

The aim of the project is to develop new chemical compounds, thanks to which it will be possible to research new directions of pharmacotherapy of extremely important neuropsychiatric diseases, especially schizophrenia.

The innovative feature of these compounds is the ability to 'intelligently' stimulate two types of receptors at the same time – serotonin 5-HT_{1A} and dopamine D₂. Usually, compounds by stimulating a given receptor cause effects that we want (therapeutic) and those that we do not want (undesirable). Compounds acting intelligently, the so-called 'biased' agonists, stimulate receptors in a functionally selective manner – activating only selected intracellular mechanisms, thanks to which it is possible to induce therapeutic effects without side effects. This offers completely new opportunities to increase the effectiveness and safety of the therapy.

In this project, for the first time, the synergy of functional selectivity towards two receptors with high potential for counteracting the symptoms of schizophrenia, i.e. 5-HT_{1A} and D₂ receptors, will be used. Particular emphasis is placed on the activity of these compounds against the so-called negative and cognitive symptoms of schizophrenia, which include, among others, anhedonia, asociality, and working memory disorders, which are very poorly controlled by the available drugs. This is a huge medical and social problem, justifying further research into more effective therapeutic solutions.

In order to achieve the goals set in the project, multidisciplinary research is necessary, including:

- designing new biologically active molecules with the use of computer modeling methods,
- chemical synthesis of designed compounds, intended for pharmacological research, defining their properties,
- in vitro pharmacological tests (with the use of i. a. cell lines), which will confirm the assumed pharmacological profile, including dual functional selectivity,
- in vivo pharmacology studies (involving advanced animal models) to investigate the potential therapeutic properties of compounds with a new pharmacological profile (dual biased agonists).

The research planned in the project will allow to obtain the first group of compounds with a previously unknown profile of pharmacological activity – dual 'biased' agonists of 5-HT_{1A} and D₂ receptors. According to the current state of the knowledge, such compounds may lead to the discovery of a new, effective and safe therapy for schizophrenia.