the global centres of plant diversity and remains to be an underexplored region for potential natural medicines. This study aimed to investigate the potential antimicrobial activities of the Bornean species *Canthium didyium* (*Psydrax dicoccos*). Powdered barks of *C. didyium* were subjected extraction successively with dichloromethane (DCM) and methanol for 24h. The resulting extracts were filtered and dried under vacuum. The extracts were further fractionated using the vacuum liquid chromatography, and assessed using Thin Layer Chromatography (TLC), and Liquid Chromatography (HPLC). The antimicrobial effects of the extracts were evaluated by disc diffusion assay and microbroth dilution method against relevant Gram-positive and Gram-negative pathogens. The DCM extract exhibited a potent activity against *Staphylococcus aureus*, showing a zone of inhibition of 20 mm and the Minimum Inhibitory Concentration (MIC) of 512 g/L. The Gram-negative strain that was used in this biological assay was *Escherichia coli* and the results were negative. More studies are currently ongoing to elucidate the potential compound or compounds responsible for this significant antimicrobial activity.

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Communication to Congress (Abstract)

ANTIBIOTIC-PRODUCING MICROBES FROM THE MARINE ENVIRONMENT

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Abstract

One of the world's most difficult challenges is antimicrobial resistance (AMR), which threatens a century of medical advancement. AMR has had an explosive rise on a worldwide scale, and a faster than expected transfer from one nation to the next. The number of fatalities from AMR currently account for 700,000 annually worldwide, and if persistent efforts are not made to manage this, deaths may rise to 10 million by the year 2050. After discovery of penicillin in the 20th century, microorganisms became an important source of novel antibiotic secondary metabolites. This study is aimed at discovering novel metabolites to overcome the issue of AMR. Fourteen water and four sediment samples were collected from a lake in University of East Anglia and River Yare in Norfolk, UK. These areas are completely unexplored with regard to the isolation of microorganisms. From these samples, 100 and 40 bacterial colonies were isolated on nutrient agar at 28 °C and 4 °C, respectively. Around 100 fungal colonies were isolated using potato dextrose agar at 28 °C. Antimicrobial bioassays of isolated colonies assessed using agar overlay and agar diffusion assay were carried out against two test microorganisms (Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli*). At this stage, five isolated fungal species were inoculated in PDA and oatmeal media caused a zone of inhibition against pathogenic bacteria. Liquid chromatography-mass spectrometry was used to investigate any differences in metabolites. Future work will isolate and elucidate the novel antibiotic compounds from antibacterial crude extracts followed by taxonomical classification of the isolated microorganism.

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Communication to Congress (Abstract)

HIGH-THROUGHPUT ANALYSIS OF NEUROACTIVE STEROIDS IN HUMAN SERUM BY UHPLC-MS/MS

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Abstract

Steroid hormones play a key role in regulating various functions of the human body, such as immune and stress responses, carbohydrate and protein metabolism, mineral and water management, and sexual development and reproduction. In addition, neuroactive steroids, a specific group of steroid substances, can modulate the function and development of the nervous system. The main sources of steroids are typically the gonads and adrenal glands. However, the skin, adipose tissue, gastrointestinal tract, gut microbiota, and nervous tissue are also equipped with a steroidogenic enzymatic system. A specific subgroup of neuroactive steroids produced in the nervous system by neurons and glial cells are known as neurosteroids. Certain pathologies affecting the human body, such as Parkinson's disease, Alzheimer's disease, multiple sclerosis, or Huntington's disease, can disrupt metabolic pathways and thus change the metabolic profile of neuroactive steroids. Current diagnostic options for neurodegenerative diseases are very limited and primarily based on characteristic clinical symptoms. Knowledge of metabolic disturbances in specific diseases can potentially serve as a tool for differential diagnosis. The aim of this work was to develop and validate a method based on ultra-high performance liquid chromatography combined with tandem mass spectrometry (UHPLC-MS/MS), which would allow simultaneous detection and quantification of selected steroid hormones with neuroactive effects in human blood serum. Selected analytes included steroids classified as progestins (pregnenolone, progesterone, and 5 α -dihydroprogesterone) and as androgens (testosterone, 5 α -dihydrotestosterone, androstenedione, dehydroepiandrosterone, and epiandrosterone).

Acknowledgements

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Communication to Congress (Abstract)

A NEW HIGH-THROUGHPUT ANALYTICAL METHOD THAT ALLOWS RELIABLE PROFILING OF STEROID SUBSTANCES COULD CONTRIBUTE TO A BETTER UNDERSTANDING OF MANY DISEASES ASSOCIATED WITH CHANGES IN NEUROACTIVE STEROID LEVELS. GIBBERELLINS: A POWERFUL TOOL IN PLANT-GROW REGULATIONSMarkéta Fuksová^{1,2} * and Jiří Pospíšil^{1,2} 

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Abstract

In modern agriculture, herbicides, pesticides, and grown retardants play an important role in influencing the development and growth of field crops. However, the negative environmental impact of these substances is leading to a search for natural and non-toxic alternatives. Gibberellins (GAs), natural growth regulators, are being investigated as alternatives to commonly used synthetic compounds. The control of plant growth can be achieved through two ways: the addition of biologically active GAs to increase endogenous GAs and promote growth and germination, or the application of growth retardants to reduce endogenous GAs and inhibit plant growth.

Recently, our research group developed and tested a new gibberellin-based plant retardant that acts as a competitive antagonist of bioactive GAs with a stronger affinity for the GA receptor in plants (GID1) than bioactive endogenous GAs. After three years of intensive field trials (optimizing the dosage, type of application, etc.) a protocol was established to enhance the grain yield of barley by 20% (t/h) and wheat by 7% (t/h). Notably, compared to negative control, no change in ear size and seed number for treated plants was observed (commercially used synthetic growth retardants showed lower numbers).

Currently, we are focusing on two important issues regarding our leading structure:

(1) increasing its bioavailability, and (2) improving its solubility in water. To achieve the first aim, we prepared a fluorinated derivative of the lead structure with the aim of enhancing the migration of the molecule through the cytoplasmic membrane to the GID1 receptor. Enzyme competitive assays show that this derivative has superior inhibitory activity compared to the best available compound. To address the second issue, we prepared several ammonium salts of the anti-gibberellin. These modifications will hopefully improve solubility and bioavailability, allowing us to reduce the amount of compound applied to plants during field trials. Newly prepared compounds will be evaluated in field trials this year. In this contribution, we present the latest results obtained during this project.

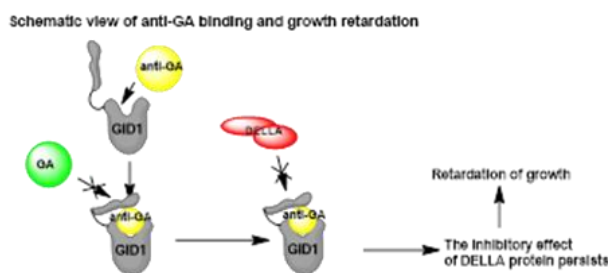




Figure 1 Schematic view of anti-GA binding and growth retardation. Anti-GA blocks the active side of GID1, which disables its activation. Inhibition prevents interaction with the DELLA protein (repressors of plant development) and its subsequent degradation. The inhibitory effect of the DELLA protein persists, and growth retardation occurs.

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Communication to Congress (Abstract)

WIDE PORTFOLIO OF PLANT STEROIDS ACROSS NATURAL PLANT PRODUCTS

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Abstract

Steroids belong to a large family of terpenoids in both plant and animal kingdoms. They are built from C5 units of isoprene, as clarified 70 years ago by Leopold Ruzicka, a Croatian chemist of Czech origin. Plant naturally occurring substances with a steroid skeleton are tetracyclic compounds containing about eighteen to thirty carbon atoms, and their biological function is also very diverse. They can fulfil the role of plant hormones and participate in plant growth and development, or they are synthesized *de novo* in plant cells as signalling molecules involved in the plant's response to environmental cues. Important plant steroid substances include phytosterols, an essential component of the membranes of all eukaryotic organisms; plant hormones brassinosteroids, phytoecdysteroids, as well as estrogens, androgens or steroidal saponins. Using the example of puncturevine (*Tribulus terrestris*) and other selected plant species, we show the diversity of the group of steroid substances the plant can produce to ensure its physiological functions and defence capacity. Many of these steroid compounds also have an effect on human health, e.g. in the form of adaptogenic, antiviral, anti-inflammatory, anti-cancer, osteoprotective, anti-diabetic, antifungal or blood lipid-lowering properties.

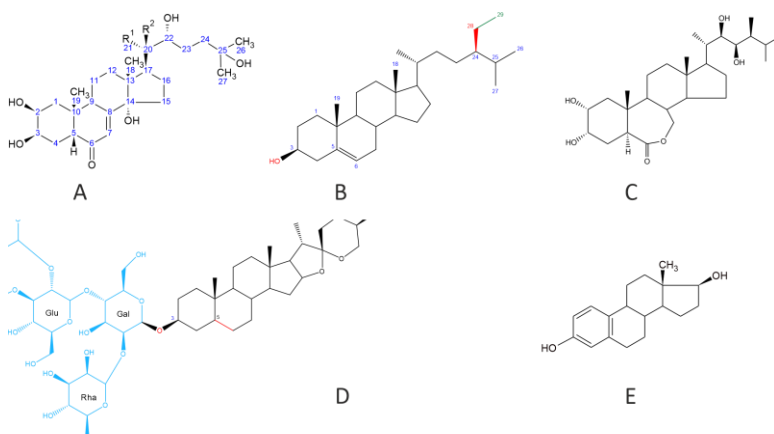


Figure 1. Chemical structures of selected representatives of various types of plant steroids. A - phytoecdysteroid 20-hydroxyecdysone (R^1 -CH₃, R^2 -OH); B - phytosterol β -sitosterol; C - brassinosteroid brassinolide; D - steroidal saponin tribulosin; E - phytoestrogen 17 β -estradiol.

Acknowledgements



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Communication to Congress (Abstract)

IDENTIFICATION OF NARCICLASINE AS *IN VITRO* ANTI-INFLAMMATORY COMPONENT OF *CYRTANTHUS CONTRACTUS* BY CORRELATION-BASED METABOLOMICS

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Abstract

The relative dearth of currently available anti-inflammatory drugs stimulates a search for new active substances. In this study, an extract from the bulbs of *Cyrtanthus contractus* showed strong anti-inflammatory activity *in vitro*. The extract was partially separated into 14 fractions and analyzed by UHPLC-QTOF-MS metabolomics where high level of polyphenols was detected. The correlation coefficients were calculated between biological activities and metabolite levels. As a result, the top-scoring phenolic alkaloid narciclasine (figure 1) is proposed as the active principle of *C. contractus*. This was confirmed by comparing the biological effect of crude extract with that of an authentic standard.

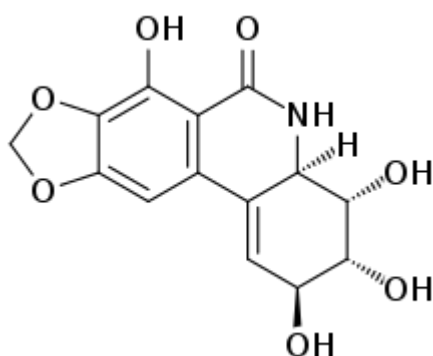


Figure 1. Narciclasine

Acknowledgements

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Communication to Congress (Abstract)

ANTIBACTERIAL AND PHYTOCHEMICAL STUDY OF BORNEAN MYRISTICACEAE AND CLUSIACEAE SPECIES

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Abstract

Antimicrobial resistance is a leading cause of morbidity and mortality worldwide. In 2019, 1.3 million deaths were directly caused by antibiotic resistant infections, with estimations that by 2050, such infections could cause 10 million annual premature deaths worldwide, as well as a large economic burden. The island of Borneo has remarkable biodiversity, which includes a variety of unexplored species, some of which belong to families known for their pharmacological activity, such as the *Myristicaceae* and *Clusiaceae*. During this project, a preliminary literature review investigated the phytochemical and biological studies of 44 plant species sampled from Borneo, revealing that over half have had no published literature on their phytochemistry or pharmacology. This project investigates the antibacterial properties of these unexplored *Myristicaceae* and *Clusiaceae* plants. Here, antibacterial assays including broth microdilution, bioautography, paper disc diffusion, as well as chromatographic techniques (thin layer chromatography, vacuum liquid chromatography and high-performance liquid chromatography), spectroscopic techniques (liquid chromatography-mass spectroscopy (LC-MS), nuclear magnetic resonance (NMR)) and X-ray crystallography are used to isolate antibacterial and novel plant metabolites. Results to date have shown crude dichloromethane extracts of two species, *Knema membranifolia* (*Myristicaceae*) and *Garcinia caudiculata* (*Clusiaceae*) to exhibit antibacterial activities against *Enterococcus faecalis* (MIC = 32 µg/mL) and *Staphylococcus aureus* (MIC = 128 µg/mL), respectively. LC-MS, X-ray crystallography and NMR analysis have allowed the identification of one known anacardic acid (Figure 1) with potent anti-*E. faecalis* activity (MIC = 2 µg/mL). Furthermore, spectroscopic analysis of 12 isolated compounds is being undertaken to identify metabolites from these species for the first time. Ongoing plant extraction, fractionation and spectroscopic analysis is being performed.

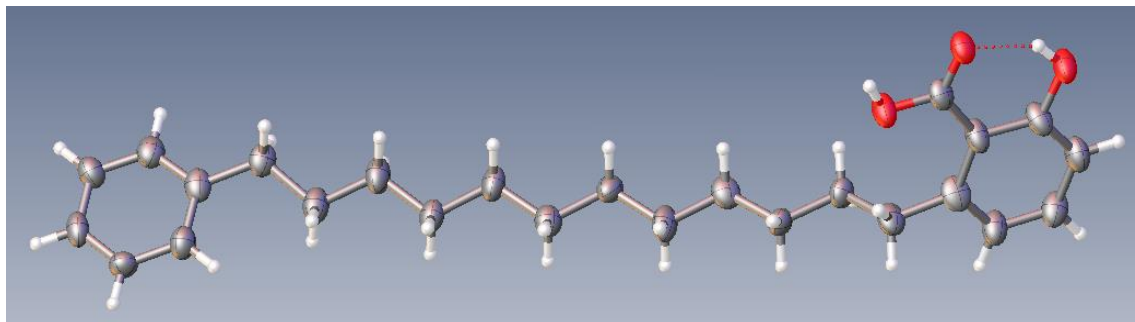


Figure 1. 2-Hydroxy-6-(12-phenyl dodecyl)benzoic acid isolated for the first time from *Knema membranifolia* (*Myristicaceae*).

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Communication to Congress (Abstract)

NATURAL ALKALOIDS AS MULTI-TARGET COMPOUNDS TOWARDS FACTORS IMPLICATED IN ALZHEIMER'S DISEASE

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Abstract

Alzheimer's disease (AD) is the most common cause of dementia in elderly people; currently, there is no efficient treatment. Considering the increase in life expectancy worldwide AD rates are predicted to increase enormously, and thus the search for new AD drugs is urgently needed. A great amount of experimental and clinical evidence has indicated that AD is a complex disorder characterized by widespread neurodegeneration of the central nervous system (CNS), with major involvement of the cholinergic system, causing progressive cognitive decline and dementia. The current treatment, based on the cholinergic hypothesis, is only symptomatic and mainly involves the restoration of acetylcholine (ACh) levels through the inhibition of acetylcholinesterase (AChE). One of the most attractive groups of natural products is, without a doubt, alkaloids. Since the introduction of the Amaryllidaceae alkaloid galanthamine as an antedementia drug in 2001, alkaloids have been one of the most attractive groups for searching for new AD drugs.

Several natural alkaloids can be recognized as multi-target compounds for the development of new anti-AD drugs. Of these, harmine is the most promising alkaloid, displaying a wide spectrum of compelling anti-AD activities. Isoquinoline alkaloids such as berberine, avicine, and chelerythrine also appear to be promising multi-target compounds, exhibiting strong inhibitory activity on key pathological enzymes of AD. Furthermore, marine flora have emerged as a viable source of multi-target compounds as well; for example, hymenialdisine has a broad range of protein kinase-inhibiting activities in a nanomolar range.

However, this topic remains open for further research on detailed mechanisms of action and the synthesis of potentially better semi-synthetic analogues.

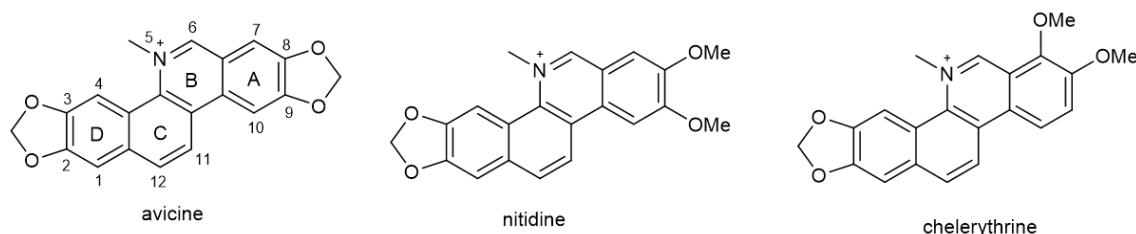


Figure 1. Structures of benzophenanthridine alkaloids with multi-target biological activity against AD

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Communication to Congress (Abstract)

MASS SPECTROMETRIC APPROACHES IN COMBATING THE COMPLEXITY OF PHYTOCHEMICALS

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Abstract

Use of herbal plants are an integral part of various indigenous medicinal systems such as Traditional Chinese Medicine (TCM) and Ayurveda. The presence of a very large number of compounds makes them complicated and pose a challenge to phytochemists. Similarly, products which contain herbs are often difficult to standardize. Many studies on the standardization of herbal medicines focus only on either HPLC-based fingerprinting or on the quantification of a few major peaks. However, environmental factors such as temperature, humidity, and soil can affect the amounts of secondary metabolites in a plant, which in-turn can lead to variations in the batch-to-batch quality of herbal medicines. It is therefore important to focus on the complete picture rather than a few specific compounds. Such knowledge can only be generated through a comprehensive metabolomics analysis that can convert analytical data into useful biological knowledge. Metabolomics data obtained through comprehensive and reliable methods for fingerprinting, profiling and quantification of active natural products can be used to study global metabolite composition, taxonomy, stress response, interaction of plant with the environment, drug lead discovery and the mode of action of an herbal drug.

We have developed several strategies for the dereplication of natural products in single and polyherbal formulations by advanced mass spectrometry tools. The strategy is based on five major steps: the collection of plant samples from different locations to observe the effects of environmental variables; LC-ESI-MS/MS-based untargeted metabolite profiling of the plant samples to identify marker compounds using extensive chemometric analysis of the obtained data; the identification of marker compounds in polyherbal products; the isolation, purification and characterization of the marker compounds; and MRM-based quantitative analysis of the isolated marker compounds using LC-ESI-MS/MS. Using this strategy, we identified a large number of compounds in plant extracts. Chemical fingerprinting of the plant led to the identification of characteristic peaks that are used to confirm presence inside complex polyherbal formulations. Moreover, marker compounds were isolated, purified and quantified in various herbal formulations containing respective plants. These methods demonstrate a comprehensive strategy based on untargeted and targeted metabolite analysis that can be used for the standardization of complex polyherbal formulations. Details will be discussed in the presentation.

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Communication to Congress (Abstract)

GLYCOSIDASE INHIBITORS IN PLANTS: THEIR DETECTION, BENEFITS AND COMMON PROBLEMS WITH PUBLICATIONS DESCRIBING THEM IN PLANTS EXTRACTS

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Abstract

The first glycosidase inhibitors from plants were reported in the 1970s and since then many have been found covering many chemical classes including iminosugars, terpenes, flavonoids and other phenolics. Glycosidase inhibitors have aroused great interest including as anti-viral agents, for anti-cancer activity and particularly alpha-glucosidase inhibitors for their ability to modulate blood sugar levels, e.g. deoxynojirimycin (1) from mulberry and derivatives such Miglitol (2) used to treat diabetes type 2. One possible problem with the myriad of papers being published in recent years on glucosidase inhibition by plant extracts is almost every plant extract shows inhibition of one alpha-glucosidase commonly used for assays (namely yeast alpha-glucosidase). The other problem is that many of these papers describe the inhibition as being better than a known alpha-glucosidase inhibitor acarbose but without stating that acarbose is a not a good inhibitor of the yeast enzyme. Glycosidase inhibitors in general need to show selectivity and not just binding to almost any protein and so it always important to compare the inhibitions of compounds or extracts on at least 3-4 different glycosidases. There are many carbohydrate-related disease targets and finding selective glycosidase activities with good uptake and distribution remains of great value but screening compounds or extracts on one enzyme is of little importance. It is also becoming clear that carbohydrate analogues can have potent activity via mechanisms not seeming to involve glycosidase inhibition at all. The presentation will discuss the problems and value in improving the screening process.

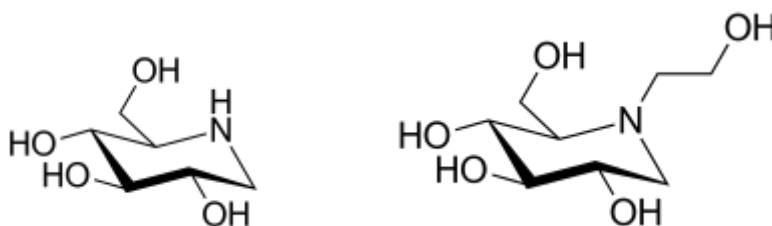


Figure 1. Deoxynojirimycin (1)

Miglitol (2)

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Communication to Congress (Abstract)

ASSESSMENT OF ANTIVIRAL AND ANTIMICROBIAL NATURAL PRODUCTS AS POTENTIALLY THERAPEUTIC AGENTS

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Abstract

Biochemicals from herbs used in traditional medicine might have a role to play in helping fight Covid-19 variants. Despite significant advancements in the administration of vaccines across the globe, concerns have grown over the capacity of new variants to escape natural and/or vaccine-induced immunity. There is a need for various treatment options for Covid-19 to slow infection rates and ease symptoms, and medicinal plants might prove to be a way forward. We found five phytochemicals could bind to the spike protein of SARS-CoV-2 and prevent the virus from entering cells and causing infection, potentially offering new avenues to prevent and treat the disease (Vellingiri et al., 2020; Kar et al., 2022). These findings generated a scope for future in vitro studies with the selected phytochemicals along with microbial biosurfactants to validate their antimicrobial therapeutic potential with the collaboration of Liverpool School of Tropical Medicine. β -amyryn, curcumin, cymaroside, friedelin, quercetin, rhamnolipid, 3- β -taraxerol, moxifloxacin were tested for their antimicrobial activity on clinically important pathogens such as *Pseudomonas aeruginosa*, Methicillin-Resistant *Staphylococcus aureus* (MRSA) and *Candida auris*. The results revealed that no compound inhibited *P. aeruginosa* except for curcumin, which reduced cell viability by ~70%. Similarly, no compound inhibited MRSA, although quercetin reduced viability by ~40%. Moxifloxacin (MOX) was used as a positive control for susceptibility testing.

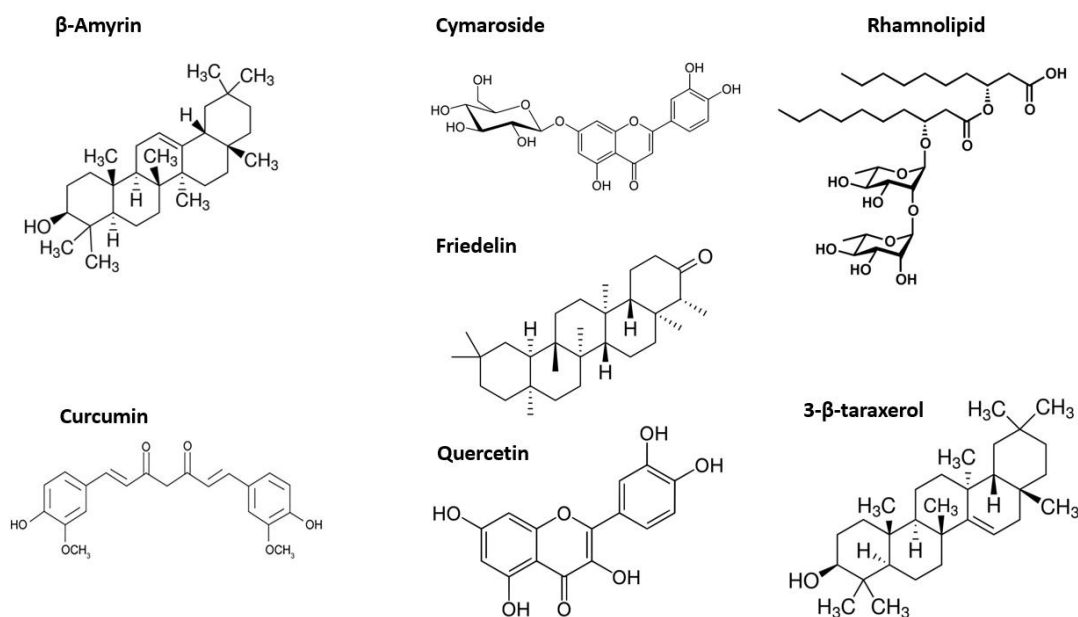



Figure1 β -amyryn, curcumin, cymaroside, friedelin, quercetin, rhamnolipid, 3- β -taraxerol

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Communication to Congress (Abstract)

ADDITION AND SUBTRACTION AS A STRATEGY FOR ACTIVATION OF MICROBIAL BIOSYNTHETIC GENE CLUSTERS

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Abstract

The potential of microbial metabolites as bioactive leads for drug discovery is largely untapped, as only ~1% of species can be successfully cultured in the laboratory. Furthermore, within this tiny fraction, the vast number of secondary metabolite producing biosynthetic gene clusters (BGCs) are expressed at very low levels under laboratory conditions that do not simulate the environmental pressures of the natural habitat. In the lecture, I will describe two recent examples of successful BGC activation that involve additions or subtractions to traditional microbial fermentation media:

- (1) induction of secondary metabolites in *Aspergillus* fungi by the addition of small molecule epigenetic modulators that are FDA approved as anticancer agents
- (2) isolation of the novel potent cytotoxic euglenatides from the photosynthetic alga *Euglena gracilis* by subtraction of amino acids and nitrogen sources.

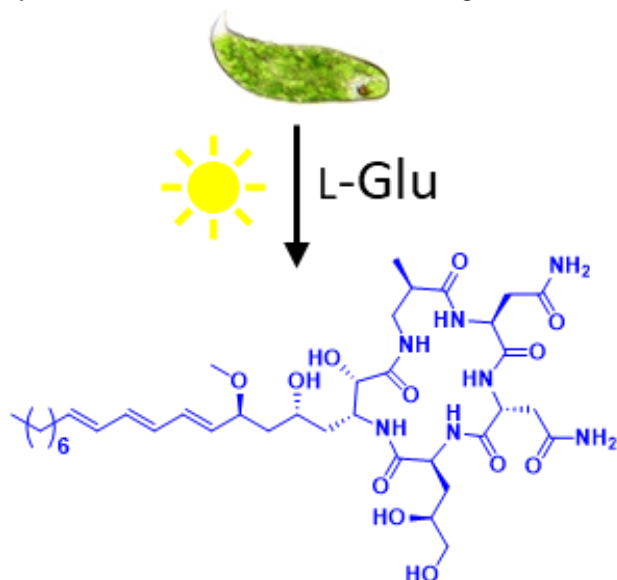


Figure1 Cytotoxic euglenatides.

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Communication to Congress (Abstract)

EFFECT OF FLAVONOIDS ON CIRCADIAN RHYTHMS AND METABOLIC SYNDROME

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Abstract

The importance of the circadian clock in maintaining human health is now widely acknowledged. Dysregulated and dampened clocks may be a common cause of age-related diseases and metabolic syndrome. Thus, circadian clocks should be considered as therapeutic targets to mitigate disease symptoms. This review highlights a number of dietary compounds that positively affect the maintenance of the circadian clock. Notably the polymethoxyflavone nobiletin has shown some encouraging results in pre-clinical experiments. Although many more experiments are needed to fully elucidate its exact mechanism of action, it is a promising candidate with potential as a chronotherapeutic agent.

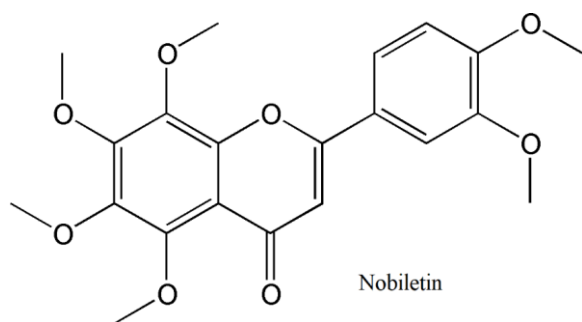


Figure 1. Nobiletin

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Communication to Congress (Abstract)

CAN FOOD WASTE YIELD HIGH VALUE NATURAL PRODUCTS?

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Abstract

Currently food waste and by-products generated are not fully exploited and their disposal continues to pose a growing challenge to the environment. Common byproducts from food such as peels, hulls, shells, husks, pods, bran, seeds, and pulp are normally discarded as wastes following consumption or utilisation of main food components. However, emerging research suggests that food waste valorisation can yield phytochemicals with high value pharmacological potentials in cosmetics, healthy living products and as ingredients in functional food products. Our investigations to identify high value natural products from food waste revealed that a freeze-dried rind extract of the pomegranate fruit (*Punica granatum*) showed significant anti-inflammatory activity in cultured human HaCaT keratinocytes through reduction of LPS-induced elevated levels of TNF α , IL-6, IL-1 β , IL8 and TSLP. It was further shown that this extract inhibited LPS-induced binding of NF-kB to its consensus DNA sequence in the nucleus. Antioxidant activity of the extract was demonstrated through reduction of LPS-induced ROS generation and enhanced binding of Nrf2 to nuclear antioxidant response element (ARE). Similar antiinflammatory and antioxidant activities were shown by freeze-dried peel extract of the mango (*Mangifera indica*) fruit in HaCaT keratinocytes. The lecture will highlight the significance and potential applications of the anti-inflammatory and antioxidant properties of these waste products in the circular economy.

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Communication to Congress (Abstract)

BIOASSAY-GUIDED ISOLATION OF POTENTIAL CANCER CHEMOPREVENTIVE PRINCIPLES FROM THE LEAVES OF *CLAOXYLON LONGIFOLIUM*

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2. Department of Thai Traditional Medicine, Faculty of Health and Sports Science, Thaksin University, 93210 Phatthalung, Thailand.
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Abstract

Cancer chemoprevention is one of the best ways to decrease cancer incidence and mortality rates. Medicinal plants and food are the major source for chemopreventive agents. *Claoxylon longifolium* (Blume) Endl. ex Hassk. (Euphorbiaceae) has been utilised in Thai traditional medicine. This species contains alkaloids, flavonoids and terpenes, with promising chemopreventive effect. This study aimed to perform bioassay-guided fractionation and isolation of chemopreventive compounds from *C. longifolium* leaves. Ground leaves were sequentially Soxhlet-extracted with n-hexane, dichloromethane and methanol followed by fractionation using solid-phase extraction and compound isolation using semi-preparative and preparative reversed-phase high-performance liquid chromatography. Chemical structures of isolated compounds were elucidated by spectroscopic methods. Crude extracts, fractions and isolated compounds were evaluated for Nrf2 induction potential using a cell-based luciferase assay in the AREc32 cell line. Six known compounds including caffeic acid, vicenin 1, vicenin 2, *p*-coumaric acid 4-*O*- β -D-glucoside, isovitexin and rosmarinic acid (Figure 1) were isolated from active methanolic fractions of *C. longifolium* leaves for the first time. This talk will primarily present the latest results on the chemopreventive potential of these isolated compounds.

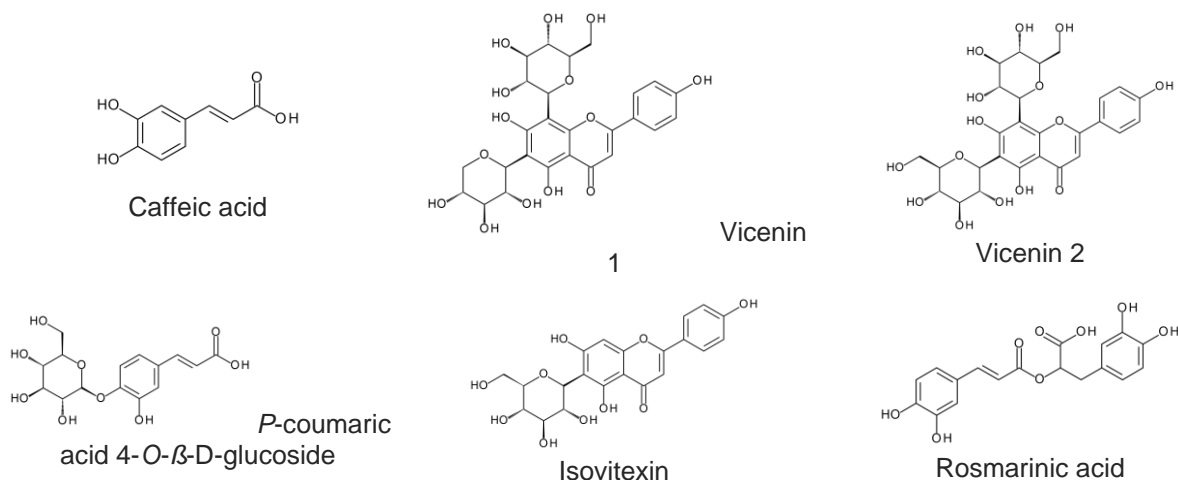


Figure 1. Chemical structures of caffeic acid, vicenin 1, vicenin 2, *p*-coumaric acid 4-*O*- β -D-glucoside, isovitexin and rosmarinic acid.

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Communication to Congress (Abstract)

A FLAVONOID-RICH EXTRACT OF BERGAMOT JUICE INDUCES ANTIPROLIFERATIVE EFFECTS ON HUMAN LEUKEMIA MONOCYTIC THP-1 CELLS TARGETING THE SIRT2/AKT/P53 PATHWAY

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Abstract

Hematological malignancies continue to represent a significant challenge, being frequently depicted as incurable diseases (Shallis et al., 2019). The acute myeloid leukemia (AML) represents one of the most alarming ones, due to its considerable genetic and clinical heterogeneity (Prada-Arismendy et al., 2017). In this regard, high levels of SIRT2 expression are associated with an unfavorable prognosis of AML (Deng et al., 2016). Therefore, the emerging scenario of AML treatment means a constant search for innovative drugs and novel approaches, including those in the landscape of natural remedies (Hwang et al., 2019), in order to obtain satisfying therapeutic outcomes and enhanced quality of life of AML patients. *Citrus x bergamia* (bergamot) was proved to possess anticancer properties (Visalli et al., 2014, Navarra et al., 2020), yet no evidence is available regarding leukemia. For the first time, we studied the potential anti-leukemic effect of a flavonoid-rich extract of bergamot juice (BJe) in THP-1 cells, investigating the underlying mechanisms. Our findings show that BJe reduced THP-1 cell proliferation, blocking the cell cycle in S-phase and inducing apoptosis. Triggering of both extrinsic and intrinsic apoptotic pathways was witnessed by cleavage of caspase-8 and -9, which in turn activated caspase-3 and PARP. Interestingly, the increased p53 acetylation in THP-1 cells underlies the SIRT2 inhibition by BJe, that was proved also in the isolated enzyme. Moreover, BJe hampered SIRT2 also by lowering its gene expression. Finally, BJe reduced AKT phosphorylation, which we hypothesized being the joining link between SIRT2 and the p53 transcription factor playing a pivotal role in BJe-induced cell cycle arrest and apoptosis in THP-1 cells. Our results suggest BJe as a potential anti-leukemic agent, via targeting of the SIRT2/AKT/p53 pathway.

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Communication to Congress (Abstract)

PHYTOCHEMICAL ANALYSIS AND CANCER CHEMOPREVENTIVE POTENTIAL OF *FOENICULUM VULGARE* GROWN IN SYRIA

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Abstract

Cancer is a global public health problem. Increased figures of new cancer cases and deaths are a major concern. Unfortunately, there is still a lack of safe and effective therapeutic options for cancer. One approach to increase cancer survival rates would be to detect cancer at the preliminary stage. An even more preferable approach would be the discovery of effective agents that can prevent cancer from developing in the first place. Recently, numerous plant products have been reported to inhibit the early stages of carcinogenesis. Accordingly, there is considerable scientific interest in the discovery of cancer chemopreventive agents as well as anticancer molecules from natural origin.

This research aims to determine the chemopreventive compounds from the aerial parts of *Foeniculum vulgare*. The ground plant material was extracted employing the Soxhlet apparatus and using three solvents, sequentially n-hexane, dichloromethane and methanol. The potential activity of these extracts to induce the Nrf2 pathway in the AREc32 cell line was assessed by applying a luciferase assay. Following a bioassay-guided protocol, further chromatographic fractionation was carried out on the bioactive extracts. Phytochemicals from the fractions with higher efficiency were later isolated and purified using high-performance liquid chromatography. Six compounds were isolated from the active fractions of methanolic and DCM extracts. The structures of the isolated compounds were characterised using the nuclear magnetic resonance (NMR) spectroscopy as quercetin 3-O-glucuronide, quercetin 3-O-glucuronide methyl ester and another newly characterised ester of p-coumaric acid and hydroxylated chlorogenic acid. Structure elucidation of the other three isolated compounds and the bioassay activity of all compounds are in progress.

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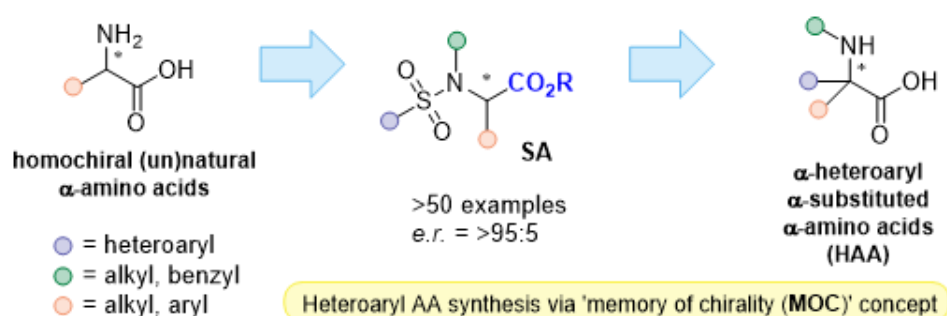
Communication to Congress (Abstract)

THE BEAUTY OF (UN)NATURAL PRODUCT SYNTHESIS: FROM CURIOSITY TO UNPRECEDENT AMINO ACIDSJiří Pospíšil^{1,2,3,*} 

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2. Laboratory of Growth Regulators, Palacký University and Institute of Experimental Botany ASCR, Šlechtitelů 27, 78371 Olomouc, Czech republic.
3. Department of Organic Chemistry, Faculty of Science, Palacký University, tř. 17. listopadu 1192/12, 771 46 Olomouc, Czech Republic.

Abstract

Over past few years we were interested in our group in the development of novel synthetic routes to various members of natural product families. Our interest was broad and in general biological activity driven. Namely we were interested in the synthesis of several class members of the following plant secondary metabolite families: phenolics (lignans and neolignans), terpenoids (various mono-, di-, and triterpenoids), and alkaloids. Recently, however, we focused our attention to a very simple building block, previously unknown and unprecedented class of unnatural amino acids. Our efforts in this field resulted in a short and efficient synthetic route to heteroaryl sulfonamides SA. With this unique and previously inaccessible class of compounds at hand, its transformations could be investigated. In this contribution, we discuss the use of natural α -amino acid SA derivatives in the context of the synthesis of α -heteroaryl α -substituted α -amino acid (HAA). Previously unknown HAA amino acids can be readily prepared from various SA in homochiral form using the concept of 'memory of chirality'. More interestingly, both possible enantiomers can be prepared starting from the same natural amino acid SA derivative in homochiral form by a simple change in reaction conditions. Our explanation of observed phenomena will be discussed within the contribution.

**Figure 1.** Synthesis of α -heteroaryl α -substituted α -amino acid (HAA).**Acknowledgements**






This work was supported by the European Regional Development Fund-Project "Centre for Experimental Plant Biology" (no. CZ.02.1.01/0.0/0.0/16_019/0000738).

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Communication to Congress (Abstract)

ANTICANCER POTENTIAL OF *ARBUTUS PAVARII* PAMPAN. AND *ASPHODELUS AESTIVUS* BROT. AGAINST PROSTATE CANCER CELLS (PC3)

Afaf Al Groshi^{1,2} , Hiba A. Jasim¹, Abdurazag Auzi², Lutfun Nahar³ , Fyaz M. D. Ismail¹ , Andrew R. Evans¹  and Satyajit D. Sarker¹ 

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2. Pharmacognosy Department, Faculty of Pharmacy, Tripoli University, Tripoli, Libya
3. Laboratory of Growth Regulators, Institute of Experimental Botany ASCR and Palacký University, Šlechtitelů 27, 78371 Olomouc, Czech Republic.

Abstract

Prostate cancer is one of the most prevalent malignancies affecting men worldwide. To explore potential therapeutic options, the cytotoxic effects of two Libyan medicinal plants, *Arbutus pavarii* Pampan. “Shmeri” and *Asphodelus aestivus* Brot. “White Asphodel or Gamon”, were investigated against prostate cancer cells using the MTT assay. The dichloromethane (DCM) extract from *A. pavarii* leaves (APL) exhibited significant cytotoxicity against prostate (PC3) cancer cells ($IC_{50} = 26 \mu\text{g/mL}$). Several compounds were isolated, including ursolic acid, which revealed considerable cytotoxicity against prostate cancer cells ($IC_{50} = 8.22 \mu\text{M}$). The DCM extract of *A. aestivus* tubers (AAT) displayed cytotoxicity against prostate (PC3) cancer cells, with an IC_{50} value of $19 \mu\text{g/mL}$. A trione glycoside, C- α -rhamnopyranosyl bianthracene, was isolated from the DCM extract of AAT which exhibited significant cytotoxicity against prostate cancer cells ($IC_{50} = 62 \mu\text{M}$). Importantly, *A. aestivus* tubers, demonstrated high selectivity towards the prostate cancer cells ($SI = 26$), indicating its safety on normal human cells. However, *A. pavarii* showed moderate selectivity towards the prostate cancer cells ($SI = 3.5$). These findings highlight the potential of *A. pavarii* and *A. aestivus* as sources of cytotoxic compounds against prostate cancer. The selective cytotoxicity of both plant extracts towards prostate cancer cells further supports their therapeutic relevance. The identified compounds, ursolic acid and C- α -rhamnopyranosyl bianthracene-9,9'-trione glycoside, which were isolated for the first time from the mentioned species, hold promise for future prostate cancer research and drug development efforts.

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Communication to Congress (Abstract)

NEOLIGNANS: NATURAL PRODUCTS WITH A POTENTIAL TO KILL

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Abstract

Neolignans are secondary metabolites derived from plants, specifically through the shikimic acid biosynthetic pathway. As structural dimers of phenylpropanoids, they emerge from the metabolism of L-phenylalanine, which generates essential building blocks. These building blocks can then undergo homodimerization or a wide range of (non-)enzymatic transformations, including acid-catalysed cyclization, methylation, and oxidation. Among the 15 subtypes that constitute the neolignan family, 2,3-dihydrobenzofurans (DHB) is a notable member. The core structure of DHB is present in numerous biologically active natural products, such as DGC-A and Licarin A. Additionally, synthetic compounds containing DHB exhibit a variety of activities, including antibacterial, antifungal, anticancer, antitubercular, and antimalarial properties. Some natural products containing DHB also demonstrate antioxidant and/or cytoprotective effects. Synthetic compounds with DHB also display a wide range of activities, including antibacterial, antifungal, anticancer, antitubercular, and antimalarial properties. In addition, some natural products containing DHB exhibit antioxidant and/or cytoprotective properties. The aim of our project is to develop a short and efficient approach to naturally occurring neolignans and to evaluate their biological activity against various targets such as antiparasitic and anticancerous activities. The latest results of our efforts will be presented and discussed.

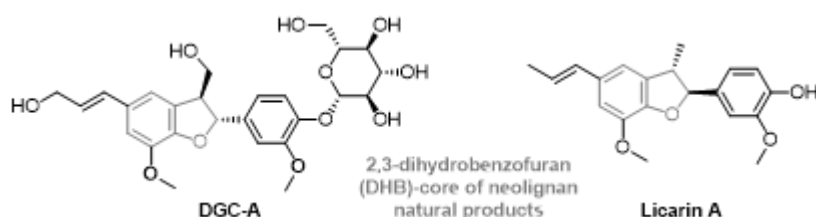


Figure 1. The neolignanes DGC-A and Licarin A

Acknowledgements

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