DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

According to report published by Royal Botanic Gardens, Kew, Apiaceae is on the 6th place among families having a significantly higher proportion of medicinal plants. From more than 4000 total number of species 600 are species with medicinal use and coumarins are key class of compounds. Coumarins, compounds with actual and potential pharmaceutical relevance, have been used in treatment of vitiligo, psoriasis or as anticoagulant.

The aim of the project is to evaluate the activity of selected coumarins in the interdisciplinary approach, combining both *in vivo* and molecular studies, as their action on the central nervous system (CNS) might be another important area of their application in medicine.

An inter- approach is proposed to study the bioavailability to assess the impact and potential mechanism of action of three selected coumarins (imperatorin, isopimpinellin and scoparone) in animal models of seizure, memory, anxiety and depressive behavior following single and chronic administration. Given that coumarins can occur naturally in plants in combination with the blood brain barrier (BBB) permeability enhancer borneol (e.g., in botanical drugs and Traditional Chinese Medicine (TCM) preparations) we going to address the effect of borneol on the CNS bioavailability of coumarins. As not much is known about the pharmacokinetics of coumarins and in particular data on their brain bioavailability is missing, detailed quantitative LC-MS analysis will be performed on brains isolates from mice exposed to coumarins – after acute and chronic administration.

Special attention will be paid to imperatorin, which exhibits strong influence on the CNS. As metabolite identification is an integral part of drug discovery and development, thus both imperatorin and its major metabolites, which are formed *in vivo*, will be screened on a panel of about 200 CNS receptors for binding interactions and activity-based protein profiling. This type of study will be performed for the first time and has a pioneer nature – both imperatorin and its metabolites will be tested.

For the proposed experiments, the required coumarins will be purified from extract of plants belonging to the Apiaceae and Asteraceae families, including e.g. *Cnidium monnieri*, *Angelica archangelica*, Heracleum sp. or Artemisia sp.

As the results of planned experiments the mechanism of action involved in the effects of coumarins will be evaluated, including those molecular, what might be potentially useful for future drug discovery efforts and targeted at novel therapies for the pharmacotherapy of anxiety or depression, and neurodegenerative diseases with memory deficits. Application of borneol, as a natural BBB permeability enhancer, can be useful for obtaining faster results of the therapy. This will be extremely helpful in the future modeling of new candidate molecules of drugs acting on the CNS, and devoid of the side effects characteristic of known synthetic drugs. It is worth to mention, that the project is based on the combination of two modern research techniques (solation and molecular), an innovative approach to the study of natural ("green") anxiolytics.