

DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

The main aim of the presented project is to find new, sustainable chemical entities which can possibly be developed as future antiepileptic drugs. Natural products are a rich source of various pharmacologically active substances, and ethnopharmacologic clues have been justified scientifically. For many years, plants from the *Apiaceae* family have been used as antiepileptic remedies all over the world. For example, the stem and seeds of *Heracleum persicum* have been used for treatment of epilepsy in Iranian traditional medicine, the essential oil of *Pimpinella anisum* was used in Persian traditional medicine, and roots of *Angelica archangelica* in Indian Ayurvedic medicine were used as antiepileptic and tranquilizers. Based on our previous experimental results, it is anticipated that the compounds called coumarins - thanks to their unique properties (lipophilic and easy penetration through brain blood barrier) will demonstrate interesting activity and may become good candidates for consideration for development as future antiepileptic drugs. The goal of this research project is to isolate the different coumarin derivatives, to determine their antiepileptic activity in zebrafish model and structure-activity relation and to select the most potent for further *in vivo* studies as a potent drug candidate.

For the isolation of the coumarins new cost-effective technique – High Performance Countercurrent Chromatography (HPCCC), with which we have extensive experience, will be used. We are operating the only instrument of this type in Poland. This technique is founded on the liquid-liquid mechanism of extraction, where the constituents of mixtures are distributed between two immiscible phases. Based on the novel instrument very pure compounds can be obtained in relatively short time (40-60 min). Active substances will be isolated from plants popularly occurring in Poland, which very often are considered as unwanted and harmful.

The evaluation of anticonvulsant activity of compounds will be assessed using new zebrafish models of epilepsy. There is proved that the behaviour of Zebrafish larvae in anticonvulsant model has direct transfer to rodents and humans. Thanks to that there is the possibility for wide screening many substances in different dosage combinations in time and cost effective way. It should be emphasized that the combination of these techniques (isolation by HPCCC and zebrafish epilepsy model) is a completely novel approach for the discovery of antiepileptic compounds from natural sources.

There is a desperate need for finding new, accessible and sustainable antiepileptic drugs. According to the World Health Organization, around 50 million people worldwide suffer from epilepsy, and nearly 80% of the people with epilepsy are found in the developing regions of the world, and their access to synthetic drugs is therefore very limited. Epilepsy responds to treatment about 70% of patients, but in 30% of patients, adequate seizure control is not achieved. About 75% of affected people in developing countries do not get the treatment they need, based on availability and cost. Experience acquired during the project will enable further scientific developments, possibly in the context of collaborative projects with the pharmaceutical industry. This project will be realised as an international cooperation which serve as a platform for exchanging skills, ideas, and techniques between Poland and Luxemburg. Considering that in this project two new techniques – HPCCC for the isolation of compounds and a zebrafish model for the estimation of anticonvulsant activity, this project may be defined as being both pioneering and innovative.