



**Fund “Nauka” Project № 24006 Resume – Special Competition-based Session
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“Investigation of psychopharmacological effects of Kochia scoparia seed extract in experimental animal models of dementia and anxiety-depressive disorder”

Project leader: Assoc. prof. Silviya Gancheva Marinova, PhD

The project aims to investigate the psychopharmacological effects of Kochia scoparia seed extract in experimental models of dementia and anxiety/depressive disorder and to establish the mechanisms involved.

Different extracts from the seeds of the plant will be prepared and their phytochemical composition will be determined. The extract with the optimal content of the main biologically active substances will be used for treatment of experimental animals. Four experiments will be conducted by utilizing different experimental models: scopolamine-induced memory impairment; alcohol-induced memory impairment and depression/anxiety; d-galactose-induced memory impairment and depression/anxiety; chronic unpredictable mild stress model for induction of depression/anxiety. In each experimental setup, the animals will be divided into five groups – a control group and four groups subjected to the corresponding experimental model, three of which will be treated with different doses of the extract. At the end of each experiment, behavioral tests will be conducted to assess the locomotor activity, anxiety- and depression-like behavior, memory and learning. Gene expression, as well as concentration or activity of cytokines, enzymes, transcription factors and growth factors related to oxidative stress and antioxidant defense, neuro-inflammation and apoptosis will be measured in the brain tissue of experimental animals. Some markers of the oxidative status will also be determined in the serum of experimental animals.

Kochia scoparia seed extract is expected to improve the symptoms of cognitive deficit, depression and anxiety in experimental animals and to favorably affect the oxidative status, neuro-inflammation and apoptosis.

The obtained results might find clinical application for prevention and/or adjunctive therapy of neurodegenerative diseases, anxiety and depressive disorders.

Expected results:

Six different extracts of Kochia scoparia seeds will be prepared by using different extractants – 70% ethanol, absolute ethanol, methanol, acetone, hexane and sterile water. The presence and concentration of momordin Ic and 20-hydroxyecdysone will be determined in each extract.

The animals not receiving the seed extract are expected to develop impairment of the memory and learning process when treated with scopolamine, alcohol, and D-galactose, and depressive- and anxiety-like behavior when treated with alcohol, D-galactose or when subjected to chronic unpredictable stress. We expect a reduction of the concentration of the growth factor BDNF in the brain tissue of these animals, increase in the gene expression of the proapoptotic Bcl-2 and decrease in the gene expression of the antiapoptotic Bax. The gene expression of pro-inflammatory cytokines (TNF- α , IL-1 β) and enzymes (iNOS, COX-2) as well as the activity of the transcription factor NF- κ B are expected to be increased. It is also expected that the oxidative status in the brain tissue of these experimental animals will be adversely affected with changes in the activity of the transcription factor NRF2 and indicators of the antioxidant status (levels of total and reduced glutathione, superoxide dismutase activity, expression of glutamate cysteine ligase) and an increase in markers of oxidative stress, such as TBARSs. In the sera of the experimental animals, similar changes in the oxidative stress and antioxidant defense markers are expected with increased levels of TBARSs and reduced total antioxidant status. In the animals with anxiety-depressive symptoms, an elevation of serum cortisol level is also expected.

Treatment of the experimental animals with increasing doses of *Kochia scoparia* seed extract is expected to improve animals' performance in the behavioral tests and to prevent the manifestations of cognitive deficits and/or anxiety- and depression-like behavior. The extract is expected to exhibit antioxidant and anti-inflammatory properties, to favorably influence the process of neuronal apoptosis and to prevent changes in the gene expression and in the concentration/activity of the measured cytokines, enzymes, transcription and growth factors.