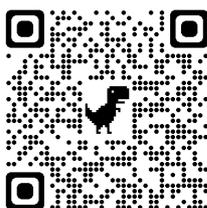


CURRENT RESEARCH TOPICS IN PHARMACY:

Herbal Drug Research

November 24th, 2022 14.00 PM ISTANBUL

FOR REGISTRATION:



First Session- Moderator: Betül OKUYAN 14.00-15.30 PM

Welcome- Prof. Hatice Kübra ELÇİOĞLU

Safety of herbal drugs- Assist.Prof. Ayfer BECEREN
Marmara University, Istanbul, Turkey

Antibacterial herbal effect applied in cosmetic emulsion preservation- Dr.Rezarta SHKRELI
Aldent University, Tirana, Albania

R&D studies in the development of traditional herbal medicinal products- Prof. İ. İrem TATLI ÇANKAYA
Hacettepe University, Ankara, Turkey

Second Session- Moderator: Betül OKUYAN 16.00-17.30 PM

The role of metabolomics in medicinal plant science-Prof.Emirhan NEMUTLU
Hacettepe University, Ankara, Turkey

Using diterpenoids from *Plectranthus* spp. As starting tool in drug development- Assoc.Prof.Patricia RIJO
Lusofona University, Lisbon, Portugal

Herbal drugs as novel antibacterials- Assoc. Prof. Entela HALOCI
University of Medicine, Tirana, Albania

The potential of certain phytochemicals as essential nutrients- Asst.Prof. Lukasz CIESLA
The University of Alabama, Tuscaloosa, USA

Chair

Prof. Hatice Kübra ELÇİOĞLU

Vice Chair

Prof. Levent KABASAKAL & Assoc. Prof. Esra TATAR

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PLECTRANTHUS: FROM TRADITIONAL MEDICINE TO BRAIN TUMOR THERAPY WITH DITERPENES

Eva María DOMÍNGUEZ-MARTÍN^{1,2}, Mariana MAGALHÃES^{3,4,5,6}, Przemysław SITAREK⁷, Ana María DÍAZ-LANZA², Ana M. GÓMEZ⁸, Thomas EFFERTH⁹, Célia CABRAL^{5,6,10}, Patricia RIJO^{1,11*}

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Cancer is one of the main causes of morbidity and mortality worldwide. Glioblastoma- GBM is the most malignant variant of intrinsic glial brain tumors. The treatments available entailed surgical resection followed by temozolomide chemotherapy and/or radiotherapy, which are associated with multidrug resistance, severe side effects, relapse and reduced survival. Therefore, new therapeutic approaches are needed to overcome these problems [1].

Natural products are an important source of bioactive lead molecules. The genus *Plectranthus* (Lamiaceae family) is known to be rich in diterpenes abietane-type royleanones (such as 7 α -acetoxy-6 β -hydroxyroyleanone (Roy), 7 β ,6 β -dihydroxyroyleanone (DiRoy), 6,7-dehydroroyleanone (DeRoy) and Parviflorone D (ParvD)) which possess, among others, antitumoral properties. The cytotoxic effect of these royleanones is due to their pro-apoptotic nature, which results, for example, in exert their activity in primary H7PX glioma cells by DNA double-strand breaks and G2/M cell cycle arrest [2]. Among the mentioned royleanones, Roy and DiRoy are frequently found in the extracts of the species *P. hadiensis* var. *hadiensis* Schweinf. and *P. grandidentatus* Gürke.

Recently, we described the bioguided isolation of compounds from the acetonic extract of *P. hadiensis* stems and investigated the *in vitro* anti-glioblastoma activity of the extract and its isolated constituents. After extraction, six fractions were obtained. Fractions V and III showed the highest

antioxidant and antimicrobial activities. None of the fractions were toxic in the *Artemia salina* assay. It was isolated the abietane-type diterpenes Roy and DiRoy, which was also in agreement with the HPLC-DAD profile of the extract. The antiproliferative activity evaluation by Alamar blue assay evidenced that after 48 h treatment, Roy exerted strong antiproliferative/cytotoxic effects against tumor cells with low IC₅₀ values among the different glioblastoma cell lines (U87, A172, U118, U373 and H4). Moreover, it was synthesized a new fluorescence derivative to evaluate the biodistribution of Roy. The uptake of BODIPY-7 α -acetoxy-6 β -hydroxyroyleanone by GB cells was associated with increased intracellular fluorescence, supporting the antiproliferative effects of Roy [3].

In conclusion, Roy is a promising lead compound to generate semisynthetic derivatives in order to its potential to be used as Active Pharmaceutical Ingredient (API) to develop new pharmaceutical formulations. Further studies should be performed to unveil the mechanism of action of Roy active against GB, which appears to be due to its accumulation in cytoplasmic vesicles and to the induction of mitochondria dependent intrinsic pathway apoptosis.

Keywords: Glioblastoma, Lamiaceae, *Plectranthus*, diterpenes, royleanones.

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