

## **Targeting the serotonin 5-HT<sub>7</sub> receptor in a search for new strategies of mental disorders treatment**

Serotonin plays an important role in the central nervous system. Its effects include the regulation of mood, sleep, appetite, sexual function and impulse control. Serotonin transmits signals between nerve cells by interacting with specialized protein receptors. These include serotonin receptors such as the 5-HT<sub>1</sub>, 5-HT<sub>2</sub>, 5-HT<sub>3</sub>, 5-HT<sub>4</sub> receptors and the 5-HT<sub>7</sub> receptor. Each of these receptors has a unique role in transmitting nerve impulses and modulating the functions of the central nervous system.

One of the recently identified serotonin receptors is the 5-HT<sub>7</sub> receptor, which is present mainly in the human central nervous system. This receptor plays an important role in nerve cells, in the processes of neurological regulation, such as cognitive, mood and neuroprotective functions. Its dysfunction can contribute to the occurrence of various mental disorders, as well as neurodegenerative diseases. Research on compounds that regulate the activity of the 5-HT<sub>7</sub> receptor is important due to their potential impact on the treatment of diseases of the central nervous system, such as depression, Parkinson's disease, schizophrenia and anxiety disorders. The development of drugs targeting the 5-HT<sub>7</sub> receptor may contribute to the development of effective therapies for these diseases.

The aim of this project is to find appropriate pharmacological tools that selectively block the activity of the serotonin 5-HT<sub>7</sub> receptor. Scientific research will be conducted within a series of compounds belonging to a common chemical group with a structure based on an arylpiperazine core. The planned modifications in the chemical structure of the compounds are aimed at increasing the affinity and selectivity of these compounds to the serotonin 5-HT<sub>7</sub> receptor, as well as improving their pharmacokinetic parameters. In addition, the inhibitory effect of the new compounds on ionotropic glutamic acid receptors will be investigated. Glutamate, which is the main excitatory transmitter in the brain, plays a very important role in learning and memory processes, and its receptors are an important therapeutic target in the treatment of neurodegenerative and psychiatric diseases.

The research includes the following stages:

**Stage 1.** Designing the structures of compounds and computer research with the use of modern, highly advanced computer software.

**Stage 2.** Chemical synthesis of a series of compounds designed in Stage 1.

**Stage 3.** *In vitro* studies of affinity and selectivity of compounds for serotonin and other non-serotonin receptors. Advanced functional tests will be carried out for selected compounds, confirming their ability to block the 5-HT<sub>7</sub> receptor.

**Stage 4.** *In vitro* studies on the affinity of compounds for selected ionotropic glutamic acid receptors

**Stage 5.** *In vitro* studies of the safety profile of compounds. Neurotoxicity and neuroprotection studies of compounds are important to assess their potential negative effects on the nervous system and identify strategies for neurological protection. Thanks to neurotoxicity studies, the effects of compounds on nerve cells will be assessed, while neuroprotection studies will allow identification of mechanisms supporting the protection of healthy nerve cells.

**Stage 6.** *In vitro* studies of permeability through biological membranes and metabolic stability. The purpose of these tests is to assess whether a given compound is able to get to the target tissues and organs, and how quickly the tested compound is transformed in the body. This information will allow the evaluation of the efficacy, safety and bioavailability of the test chemical.

As a result of the conducted research, chemical compounds with a strong affinity and appropriate selectivity for the serotonin 5-HT<sub>7</sub> receptor will be obtained. The potential antidepressant and anxiolytic effects of these compounds will be further analyzed in animal studies, which may contribute to the development of new therapies for people suffering from depression and anxiety disorders. The results of these studies will be published in international scientific journals and presented at conferences in the field of medicinal chemistry.