EXPERIMENTAL INVESTIGATION OF ANTIEPILEPTIC POTENTIAL AND MECHANISMS OF ANTICONVULSANT ACTION OF DRY EXTRACT OF *FUMARIA SCHLEICHERI*

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According to the data of WHO almost 0.68 per cent of world population suffers from epilepsy and this showing is only increasing. It is well known that treating chronic diseases including epilepsy is a rather long-term if not lifelong process. That is why in this case implementing medicinal plants is relevant as they are highly safe even in the situation of a long-term using.

The aim of the present study is to study the antiepileptic potential of perspective herbal anticonvulsant drug – dry extract of *Fumaria schleicheri* (FSDE) – taking into consideration its ability to prevent primarily generalized convulsions on the model of seizures induced by the maximal electroshock (MES) and the ability to inhibit epileptogenesis under the conditions of pentylenetetrazole-induced kindling, and also to examine the potential mechanisms of anticonvulsant action of FSDE analyzing the changes of neurotransmitter amino acids content in mice brain.

Materials and methods. For the MES test the animals of experimental group received intragastically the water solution of FSDE at the conditionally effective dose of 100 mg/kg during 3 days with the last time 30 minutes before conducting the experiment. The comparison groups received intragastically classic antiepileptic medications – sodium valproate at a dose of 300 mg/kg and carbamazepine at a dose of 40 mg/kg in the same mode. The control group of mice received intragastically the distilled water (0.1 ml for 10 g of body weight). Then the animals through the corneal electrodes were influenced by electric stimuli with the duration of 0.2 sec, frequency 50 Hz and current 50 mA.

For the pentylenetetrazole-induced kindling the animals of experimental group received intragastically water solution of FSDE at the conditionally therapeutic dose of 100 mg/kg in the treating and preventive mode during 27 days once a day 30 min before injecting the convulsant. The comparison group received intragastically a classic anticonvulsant drug of sodium valproate at a dose of 300 mg/kg in the same mode. Mice from control group received intragastically distilled water (0.1 ml for 10 g of body weight). The water solution of pentylenetetrazole (corasole) was injected intraperitoneally at the under-edge dose of 30 mg/kg in the same mode.

The influence of FSDE on the content of inhibitory and excitatory amino acids in the brain of intact mice has been studied. Water solution of FSDE at the conditionally effective anticonvulsive dose of 100 mg/kg and the reference drug of sodium valproate at the dose of 300 mg/kg were administered intragastrically in the preventive regimen for 3 days. Thirty min after the last injection mice were sacrificed, the brain was immediately removed and frozen with liquid nitrogen, powdered and extracted. The content of GABA, glutamate and aspartate was determined in the obtained extracts.

Results and discussion. In the MES test FSDE showed clear anticonvulsant properties. FSDE decreased the duration of convulsions in 2.1 times compared with control, and also decreased the time of recovery of the survived animals in 3 times.

On the model of pentylenetetrazole-induced kindling FSDE continued the latent period of the first convulsions occurrence with statistical significance, validly decreased the general amount of days with seizures and the percentage of mice with convulsions in the group from the 23^{rd} to the 27^{th} day including the last one.

Under administration of FSDE there were significant changes in the quantitative content of all studied amino acids in the mice brain. The GABA level was increased by 2.3 times, and the glutamate and aspartate levels were decreased by 8.3 and 30.8%, respectively. Sodium valproate significantly increased the level of GABA in the brain of mice 3.4 times, as well as a significantly decreased the content of glutamate by 34.6% and increased the level of aspartate by 8.9% compared to control group. Correlation analysis showed that there is a strong negative relationship between GABA and glutamate levels in the brain of mice treated with FSDE and sodium valproate. Between GABA and aspartate levels in the control group and in the background of sodium valproate there was a weak correlation and negative correlation of medium strength in the group of animals treated with FSDE.

Conclusions. Under the conditions of the MES test it was established that FSDE showed considerable anticonvulsant properties which were not inferior to the effect of sodium valproate though did not reach the level of carbamazepine. On the model of pentylenetetrazole-induced kindling it was shown that FSDE has an ability to prevent convulsions under the conditions of experimental chronic epileptogenesis. A pronounced influence of FSDE on the balance of neurotransmitter amino acids in the intact mice brain was indicated. Correlation analysis proved a significant intervention of FSDE in processes of the exchange of neurotransmitter amino acids in the CNS.