Epilepsy belongs to the most common neurological diseases significantly reducing patients' quality of life and the possibility of their daily functioning as well. Currently healthcare offers a large number of antiepileptic drugs, both conventional (classical) used for many years, as well as so-called new generation drugs (second and third), implemented for the treatment since the 90s. Analysis of their effectiveness, however shows that 30% of patients do not respond satisfactorily to the treatment, and this type of disease is known as drug resistant epilepsy. In addition, many of the currently used antiepileptic drugs is known to cause numerous side effects which substantially limit patients' compliance with pharmacotherapy planned. In a view of the fact that anticonvulsants are the most commonly used drugs in the treatment of neuropathic pain, there is a high probability that the compounds exhibiting anticonvulsant activity will also be effective in inhibiting pain stimuli caused by damage or dysfunction of the central or peripheral nervous system (e.g. as a result of diabetes, chemotherapy or surgical procedure). It should be stressed that current data indicate that in only 50% of patients one observes a reduction of neuropathic pain by only 30–50%, in the remaining patients no improvement by administration of any of the drugs used is observed. Therefore, there is a continuous need for new, more effective and well tolerated substances for treatment of aforementioned neurological diseases.

The current research and development studies of new drug candidates are focused mainly on substances with novel mechanism of action. Only such molecules may constitute a real breakthrough in the pharmacotherapy of given disorder. Thus, one of the newest, extremely interesting (bearing in mind the wide expression in human body) and widely explored molecular targets is transient receptor potential cation channel vanilloid type 1 (TRPV1). This channel is expressed in primary afferent sensory neurons of the pain pathway and its activation has been linked to among others chronic inflammatory pain conditions and neuropathic pain. For these reasons the substances which block TRPV1 receptor are recognized as potential drugs useful for the treatment of pain associated with inflammation, neuropathic pain, and migraine. Furthermore, the current neurobiological studies indicate the involvement of TRPV1 stimulation in induction of epileptic seizures, and thus blockers of the aforementioned channel may be a candidates for new anticonvulsants with novel mechanism of action. Notably, it should be stressed that this hypothesis has not been confirmed enough in wide chemical and pharmacological studies. Therefore, the main objective of the current project is to obtain chemically original TRPV1 antagonists that will be effective in different animal models of epilepsy which correspond to human tonic–clonic epilepsy, partial convulsions with or without secondary generalization, generalized absence epilepsy, myoclonic convulsions, and notably drug resistant epilepsy. Taking into consideration blocking of TRPV1, these substances may suppress pain following inflammation or injury/dysfunction of the central or peripheral nervous system, thus they should be also effective in different animal pain models including models of neuropathy induced by mechanical stimuli (model of post-surgical neuropathic pain), metabolic stimuli (model of diabetic neuropathy), and chemical stimuli (model of neuropathy during the chemotherapy). It should be emphasized that till know TRPV1 blockers with so wide pharmacological activity in the preclinical studies have not been described. When identifying new biologically active substances, it is important to assess the more detailed molecular mechanism determining pharmacological effect. For this reason, the project involves *in vitro* tests towards the affinity for different (and additional to TRPV1) ion channels and receptors involved in the regulation of nerve cells' excitability. Supplementation of the proposed studies will be determination of pharmacokinetics and toxicity of new substances in the *in vitro* and *in vivo* tests.

In more distant perspective, the results of this project may be useful for many studies aimed at highly effective and well-tolerated antiepileptic drugs (with potent antinociceptive activity), which introduction into the treatment may constitute an important progress in the pharmacotherapy of epilepsy and neuropathic pain, resulting in the reduction of treatment costs for both, the budget and the patients as well. Importantly, the literature on TRP1 channel shows that it may be implicated also in many other diseases, e.g. anxiety, neurodegenerative disorders (including Parkinson's disease), diabetes, obesity (and other metabolic disorders), cardiovascular disorders, urinary urge incontinence, chronic cough (asthma), irritable bowel syndrome, and hearing loss.