Epilepsy is a serious and widespread neurological disorder affecting approximately 1% of the population. Despite the availability of numerous antiepileptic drugs, as many as one-third of patients suffer from drug-resistant epilepsy, which does not respond to conventional pharmacological treatment. This condition is associated with a significant deterioration in quality of life, an increased risk of injury, psychiatric comorbidities, and higher mortality. Current therapies are often burdened by adverse effects such as sedation, cognitive impairment, or mood disturbances, which further limit their applicability. An independent but related clinical problem is chronic neuropathic pain, which affects up to 6–10% of the population. It is characterized by hypersensitivity to stimuli, a burning sensation, and pain occurring without a clear physical cause. In the face of ineffective treatment options, opioids are increasingly used, potent analgesics that carry substantial risks. Addiction, tolerance, respiratory depression, and even death are among the serious consequences of opioid misuse. For this reason, chronic pain has become one of the major areas of concern in the growing global opioid crisis. In this context, the development of effective and safe non-opioid therapies has become not only a clinical need but also a societal imperative. A common denominator of both epilepsy and neuropathic pain is the phenomenon of neuronal hyperexcitability, driven in part by dysregulated neurotransmission and abnormal function of ion channels and glial cells.

In response to these pressing clinical and societal needs, this project aims to develop novel chemical compounds with a dual mechanism of action, selectively targeting two distinct but complementary biological systems: the glutamate transporter EAAT2 and Kv7.2/3 potassium channels. Both targets play a key role in regulating neuronal excitability — the former removes excess glutamate from the synaptic cleft, while the latter stabilizes the membrane potential and suppresses abnormal neuronal discharges. This combined approach seeks to simultaneously restore synaptic balance and reduce excitability through membrane stabilization. Using a single compound that modulates both systems may enable strong therapeutic efficacy at lower doses and with fewer side effects. The project involves the design, synthesis, and evaluation of a series of compounds acting on these two targets. It will employ advanced molecular design techniques, synthesis of novel structures, and biological testing in animal seizure models, including drug-resistant forms, as well as in well-established models of neuropathic pain, such as diabetic neuropathy, chemotherapy-induced pain, and inflammatory pain. The aim is not only to demonstrate efficacy in seizure suppression and pain reduction but also to assess the safety, selectivity, and pharmacokinetic properties of the selected lead compounds. A key advantage of the proposed approach lies in its moderate but synergistic modulation of two core mechanisms, which may reduce toxicity and adverse effects commonly seen with high-dose, single-target therapies. Importantly, using a multifunctional compound simplifies treatment strategies and reduces the risk of drug–drug interactions, which may translate into better disease control and improved patient outcomes.

The expected outcome of this project is the identification of promising drug candidates with both antiseizure and analgesic potential, suitable for further preclinical and clinical development. This work addresses major unmet challenges in contemporary neurology and neuropharmacology by offering a realistic alternative to ineffective or risky treatments, both for drug-resistant epilepsy and for chronic pain, whose growing prevalence and link to the opioid crisis constitute one of the most serious public health threats in recent years.