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Meeting Report

11th National Meeting of Organic Chemistry and 4th Meeting of Therapeutic Chemistry

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Academic Editor: Jean Jacques Vanden Eynde
Received: 23 February 2016; Accepted: 26 February 2016; Published: 17 March 2016

Abstract: For the first time under the auspices of Sociedade Portuguesa de Química, the competences of two important fields of Chemistry are brought together into a single event, the 11st National Organic Chemistry Meeting and the the 4th National Medicinal Chemistry Meeting, to highlight complementarities and to promote new synergies. Abstracts of plenary lectures, oral communications, and posters presented during the meeting are collected in this report.

Keywords: organic synthesis; spectroscopic methods; natural compounds; drug metabolism and disposition; beyond small molecules; drug design; antitumor and anti-infective drugs; industrial applications

1. Aim and Scope of the Meeting

The Scientific Committee has put high expectations on the excellence of the scientific program, which includes plenary/keynote lectures from renowned scientists whose work has been an inspiration for researchers in Organic and Medicinal Chemistry. Oral communications focused on topics from the following main research fields: organic synthesis, spectroscopic methods, organic natural compounds, drug metabolism and disposition, beyond small molecules, computational methods and drug design, antitumor and anti-infective drugs, industrial applications.

This meeting is expected to bring together researchers with different expertise and perspectives, from senior to young scientists, to discuss and share their latest achievements in a stimulating

In conclusion, thirteen new coumarin derivatives were obtained, *i.e.*, two propynyl, three acetyl glucosides, three glucosides, and five sulfated derivatives, and the structure elucidation of the synthesized compounds was stablished by IR, NMR, and HRMS for the first time. This small library of compounds will allow the study of the effect of the presence of the triazole moiety on the anticoagulant activity and mode of action of these new anticoagulant hybrids.

4.19. Identification of Complexes Formed Between Salivary Proteins and Procyanidin B3 by LC-MS. Effect of Concentration and Saliva Profile (P27)

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Astringency is an important factor in food quality. Different theories about astringency mechanism have been attributed but the most established process is the interaction between food tannins and human salivary proteins (Kallithraka, S., *et al. J. Sens. Stud.* 1998, *13*, 29–43). Several factors could influence the tannin-protein interaction such as the human salivary protein profile, the tannin tested and the tannin/protein ratio (Soares, S., *et al. Food Res. Int.* 2012, *49*, 807–813). Highlight the astringency mechanism through the study of tannin-protein interactions became relevant. The goal of this study aims to study the effect of different salivas (A, B and C) and different tannin concentration (0.5 and 1 mg/mL) in the interaction process. Human salivary proteins are divided into different groups mainly histatins (His), statherins (Stah), proline rich proteins (PRPs) and cystatins (Huq, N.L., *et al. Int. J. Pep. Res. Ther.* 2007, *13*, 547–564). This study is is focused in the identification of new procyanidin B3-salivary protein complexes complexes created between a common food tannin, the procyanidin B3 (B3), and the Stath, His and PRPs originating from saliva with different protein profiles.

4.20. Determination and Comparison of the Chemical Composition of Calendula L. species Growing in Continental Portugal (P28)

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The flora of Continental Portugal includes three species of *Calendula* L. (*Calendula officinalis* L., *C. arvensis* L., *C. suffruticosa* Vahl), one of which comprises three subspecies (*C. suffruticosa* subsp. *algarbiensis* (Boiss.) Nyman, *C. suffruticosa* subsp. *lusitanica* (Boiss.) Ohle and *C. suffruticosa* subsp. *cinerea* (Ohle) P.Silveira & A.C.Gonç.). *C. officinalis* is recognised for its medical properties and its chemical composition has been widely studied (Muley, B. P., *et al. J. Pharm. Res.* 2009, *8*, 455; Safdar, W., *et al. Int. J. Cell Mol. Biol.* 2010, *1*, 108). Nevertheless, little is known about the chemical composition of *C. arvensis* and even less regarding the different subspecies of *C. suffruticosa*. Therefore, the present study aims the elucidation of these plants' chemical composition and to compare and identify differences and/or similarities among them.

To accomplish this, one sample of each *taxon*, *C arvensis*, *C. officinalis*, and *C suffruticosa* subsp. *lusitanica*, and two samples, from two different populations, of *C. suffruticosa* subsp. *algarbiensis* were collected in the field, washed with running water, and dried in a woven at 40 °C until stabilization of weight was reached. The hexane extract of each *taxon* was obtained from dried and powdered plant and completely characterized by GC-MS after silylation, which allowed the identification and quantification of their constituents.

The achieved data showed the presence of mono- and disaccharides, terpenoids, fatty acids, sterols, alkanes, long chain alcohols and some amino acids. It was found that the monosaccharides and fatty acids are the most abundant families in *C. officinalis* being the palmitic acid and α-linoleic acid the most abundant compounds. The last one was also found in higher quantities in *C. arvensis*. Fatty acids like α-linoleic acid, palmitic acid and linoleic acid are also the most abundant in *C. suffruticosa* subsp. *lusitanica*. Lastly, the two samples of *C. suffruticosa* subsp. *algarbiensis* showed in major quantities a branched alkane and one compound from the ursano family. Some carbohydrates as well as lignoceric acid and linoleic acid were described for the first time in the *Calendula* L. genus.

Through the accomplished findings, including a preliminary Principal Component Analysis (PCA), a taxonomic differentiation among the *taxa* can be made. Irrelevant variations were also found in the two samples of the subsp. *algarbiensis*. The compounds detected for the first time improved our knowledge of the chemical profile of this genus. Additionally, some of the reported compounds have a major importance on a nutritional level.

Acknowledgments: We thank the Instituto da Conservação da Natureza e das Florestas for allowing the collection of the samples of *C. suffruticosa* subsp. *lusitanica*. We would like to thank University of Aveiro and FCT/MEC for the financial support to the QOPNA Research Unit (FCT UID/QUI/00062/2013), and to the CESAM RU (UID/AMB/50017), through national founds and where applicable co-financed by the FEDER, within the PT2020 Partnership Agreement.

4.21. Development of Antitumoral Monastrol Analogues: Synthesis, Cytotoxicity Evaluation and SAR Studies (P30)

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Cancer persists as one of the major global public health concerns due to its large incidence and mortality. Searching for novel anticancer agents with higher potency and lower toxicity, our work aims the development of monastrol analogues. For this, forty five dihydropyrimidin(thi)ones were synthesized *via* the Biginelli reaction by condensation of an aldehyde, a β-ketoester and urea/thiourea. The screening of the antiproliferative effects of the compounds was evaluated at 30 μM on MCF-7, T47D, LNCaP, HepaRG, Caco-2 and NHDF cell lines by the MTT assay. The concentration inducing 50% inhibition of cell growth (IC_{50}) was assessed for the most toxic compounds using different concentrations (0.01, 0.1, 1, 10, 50 and 100 μM). The results revealed that the compounds did not show significant toxicity neither in normal dermal cells (NHDF) nor in prostatic and breast (T47D) cancer cell lines; however, the chloro-containing compounds of the urea series showed selective toxicity for HepaRG cells (5.28 μM $\leqslant$ IC_{50} $\leqslant$ 15.9 μM) whereas their thiourea analogs evidenced lower selectivity, being significantly toxic for hepatic, colon and breast (MCF-7) cancer cell lines (0.749 μM $\leqslant$ IC_{50} $\leqslant$ 31.9 μM for HepaRG; 5.51 μM $\leqslant$ IC_{50} $\leqslant$ 13.7 μM for Caco-2; and 2.95 μM $\leqslant$ IC_{50} $\leqslant$ 10.9 μM for MCF-7). Thus, it was found that the molecules containing chloro atoms in their structure, particularly those belonging to urea series, demonstrated selective toxicity for hepatic cancer cells. Additional studies are ongoing to understand what mechanisms of action are involved in the toxicity of these molecules as well as the existence of differences between the two series.

Acknowledgments: We thank the Fundação para a Ciência e Tecnologia (SFHR/BD/85279/2012) for financial support as well as POPH-QREN which is co-funded by FSE and MEC.