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BIOACTIVE NATURAL PRODUCTS RESEARCH MEETING

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Venue: Universidade Lusófona, Campo Grande 376, 1749-024 Lisbon, Portugal

ability to modulate this important signaling protein. These findings provide a strong basis for further exploration of derivative **2**, including studying the mechanisms of PKC modulation and evaluating its therapeutic efficacy in preclinical models of breast cancer.

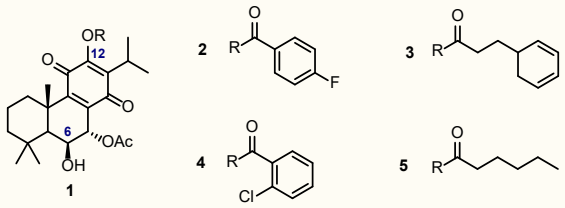

Figure 1 - Abietane diterpenoids: natural 7α-acetoxy-6β-hydroxyroyleanone (**1**) obtained from *P. grandidentatus* and semi-synthetic derivatives evaluated as PKC-α activators (**2** to **5**)

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Centauri Honey: A Promising Medicinal Ingredient?

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Abstract:

Honey is a natural product that has been used over the centuries as a medicine due to its biological activities. Centauri Cave Nymph Honey is a Cave honey extracted from 2500 meters high altitude above sea level from a deep cave by professional speleologists and is located at Caucasus Mountains of Turkey. The *Apis mellifera* Caucasica bee colony is located 50 kilometers away from human residences, ensuring its isolation from other colonies and maintaining a varroa mite-free status. The aim of this work is to analyze the physicochemical parameters and the bioactivity of Centauri honey. The physiochemical parameters that have been examined include color, moisture content, conductivity, pH, acidity, HMF (5-hydroxymethylfurfural), diastase index, and proline. In addition, it was also evaluated the ash, protein, sugars, carbohydrates, and energy. The biological activity was evaluated through the antioxidant (TBARS), antimicrobial activities and cytotoxicity in different cell lines (AGS, CaCo-2, MCF-7, NCI-H460, PLP2, HFF-2, and HaCat), and anti-inflammatory activity (RAW 264.7 macrophages). Ongoing research is focusing on the potential protetive effects of consuming

Centauri Cave Honey against lung and prostate cancers. In vivo studies are expected to shed more ligt on the additional health benefits that this honey may offer.

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Molecular Docking Studies and In Vitro Analysis of P-gp Inhibitors from *Plectranthus* Diterpenoids

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Abstract:

As cancer cases worldwide continue to increase, there is an urgent need to discover new treatments to combat the disease. Unfortunately, in the case of multi-drug resistant (MDR) cancers, effective therapy is hindered by the overexpression of membrane transport proteins such as P-glycoprotein (P-gp). Plectranthus species, well-known for their medicinal properties, are a valuable source of diterpenes, such as the 7α-acetoxy-6β-hydroxyroyleanone (Roy) and Coleon U, which have demonstrated cytotoxicity against various cancer cell lines[1]. Based on molecular docking, SwissADME and ADMET simulations[2], semi-synthetic derivatives of Roy and Coleon U, that displayed strong P-gp interactions in silico, were prepared. To evaluate the potential antitumor activity of the compounds, resistant human cancer cell lines NCI-H460/R and DLD1-TxR were tested. The MTT assay was used to assess cell viability, while Annexin V/PI was used to determine cell death induction. The findings revealed that Roy derivatives 2, 3, and 4 exhibited significant selectivity (2.7, 2.3, and 2.6 times, respectively) for cancer cells compared to normal lung fibroblasts (MRC5). Additionally, Roy derivatives 2, 3, and 4 demonstrated a reduction in P-gp activity in the Rho123 accumulation assay and showed P-gp inhibition in the DOX accumulation assay for resistant cell lines NCI-H460/R and DLD1-TxR. These results demonstrate that abietane diterpenoid derivatives are capable of inducing P-gp inhibition in MDR cancer cell lines, presenting a novel set of selective compounds for the treatment of lung and colon cancer. Further investigations are ongoing to ascertain the anticancer activity of the Coleon U derivatives to obtain hit P-gp modulators.

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