

Epilepsy is one of the most common neurological disorders, affecting about 1-2% population. It is a disorder characterized by an extremely complicated pathomechanism and multifactorial character. Clinically manifested by spontaneous and recurrent seizures arising from abnormal electrical activity some parts of the brain. Despite the fact that currently medicine has many drugs, pharmacotherapy is not always successful. Patients who have seizures that do not efficiently respond to currently available antiepileptic drugs are claimed to have drug-resistant epilepsy. Drug resistance epilepsy has recently become a serious clinical problem, because affects up to 40% of patients. Uncontrolled seizures significantly reduce the quality of patients life and may contribute to an increased risk of psychosocial disorders, psychiatric and medical complications, and in extreme cases even early dead. Currently the treatment to control seizures of patients with drug-resistant epilepsy requires monotherapy or combination therapy. Advantages of monotherapy include less risk of drug-drug interactions, side effects, decreased toxicity and lower costs. However, majority of patients achieve seizure control with the combination of two or more drugs.

Bearing in mind the relatively low efficacy of pharmacotherapy the continued search for novel anticonvulsants effective in drug-resistant seizures is urgently necessary. That's why a lot of research is being carried out in the world to develop new screening methods that will allow the selection of effective substances in the treatment of drug-resistant seizures. The world leader in the search for new antiepileptic drugs is the American program: Epilepsy Therapy Screening Program (ETSP). ETSP's successes include the participation in launch on the market the newest antiepileptic drugs (including lacosamide, levetiracetam), and recently the development a new *in vivo* screening model allowing to maximize the selection of substances with potential activity in drug-resistant seizures. As a result, substances with activity in the mice 6 Hz (44 mA) seizure model are the most promising, importantly the range of marked antiepileptic drugs currently are not active therein. Therefore, the 6 Hz (44 mA) seizure model in mice is used as the first step in identifying substances that are potentially effective in the pharmacotherapy of drug-resistant seizures. According to the ETSP guidelines, high activity in the 6 Hz model (44 mA) allows to qualify the compounds for the next and more advanced phases of *in vivo* studies. Therefore, the main goal of the presented project is to obtain a series of original compounds characterized by high activity in animal model of 6 Hz drug-resistant epilepsy (44 mA). The planned compounds are hybrids substances with join structural fragments of well-known antiepileptic drugs as well as fragments from anticonvulsant compounds selected on research conducted by our team over many years.

The desired effect of the presented project will be obtaining highly active substances in the said 6 Hz (44 mA) model, that will be promising candidates for new antiepileptic drugs potentially effective in the treatment of drug-resistant seizures. In addition, the similarity of the chemical structure of the presented compounds to safinamide (a drug that is used to treat Parkinson's disease as an inhibitor of the MAO-B enzyme) may ensure potential activity in Parkinson's disease. Importantly, recent studies show that Parkinson's disease is associated with an increased risk of epileptic seizures.