Biomedical and Biopharmaceutical Research
Jornal de Investigação Biomédica e Biofarmacêutica

Supplement | *Suplemento* *Biomed Biopharm Res.*, 2021; 18(1): S139-155

doi:10.19277/bbr.18.1.260

Fascination of Plants Day May 2021

Organizado por / organized by:

cbios UNIVERSIDADE LUSÓFONA
RESEARCH CENTER FOR HEALTH BIOSCIENCES & TECHNOLOGIES

BIO. NATURAL

Vem conhecer melhor os Medicamentos à base de plantas
"Get to know herbal medicines better"

Dia Internacional do Fascínio das Plantas 2021

Livro de Resumos / *Book of Abstracts*

18 Maio, 2021 / May 18th 2021

ULHT + virtual, Lisboa, Portugal

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CBIOS

Research Center For Biosciences & Health Technologies
Universidade Lusófona de Humanidades e Tecnologias

O CBIOS foi criado em 2011 como uma estrutura da COFAC / U.Lusófona, para promover a investigação em ciências da saúde como parte da Escola de Ciências e Tecnologias da Saúde da universidade.

Como parte da nossa visão, o CBIOS desenvolve Estratégias Integradas de Saúde destinadas a apoiar o progresso das sociedades lusófonas.

O CBIOS atualmente inclui 23 membros integrados, 19 alunos de doutorado, 16 colaboradores e uma ampla rede colaborativa, operando em cinco domínios de investigaçãon - ***Bioativos naturais (Bio.Natural), Desenvolvimento de Sistemas de Veiculação, Farmacologia e Mecanismos Moleculares, Sistemas de Modelação (MoSys) e Nutrição e Promoção da Saúde***.

Por ser uma unidade universitária, o CBIOS está altamente comprometido com a Diversidade, Equidade e Inclusão. Também tem o privilégio de operar dentro de um ambiente multidisciplinar e de mente alargada, essencial para fomentar a inovação, promover um ensino avançado e atrair jovens investigadores dinâmicos de diferentes origens e culturas.

CBIOS was created in 2011 as a structure of COFAC / U. Lusófona, to promote research in health sciences as part of the university's School of Health Sciences and Technologies.

As part of our vision, CBIOS develops Integrated Health Strategies designed to support the progress of Lusophone societies.

CBIOS currently includes 23 integrated members, 19 Ph.D. students, 16 collaborators, and a wide collaborative network, operating in five research domains – **Natural Bioactives (Bio.Natural)**, **Development of Delivery Systems**, **Pharmacology, and Molecular Mechanisms**, **Modeling Systems (MoSys)**, and **Nutrition and Health Promotion**.

Being an university-based unit, CBIOS is highly committed to Diversity, Equity, and Inclusion. It is also privileged to operate within a broad-minded, multidisciplinary environment essential to foster innovation, promote advanced learning, and attract dynamic young researchers from different backgrounds and cultures.

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Dia Internacional do Fascínio das Plantas

Descrição / Description

As plantas são importantes não só na promoção de um estilo de vida saudável através de nutrientes e condimentos, como na prevenção e tratamento de doenças, através dos seus constituintes químicos naturais com ação farmacológica. Em todos os casos, a saúde do consumidor só é protegida pela garantia da qualidade dos produtos e sua segurança por meio de uma relação dose-efeito padronizada, procurando-se entender cada vez mais o seu modo de ação. Neste evento, reuniremos diversos trabalhos que mostram a importância do uso tradicional como suporte para os medicamentos à base de plantas. Serão apresentadas as características gerais dos medicamentos à base de plantas atualmente validados pela Agência Europeia de Medicamentos, com destaque para os de uso tradicional autorizados em Portugal. Este evento com palestras, posters e demonstrações com visitas aos laboratórios do Bio.Natural do CBIOS tem o objetivo de dar a conhecer melhor o que são os medicamentos à base de plantas.

Plants are important not only in promoting a healthy lifestyle as nutrients and seasonings, but also in the prevention and treatment of diseases through their natural chemical constituents with pharmacological activity. In all cases, the consumer's health is only protected by a guaranteed quality of the products and their safety through a standard dose-effect relationship, seeking to continually better understand their mode of action. In this event, we bring together different works that show the importance of traditional use as a support for herbal medicines. Traditionally used and well-established drugs currently validated by the European Medicines Agency will be introduced, highlighting those authorized in Portugal. This event, with lectures, posters, and demonstrations with visits to Bio.Natural laboratories of CBIOS, aims to give attendees a better understanding of herbal medicines.

Organização/ Organization

Patrícia Rijo, CBIOS, ULHT (Local Organizer / Organizadora ULHT/CBIOS)
Maria do Céu Costa, CBIOS, ULHT
Andreia Rosatella, CBIOS, ULHT

Agradecimentos: A comissão organizadora agradece a Instituto Lusófono de Investigação e Desenvolvimento (ILIND) pelo projeto COFAC/ILIND/CBIOS/1/2020 e Fundação para a Ciência e Tecnologia (FCT) pelos projetos UIDB/04567/2020 e UIDP/04567/2020.

Acknowledgments: The organizing committee gratefully acknowledges Instituto Lusófono de Investigação e Desenvolvimento (ILIND) for the project COFAC/ILIND/CBIOS/1/2020 and Fundação para a Ciência e Tecnologia (FCT) for the projects UIDB/04567/2020 and UIDP/04567/2020.

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"Get to know herbal medicines better"

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18 de Maio de 2021 – Sala I.1.2.

Presencial/Presential: I.1.2. (ULHT)

Virtual: Zoom

Programa / Program

14:00-14:15	Welcome reception
14:15-14:30	**Opening:** L. Monteiro Rodrigues - CBIOS Director and Patrícia Rijo – Local Organizer, CBIOS
Session 1 | Presential Chair: Patrícia Rijo (CBIOS, Lisboa, Portugal) Virtual Chair: Andreia Rosatella (CBIOS, Lisboa, Portugal)	
14:30-15:00	Talk #1 Herbal Medicines - Traditional and Well-established use Maria do Céu Costa (SPFito, Lisboa, Portugal)
15:00-15:15	Talk #2 Medicinal cannabis in Europe – an overview João Anes (EXMceuticals Portugal)
15:15-15:45	*Coffee Break / Posters*
Session 2 | Presential Chair: Patrícia Rijo (CBIOS, Lisboa, Portugal) Virtual Chair: Andreia Rosatella (CBIOS, Lisboa, Portugal)	
15:45-16:00	Talk #3 Hydroalcoholic extract of *Calendula officinalis* L. (Asteraceae) inflorescences promotes gastric ulcers healing in rats Sergio Faloni de Andrade (CBIOS, Lisboa, Portugal)
16:00-16:15	Talk #4 Which place for the biorefinery in the circular bioeconomy? Forest biomass as a source of bioactives but not for HMP – the case of *Cupressus lusitanica* Mill Paula Pereira, Maria João Cebola, Oriana Pestana, José Nogueira, Maria Graça Miguel, Susana Dandlen, Patricia Rijo, Maria do Céu Costa (CBIOS, Univ Algarve, FCUL Lisboa, Portugal)
16:15-16:30	Q & A - Highlights & Lessons Learned Maria do Céu Costa (CBIOS, Lisboa, Portugal)
16:30-16:45	Closing session

Vem conhecer melhor os Medicamentos à base de plantas

"Get to know herbal medicines better"

Oral Communications

Talk #1 Herbal Medicines - Traditional and Well-established use

Maria do Céu Costa

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SPFITO- Portuguese Society of Phytochemistry and Phytotherapy (member of ESCOP, https://escop.com/), Rua da Sociedade Farmacêutica, 18, 1169-075 Lisboa (https://spfito.pt/)

General concepts of regulation of herbal medicines of traditional use and of well-established use. ACM-Drug Marketing Authorization: case of Cannabis.

Since the Medicinal Plant is defined as any plant that in one, or more than one, of its organs, contains substances that can be used for therapeutic purposes or that are precursors for chemical-pharmaceutical hemi-synthesis, it is important to clarify the concepts of herbal substance and of herbal medicine. Herbal substances are any whole, fragmented or cut plants, unprocessed, dried or fresh plant parts, algae, fungi and lichens and some exudates not subject to specific treatment, defined through the part of the plant used and the botanical taxonomy, including the species, the variety, if any, and the author (Dec. Law 176/2006, paragraph 1 of art. 3). Herbal preparations, are preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation, such as substances derived from powdered or powdered plants, tinctures, extracts, essential oils, squeezed juices and processed exudates. In this presentation, an overview of herbal medicines in the EU and Portugal will be presented.

Talk #2 Medicinal cannabis in Europe – an overview

João Anes[1] and Adília Charmier[1,2]

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Plants have been used for medicinal purposes long before prehistoric period. Among these ancient medicinal herbs, Cannabis, a flowering plant of the family *Cannabaceae*, originating from Central and South Asia, was used due to its broad-spectrum applications over the centuries. Its uses ranged from ropes, clothing, paper to its psychoactive properties, making it a very appealing plant. From the 1900's onwards cannabis consumption was deemed illegal in several countries around the world due to its overuse consequences [1].

The lack of scientific information regarding the mechanism of action of its constituents was a direct consequence from the illegal status given in the 1900's. Recently, this has changed, cannabis pre-clinical studies have shown several medicinal properties which helped cannabis gained traction and legal status for its medicinal use in most of North and South America, and in some European countries, lifting some of the old prejudice. In Europe, medicinal cannabis usage is still growing. Several cannabinoid-containing medicinal products are already available in the market [2,3].

EXMceuticals Portugal is one of the European Pharmaceutical companies working with medicinal cannabis that is specialized in extraction and purification of cannabinoids and terpenes for pharmaceutical grade ingredients. Most recently, due to the COVID-pandemic our research efforts have been put to "BioBlock COVID", a project that focus on antiviral properties of terpenes from cannabis and other medicinal plants for inactivation o the virus SARS-CoV-2, and its applications in tissues, hand and surface disinfectants.

References

[1] Zuardi A.W. (2006) History of cannabis as a medicine: a review. *Brazilian Journal of Psychiatry, 28*(2), 153-7.

[2] Freeman, T. P., Hindocha, C., Green, S. F., & Bloomfield, M. (2019). Medicinal use of cannabis based products and cannabinoids. *BMJ (Clinical research ed.), 365*, l1141. https://doi.org/10.1136/bmj.l1141

[3] Lipnik-Štangelj, M., & Razinger, B. (2020). A regulatory take on cannabis and cannabinoids for medicinal use in the European Union. *Arhiv za higijenu rada i toksikologiju, 71*(1), 12–18. https://doi.org/10.2478/aiht-2020-71-3302

Talk #3 Hydroalcoholic extract of *Calendula officinalis* L. (Asteraceae) inflorescences promotes gastric ulcers healing in rats

Luisa Mota da Silva[1], Ana Carolina de Araújo[1], Viviane Silva Bunn[1], Luisa Nathalia Bolda Mariano[1], Lincon Bordignon Somensi[1], Luiz Carlos Klein Jr.[1], Sérgio Faloni de Andrade[1,2*]

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Calendula officinalis L. (Asteraceae), popularly known as Marigold in Europe and "Calêndula" in Brazil, is a medicinal plant widely distributed in the world. The plant is listed in German Commission E, European Scientific Cooperative on Phytotherapy, British Herbal Pharmacopeia, World Health Organization monographs and "Formulário de Fitoterápicos da Farmacopeia Brasileira (Brazilian Pharmacopeia)" for wound healing and anti-inflammatory actions. Its inflorescences have been used for centuries to treat a wide variety of ailments including skin diseases, wounds, burn and gastrointestinal ulcers. Despite the folk use, there are no studies about the potential of *C. officinalis* extract to heal gastric ulcers. Therefore, this study aims to fill out this lack. The healing gastric ulcer potential of *C. officinalis* inflorescences extract was evaluated using chronic gastric ulcer induced by acetic acid in Wistar rats. Different groups (n=6) were treated orally with vehicle (water plus 0.5% Tween 80, 1mL/100 g), omeprazole (20 mg/kg), or *C. officinalis* inflorescences extract (10, 30 and 100 mg/kg), twice a day by seven days. The results showed that *C. officinalis* inflorescences extract is rich in phenolic substances and displays healing gastric chronic ulcer activity. The data suggest that effectiveness is related, at least part, to the capacity of extract to increase protective factors of gastric mucosa such as mucus and antioxidant factors as well as an increase in collagen synthesis. In addition, the findings of this study suggest that phytotherapeutic products can be obtained from *C. officinalis* inflorescences for the development of new drugs to treat gastric ulcers. It also contributed to the validation of the folk use of this species for the treatment of gastric ulcers.

References

Chandra P, Kishore K, Ghosh A.K. (2015) Evaluation of antacid capacity and antiulcer activity of *Calendula officinalis* L. in experimental rats. *Oriental Pharmacy and Experimental Medicine, 15*, 277-285.

Formulário de Fitoterápicos da Farmacopéia Brasileira / Agência Nacional de Vigilância Sanitária. Brasília: Anvisa, 2011. 126p.

Yadav AK, Mishra PK, Jain PK, Rao CV, Tiwaril S, Singh V. (2016) Investigation of *Calendula officinalis* whole plant as a gastroprotective and antioxidant in peptic ulcer. *British Journal of Medical and Health Research. 3*(7).

Yoshikawa M, Murakami T, Kishi A, Kageura T, Matsuda H. (2001) Medicinal Flowers. III.1) Marigold. (1): Hypoglycemic, Gastric Emptying Inhibitory, and Gastroprotective Principles and New Oleanane- Type Triterpene Oligoglycosides, Calendasaponins A, B, C, and D, from Egyptian *Calendula officinalis*. *Chemical and Pharmaceutical Bulletin, 49*: 863-870.

Talk #4 Which place for the biorefinery in the circular bioeconomy? Forest biomass as a source of bioactives but not for HMP – the case of *Cupressus lusitanica* Mill

Paula Pereira[1,2], Maria João Cebola[1,2,3], Oriana Pestana[4], José Nogueira[4], Maria GraçaMiguel[5], Susana Dandlen[6], Patricia Rijo[1], Maria do Céu Costa[1]*

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Several by-products such as essential oils and extracts from medicinal and aromatic plants (MAP) can be obtained within the biorefinery concept from forest biomass as they are high value, low volume commodities, extremely attractive for the perfume, cosmetic and flavour industries and are also known to possess different pharmacological activities. *Cupressus lusitanica* Mill ("cipreste-do-Buçaco" in Portuguese), also known as Cedar-of-Goa or Mexican cypress, was introduced in Portugal more than 300 years ago and is still widely used as an ornamental plant and for reforestation [1]. It is frequent in Portuguese landscape, and large amounts of their waste products are obtained from forest management. Recent studies reported for the first time the chemical composition of the essential oil and hydrolate volatiles and their antioxidant and anti-inflammatory properties [2]. The supercritical extraction of the volatile oil of *C. lusitanica* has not been studied in literature. So, the aim of this work was to evaluate the extracting capability of supercritical CO2, to recover volatiles contained in *C. lusitanica*, in order to determine its chemical composition and to assess its potential as a source of drug leads.

From Biomass it is not possible to prepare qualified extracts for medicines (Good Agricultural Practices, contaminants, impurities, wastewater ...) but it is possible, for example, to extract compounds with antiviral action, such as ferruginol, the major component of CO_2 extraction.

References

[1] Proença da Cunha, A., Roque, O.R., Nogueira, M.T. (2012). Plantas Aromáticas e óleos Essenciais. Composição e Aplicações. Edição da Fundação Calouste Gulbenkian, Lisboa.

[2] Tavares, C. S.; Martins, A.; Faleiro, M. L.; Miguel, M. G.; Duarte, L. C.; Gameiro, J. A.; Roseiro, L. B.; Figueiredo, A. C., (2020) Bioproducts from forest biomass: Essential oils and hydrolates from wastes of *Cupressus lusitanica* Mill. and *Cistus ladanifer* L. *Industrical Crops and Products 144*, 112034. doi: 10.1016/j.indcrop.2019.112034

Poster Communications

PC #1 Naturally occurring diterpenoids from *Plectranthus mutabilis* Codd. with cytotoxic Activity

Epole Ntungwe[1,2], Vera Isca[1,3], Lucilia Saraiva[4], Ana María Díaz-Lanza[2], Attila Hunyadi[5], Noélia Duarte[3], Milica Pesic[6], Patrícia Rijo[1,3]*

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Despite the great development in Human medicine, cancer is still a serious threat to public health and consequently, research on new anticancer agents should be continued [1]. Natural products from medicinal plants (e.g., *Plectranthus* species) continue to be a substantial resource to treat different diseases, particularly in developing countries [2]. Plectranthus species are rich in diterpenoids, which are reported to be responsible for various pharmacological activities such as cytotoxic activity [3]. *P. mutabilis* Codd. is a perennial succulent herb containing Nepetoidins A and Nepetoidins B in its essential oils and have limited information available in the literature [4].

In this study, we performed an ultrasound-assisted acetone extraction of air-dried *P. mutabilis* whole plant followed by a bio-guided fractionation using the *Artemia salina* general toxicity assay that resulted in the identification of four compounds: Coleon U quinone (1), 8α,9α- Epoxycoleon U quinone (2), Coleon U (3) and 7-hydro,14-deoxycoleon U (4) [4]. The cytotoxicity of the isolated compounds and P. mutabilis extract was evaluated using a model system of sensitive (NCI-H460) and MDR (NCI-H460/R) cells, along with normal human embryonal bronchial epithelial cells (MRC-5). Studies of modulation of P-gp activity are ongoing to unveil the interaction of these compounds and xtract with P-gp.

Acknowledgments: The authors gratefully acknowledge Fundação para a Ciência e Tecnologia (FCT) for the financial support under the reference CBIOS/COFAC/FIPID/1/2019, UIDB/50006/2020, UID/MULTI/04378/2013, and projects UIDB/04567/2020, UIDP/04567/2020,, CBIOS/COFAC/FIPID/1/2019 and COFAC/ILIND/CBIOS/1/2020. This work was also supported by PADDIC 2019 (ALIES-COFAC) as part of the PhD Program in Health Sciences from Universidad de Alcalá and Universidade Lusófona de Humanidades e Tecnologias.

References

[1] Mothana, R. A., Khaled, J. M., Noman, O. M., Kumar, A., Alajmi, M. F., Al-Rehaily, A. J., & Kurkcuoglu, M. (2018). Phytochemical analysis and evaluation of the cytotoxic, antimicrobial and antioxidant activities of essential oils from three Plectranthus species grown in Saudi Arabia. *BMC complementary and alternative medicine, 18*(1), 237.

[2] Ntungwe, E., Domínguez-Martín, E. M., Teodósio, C., Teixidó-Trujillo, S., Armas Capote, N., Saraiva, L., Díaz-Lanza, A. M., Duarte, N., & Rijo, P. (2021). Preliminary Biological Activity Screening of Plectranthus spp. Extracts for the Search of Anticancer Lead Molecules. *Pharmaceuticals (Basel, Switzerland), 1*4(5), 402.

[3]. Matias, D., Nicolai, M., Saraiva, L., Pinheiro, R., Faustino, C., Diaz Lanza, A., Pinto Reis, C., Stankovic, T., Dinic, J., Pesic, M., & Rijo, P. (2019). Cytotoxic Activity of Royleanone Diterpenes from Plectranthus madagascariensis Benth. ACS omega, 4(5), 8094–8103.

[4] Grayer, R. J., Eckert, M. R., Veitch, N. C., Kite, G. C., Marin, P. D., Kokubun, T., Simmonds, M. S., & Paton, A. J. (2003). The chemotaxonomic significance of two bioactive caffeic acid esters, nepetoidins A and B, in the Lamiaceae. *Phytochemistry, 64*(2), 519–528.

PC #2 Natural diterpenoids from *Plectranthus* spp. as anti-apoptoticagents

Vera M. S. Isca [1,2], Epole Ntungwe[1,3], Eva Domínguez-Martín[1,3], Tomasz Śliwiński[4], Przemysław Sitarek[5], Tomasz Kowalczyk[6], Michał Bijak [7], Carlos Afonso [2], Patrícia Rijo [1,2]*

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Medicinal plants have been used for centuries to treat several illnesses. *Plectranthus* plants (Lamiaceae) are widely known for their ethnomedicinal uses [1]. Consequently, several bioactive abietane diterpenes were already discovered in *Plectranthus* spp., such as Parvifloron D (**Parv**) [2], 7β,6β-Dihydroxyroyleanone (**Diroy**) [3], 7α-acetoxy-6β-hydroxyroyleanone (**Roy**) [3], and 6,7-dehydroroyleanone (**Deroy**) [4].

In this study, we explored the cytotoxic effect of **Roy**, **Deroy**, **Diroy**, and **Parv** in acute lymphocytic leukemia (CCRF-CEM) and lung adenocarcinoma cell lines (A549) and their ability to induce apoptosis.

The natural diterpenoids tested induced cell apoptosis by altering the level of pro- and anti- apoptotic genes and, consequently, inhibited the proliferation of CCRF-CEM and A549 cells in vitro. **Roy** and **Parv** displayed the most promising results in both human cancer cell lines, changing the permeability mitochondrial membrane potential and reactive oxygen species (ROS) levels. Consequently, **Roy** and **Parv** could be used in the future as natural chemotherapeutic agents.

Acknowledgments: The authors thank Fundação para a Ciência e a Tecnologia (FCT), Portugal for the projects UIDB/04567/2020 and UIDP/04567/2020, and grants CBIOS/PRUID/BI1/2017 and SFRH/BD/137671/2018.

References

[1] Ladeiras, D., Monteiro, C. M., Pereira, F., Reis, C. P., Afonso, C. A., & Rijo, P. (2016). Reactivity of Diterpenoid Quinones: Royleanones. *Current pharmaceutical design, 22*(12), 1682–1714.

[2] Burmistrova, O., Perdomo, J., Simões, M. F., Rijo, P., Quintana, J., & Estévez, F. (2015). The abietane diterpenoid parvifloron D from *Plectranthus ecklonii* is a potent apoptotic inducer in human leukemia cells. *Phytomedicine : international journal of phytotherapy and phytopharmacology, 22*(11), 1009–1016. .

[3] Matias, D., Nicolai, M., Saraiva, L., Pinheiro, R., Faustino, C., Diaz Lanza, A., Pinto Reis, C., Stankovic, T., Dinic, J., Pesic, M., & Rijo, P. (2019). Cytotoxic Activity of Royleanone Diterpenes from *Plectranthus madagascariensis* Benth. *ACS omega, 4*(5), 8094–8103.

[4] Garcia, C., Silva, C. O., Monteiro, C. M., Nicolai, M., Viana, A., Andrade, J. M., Barasoain, I., Stankovic, T., Quintana, J., Hernández, I., González, I., Estévez, F., Díaz-Lanza, A. M., Reis, C. P., Afonso, C. A., Pesic, M., & Rijo, P. (2018). Anticancer properties of the abietane diterpene 6,7-dehydroroyleanone obtained by optimized extraction. *Future medicinal chemistry, 10*(10), 1177–1189.

PC #3 Synopsis of the Bioactivity of Abietane Diterpene isolated from *Plectranthus ecklonii* Benth

Gabrielle Bangay[1], Eva María Domínguez-Martín[1,2], Ana Margarida Antão[1,3], EpoleNtungwe[1,2], Vera Isca [1,3], Ana María Díaz-Lanza[2], Patrícia Rijo[1,3*]

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In recent years, the world has witnessed a resurgence in the use of herbal medicine, as an alternative and complimentary approach to the prevention and treatment of disease. It is estimated there are around 28,137 recorded medicinal plants, from which, species of the Lamiaceae family are popularly used for their medicinal properties and application, especially in folk medicine. In particular, species of the *Plectranthus* genus have widespread ethnobotanical and traditional uses. In parts of southern Africa, *Plectranthus ecklonii* Benth., is used to treat tuberculosis- and listeriosis-related problems, gastrointestinal infections and skin diseases [1]. The broad catalogue of uses suggests that this species, and others from the same genus, are promising plants for the discovery of medicinal compounds. *Plectranthus* species contain many bioactive compounds and exhibit several biological effects, including anti- inflammatory, antioxidant, anti-infective and antitumour [2]. In this work, search terms, including '*Plectranthus ecklonii*', 'parvifloron D', 'parvifloron E', 'parvifloron F' and 'sugiol', were used and databases, including PubMed, Web of Science and ScienceDirect, were examined. Herein lies the information currently present in the literature on the isolated abietane diterpenes of *P. ecklonii*, parvifloron D, E, F and sugiol, and comments on their bioactivities, in order to reveal their potential for novel pharmaceutical drug development [3].

Acknowledgments: This research was funded by Fundação para a Ciência e a Tecnologia (FCT, Portugal), through projects UIDP/04567/2020 and UIDB/04567/2020. E.M.D-M gratefully acknowledges being the recipient of a predoctoral FPU 2019 fellowship from the University of Alcalá de Henares.

References

[1] Lukhoba, C.W., Simmonds, M.S.J., & Paton, A.J. (2006). Plectranthus: a review of ethnobotanical uses. *Journal of Ethnopharmacology, 103*(1), 1–24.

[2] Garcia, C., Teodósio, C., Oliveira, C., Oliveira, C., Díaz-Lanza, A., Reis, C., Duarte, N. and Rijo, P. (2019). Naturally Occurring Plectranthus-derived Diterpenes with Antitumoral Activities. *Current Pharmaceutical Design, 24*(36), 4207-4236.

[3] Sitarek, P., Toma, M., Ntungwe, E., Kowalczyk, T., Skała, E., Wieczfinska, J., Śliwiński, T. and Rijo, P. (2020). Insight the Biological Activities of Selected Abietane Diterpenes Isolated from *Plectranthus* spp.*Biomolecules, 10*(2), 194.

PC #4 LOXL2 inhibitory activity of pimaranes from medicinal plants

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LOX (Lysyl oxidase) and LOXL 1-4 are amine oxidases, that catalyze the cross-linking of elastin and collagen in the extracellular matrix of tumors, facilitating the formation of metastases. LOXL2 inhibitors have been suggested as a promising treatment to prevent metastasis and invasion of breast cancer [1]. These compounds may also have clinical interest in fibrotic diseases. BAPN (β-aminopropionitrile) is a phytochemical compound that was the first LOX inhibitor known. Medicinal plants are important sources of natural bioactive products and constitute a potential source of novel LOXL2 inhibitors, such as pimarane diterpenoids [2]. In this work, two pimaranes, lagascatriol (1) and 7, 15-isopimaradien-19-ol (2) were tested [3]. Pimarane-type diterpenoids are a potential source of novel human LOXL2 (hLOXL2) inhibitors. These bioactive compounds have been described for their therapeutic properties like antitumor, anti-inflammatory, analgesic and antibacterial activities [2]. However, their effect on LOXL2 activity was never studied before. For the screening of the LOXL2 inhibitory activity of these compounds, the Amplex ultra red (AUR) technique was used [4]. The method was validated using BAPN, and an IC_{50} value in accordance with previous reports was obtained [4]. Our results indicate that pimarane 1 has no inhibitory activity for LOXL2. For pimarane 2, an IC_{50} value of 174 µM was found. Although the pimarane 2 has the ability to inhibit LOXL2, it presents a very high IC_{50} value when comparing to the positive control BAPN. Further studies will be carried out to identify novel compounds able to inhibit LOXL2 with potential therapeutic interest.

Acknowledgments: This work is funded by national funds through FCT - Foundation for Science and Technology, I.P., under the UIDB/04567/2020 and UIDP/ 04567/2020 projects. Research developed with funding from COFAC/ILIND (ILIND/F+/EI/01/2020).

References

[1] Ferreira, S., Saraiva, N., Rijo, P., & Fernandes, A. S. (2021). LOXL2 Inhibitors and Breast Cancer Progression. *Antioxidants (Basel, Switzerland), 10*(2), 312.

[2] Isca, V., Andrade, J., Fernandes, A. S., Paixão, P., Uriel, C., Gómez, A. M., Duarte, N., & Rijo, P. (2020). In Vitro Antimicrobial Activity of Isopimarane-Type Diterpenoids. *Molecules (Basel, Switzerland), 25*(18), 4250..

[3] Reveglia, P., Cimmino, A., Masi, M., Nocera, P., Berova, N., Ellestad, G., & Evidente, A. (2018). Pimarane diterpenes: Natural source, stereochemical configuration, and biological activity. *Chirality, 30*(10), 1115–1134..

[4] Hutchinson, J. H., Rowbottom, M. W., Lonergan, D., Darlington, J., Prodanovich, P., King, C. D., Evans, J. F., & Bain, G. (2017). Small Molecule Lysyl Oxidase-like 2 (LOXL2) Inhibitors: The Identification of an Inhibitor Selective for LOXL2 over LOX. *ACS medicinal chemistry letters, 8(*4), 423–427.

PC #5 Antioxidant, antimicrobial activity and general toxicity of methanolic ultrasound-assisted *Plectranthus* spp. extracts and theirpotential use in dermocosmetics

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The search for natural products as active ingredients in cosmetics has gained strength due to the large demand from the general population concerned with daily care and health. *Plectranthus spp.* is a well-known genus used in traditional medicine for skin conditions. It belongs to the Lamiaceae family that grows in the warm and tropical areas of the globe. The aim of this study is to select, through literature, *Plectranthus* species related to skin disorders and evaluate their antioxidant, antimicrobial activities and general toxicity for its potential cosmetological use. Considering the ethnopharmacological use, 8 species were selected (*P. amboinicus, P. barbatus, P. cylindraceus, P. ecklonii, P. fruticosus, P. grandidentatus, P. hadiensis and P. madagascariensis*).

Methanolic ultrasound-assisted extracts were prepared for all eight selected species (10% (w/v)). The antioxidant activity was evaluated by the 2,2-diphenyl-1-picrylhydrazyl, DPPH radical method, using the extracts at 10 mg/mL. The extracts of *P. ecklonii* and *P. grandidentatus* showed high antioxidant activity - 98,15% and 72,34% respectively.

All extracts were screened for their antimicrobial activity, using the microdilution test at 10 mg/mL, against Gram-positive bacteria and yeast strains related to skin microbiota (*S. aureus* and *C. albicans*). The extracts of *P. amboinicus, P. fruticosus, P. grandidentatus, P. hadiensis* and *P. madagascariensis* showed moderated antimicrobial activity against Gram-positive bacteria and yeasts tested.

The general toxicity was tested using the *Artemia salina* L. model and was tested at 0.1 mg/mL. None of the extracts were revealed to be toxic.

The *Plectranthus* extracts seem to be promising ingredients to be used in dermocosmetic formulations. However, further studies addressing safety, namely cytotoxicity, and other areas of efficacy, such as physical and chemical stability must be conducted.

Acknowledgments: This research was funded by *Fundação para a Ciência e a Tecnologia* (FCT, Portugal), through projects UIDP/04567/2020 and UIDB/04567/2020.

PC #6 Mutagenic and antimutagenic activity of Myrtle extracts

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Myrtus communis L. is an evergreen shrub belonging to the Myrtaceae family that grows wild around all the Mediterranean region, Portugal included. Many medicinal properties have been attributed to myrtle, which has been used since ancient times in folk medicine. It is traditionally used as an antiseptic disinfectant, with anti-hemorrhagic, antimicrobial and antioxidant properties. Toxicity screening, particularly the study of the mutagenicity, is a necessary aspect of the preliminary safety evaluation of plant-derived extracts and compounds prior to further development and commercialization [1]. On the other hand, the search for antimutagenic agents is an important one, since such compounds maybe helpful in preventing cancer and other mutation-related diseases [2].

In this study, the mutagenic and antimutagenic activities of a supercritical myrtle extract was assessed using the Salmonella mutagenicity assay (Ames test). No mutagenic effects were observed for concentrations up to 5.0 mg/plate, which corresponds to the recommended maximum test concentration according to the OECD guidelines for testing of chemicals. On the other hand, the extract was able to inhibit up to 45% the mutagenic activity of tert-Butyl hydroperoxide. As tert-Butyl hydroperoxide is an oxidative mutagen, the antimutagenic effect could be related to the antioxidant activity of the extract. The antimutagenic activity detected could make this extract a promising candidate for future applications in human healthcare.

Acknowledgments: This work was financially supported by Fundação para a Ciência e Tecnologia, through funding UID/DTP/04567/2019 and UIDB/0456/2020.

References

[1] Eloff, J.N. and McGaw, L.J. (2006). Plant Extracts Used to Manage Bacterial, Fungal, and Parasitic Infections in Southern Africa. In Modern Phytomedicine (eds I. Ahmad, F. Aqil and M. Owais). https://doi.org/10.1002/9783527609987.ch5.

[2] Chandela, M., Kumara, M., Kumarb S., Kaur, S. (2012) Inhibition of 2-aminofluorene and 4-nitro-O-phenylenediamine mutagenicity by natural food colorant plant *Rubia cordifolia* L. *International Journal of Pharmacy and Pharmaceutical Sciences, 4*, 235-239.

PC #7 Initial studies on the phytochemical and antitumoral activity of *Plectranthus hadiensis* (Forssk.) Schweinf. ex Sprenger aerial parts

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The *Plectranthus* genus belongs to the Lamiaceae family and consists of around 300 species distributed from Africa to Asia and Australia. Several studies have reported that *Plectranthus* species are rich in abietane-type diterpenes, such as royleanones, which are interesting in the treatment of various diseases. One of such species is *Plectranthus hadiensis* (Forssk.) Schweinf. ex Sprenger, which has been documented to be useful in several types of cancer [1]. The objective of this work is to present the preliminary results of extraction, fractionation, isolation and bioactivity of the aerial parts of this plant. These data indicate a great difference between the acetonic extracts from leaves and those from stems, mainly in their content of 7α-acetoxy-6β- hydroxyroyleanone (Figure 1), which has cytotoxic properties [2,3]. Currently, phytochemical studies are ongoing to elucidate the main abietanes responsible for the biological activity.

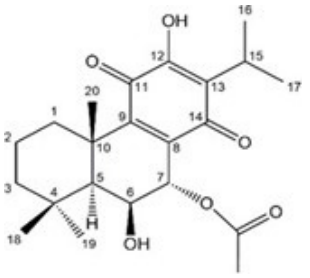

Figure 1. Structure of 7α-acetoxy-6β-hydroxyroyleanone

Acknowlegments: This work was supported in part by FCT – *Fundacão para a Ciência e Tecnologia* grants PEst-OE/SAU/UI4013/2014, UID/DTP/04567/ 2016, UIDB/04567/2020 and UIDP/04567/2020.

E.M.D-M gratefully acknowledges being the recipient of a predoctoral FPU 2019 fellowship from University of Alcalá.

References

[1] Schultz, F., Anywar, G., Wack, B., Quave, C. L., & Garbe, L. A. (2020). Ethnobotanical study of selected medicinal plants traditionally used in the rural Greater Mpigi region of Uganda. *Journal of ethnopharmacology, 256,* 112742.

[2] Sitarek, P., Toma, M., Ntungwe, E., Kowalczyk, T., Skała, E., Wieczfinska, J., Śliwiński, T., & Rijo, P. (2020). Insight the Biological Activities of Selected Abietane Diterpenes Isolated from *Plectranthus* spp. *Biomolecules, 10*(2), 194.

[3] Śliwiński, T., Sitarek, P., Skała, E., Isca, V., Synowiec, E., Kowalczyk, T., Bijak, M., & Rijo, P. (2020). Diterpenoids from *Plectranthus* spp. as Potential Chemotherapeutic Agents via Apoptosis. *Pharmaceuticals (Basel, Switzerland), 13*(6), 123.

PC #8 Glycine-based IL to improve the performance of O/W emulsions containing rutin

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The development of new drug delivery systems faces several challenges, like the poor drug solubility of many substances, such as phenolic compounds, as well as the low stability of various delivery systems [1-2].

Rutin is a polyphenolic bioflavonoid widely found in natural sources, including fruits (e.g., apples, grapes, lemons), vegetables (e.g., carrots, potatoes), and beverages (e.g., tea and wine) [2]. In the last years, several relevant pharmacological activities have been attributed to this phenolic compound, including antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and anticancer [2]. Hence, this compound presents vast potential, but since it presents low aqueoussolubility its incorporation into delivery systems may be impaired.

Considering this, ionic liquids (ILs) are a multifunctional tool that may be valuable to overcome this challenge [2,3].

Thus, this work aimed to study the influence of the biobased IL (2- hydroxyethyl)trimethylammonium-L-glycinate [Cho][Gly], on the solubility and loading of rutin into oil-in-water (O/W) emulsions and to access its impact on the stability of the developed formulations.

Our results showed that the [Cho][Gly] allowed a considerable increase in the solubility of rutin, even compared with other previously studied ILs, thus granting a higher rutin loading into the emulsions. This IL was also crucial to stabilize the developed formulations.

Acknowledgments: This work was financially supported by Fundação para a Ciência e Tecnologia, through funding UID/DTP/04567/2019 and UIDB/0456/2020 (both general funding to CBIOS), and by funding from Universidade Lusófona/ILIND (Grant Programme FIPID 2019/2020). A.J. and R.C. would like to thank ALIES for the grant PADDIC 2018-2019 and PADDIC 2019-20.

References

[1] Fernández-García, R., Lalatsa, A., Statts, L., Bolás-Fernández, F., Ballesteros, M. P., & Serrano, D. R. (2020). Transferosomes as nanocarriers for drugs across the skin: Quality by design from lab to industrial scale. International journal of pharmaceutics, 573, 118817.

[2] Caparica, R., Júlio, A., Araújo, M. E. M., Baby, A. R., Fonte, P., Costa, J. G., & Santos de Almeida, T. (2020). Anticancer Activity of Rutin and Its Combination with Ionic Liquids on Renal Cells. Biomolecules, 10(2), 233. MDPI AG..

[3] Santos de Almeida, T., Júlio, A., Saraiva, N., Fernandes, A. S., Araújo, M., Baby, A. R., Rosado, C., & Mota, J. P. (2017). Choline- versus imidazole-based ionic liquids as functional ingredients in topical delivery systems: cytotoxicity, solubility, and skin permeation studies. *Drug development and industrial pharmacy, 43*(11), 1858–1865.