

Schizophrenia is a debilitating mental disorder, affecting 1 in 222 adult people and manifesting by positive (e.g. hallucinations), negative (e. g. social withdrawal) and cognitive (e. g. memory impairment) symptoms. Noteworthy, schizophrenic patients often suffer from reduced quality of life, caused mainly by the schizophrenia symptoms severity. The life expectancy of people diagnosed with the illness is 15-20 years lower compared to the general population due to higher cardio-vascular risk and metabolic issues. Despite the years of SCZ-related studies, neither SCZ triggering factors nor satisfying pharmacotherapy has been found, as currently used antipsychotics are burdened with numerous side effects. Noteworthy, only one third patients respond to pharmacological treatment, therefore searching for safer and more efficient drugs is urgently needed. Bulk of studies suggest variety of molecular changes observed in central nervous system of schizophrenic subjects such as inflammatory response or accelerated oxidative stress and these may lead to highly disturbed functioning of central nervous system. Results of previous research indicate that manifestation of schizophrenia symptoms (e. g. cognitive decline) and course of the illness may be linked to above mentioned oxidative and neuroinflammatory processes.

Endocannabinoid (eCB) system is a widespread neuromodulatory network regulating various physiological processes, e. g. immunological system regulation, central nervous system development, synaptic plasticity (underlying memory and learning processes) or cognitive function. Endocannabinoids acts on CB1 and CB2 receptors carrying diverse functions in nervous system. Numerous natural, plant-derived compounds may interact with eCB system exerting beneficial effects. One of these compounds is BCP ( $\beta$ -caryophyllene), contained in e. g. black pepper, basil or *Cannabis sativa*. Recent research showed anti-oxidative, anti-inflammatory, antidepressive and analgesic action of BCP. Moreover, BCP administration, even in high doses, does not lead to toxic effects. BCP selectively activate CB2 receptor with a good safety profile. Importantly, CB2 receptor activation by BCP lacks the psychoactive effects, in contrast to CB1 activation by e.g. THC ( $\Delta$ -9-tetrahydrocannabinol). CB2 receptors are less expressed in neuronal cells of the healthy brain, however, their expression highly increases on on-neuronal cells (e. g. microglia or astrocytes) while ongoing neuroinflammation. Bulk of studies indicates beneficial effects of CB2 receptor activation in inflammatory and oxidative stress processes, e. g. in animal model Alzheimer disease, which gives hope for similarly favorable results in other studied conditions with presence of oxidative stress and inflammation.

Presented project aims to evaluate antipsychotic, pro-cognitive and anxiolytic actions of BCP in rat model of schizophrenia with battery of behavioral test employed. Additionally, using molecular methods, effect of BCP administration on inflammatory status in brain structures will be assayed. Thanks to the cooperation with Institute of Biomolecular Chemistry (Naples, Italy), the BCP influence on oxidative stress reactions will be investigated using high-tech mitochondrial functions analyzing method.

Regarding the precious research of BCP in animal models of various diseases, we expect the potential therapeutic action of this natural, however still undervalued, compound. We expect that subchronic administration of BCP in animal schizophrenia model will attenuate, or completely reverse both behavioral and molecular disease-relevant symptoms. Employing various research methods, reliable results will be delivered and these may be supportive for future clinical studies, using BCP in treatment of neuropsychiatric conditions such as schizophrenia.