Administration of Saperavi flavonoids (SF) to the rats reduces the number and duration of behavioral seizures: involvement of the brain NO system in antyseizure effects of SF

Nanuli Doreulee, Mariam Qurasbediani, Butsiko Chkhartishvili, Manana Chikovani, Roza Bukia, Militsa Svanidze, Gia Kutelia

e-mail: nanuli.doreuli@tsu.ge

Department of Biology, Faculty of Exact and Natural Science, Iv.Javakhishvili Tbilisi State University, University str.2, 0143 Tbilisi, Georgia

Temporal lobe epilepsy (TLE) is one of the common human seizure disorder characterized by seizures poorly controlled with anticonvulsant medications [1]. The development of epileptogenesis is associated with a diversity of plastic changes which functionally affect different system levels, resulting in epilepsy-related cognitive impairment and psychiatric comorbidities. Culmination for epileptogenesis is the development of chronic spontaneous seizures. Different types of alteration associated with epileptogenesis were revealed in the brain, for example blood–brain barrier damage, neurodegeneration, neuroinflammation, neurogenesis and synaptic reorganization [2]. In several investigations reduction of the total antioxidant status and increases of production of nitric oxide (NO) in epileptogenesis were demonstrated [3]. In the studies of the determination of new approaches of TLE treatment plant flavonoids are very important, because of their abilities to scavenge reactive oxide species and to inhibit pathological NO. In our previous experiments antioxidant potency of the active fraction of flavonoids from saperavi was revealed: saperavi flavonoids (SF) effectively prevented age-related increase of quantity of malondialdehyde in the brain of adult rats. It has been shown that in kainate–induced rat model of epilepsy (KA-SE) SF corrects epilepsy-associated behavioral and memory disturbances.

The aim of the present work was to define a role of supplementation of rats during the early stages of epileptogenesis with SF (8 days, 25mg/kg per day, after single i.p. injection of kainic acid (15mg/kg)) on a number and duration of the behavioral seizure attacks. The effects of SF were studded in comparison with quercetin and L-NAME (a non-selective inhibitor of NO synthase) (8days of administration, 25mg/kg and 40mg/kg per days, respectively). Behavioral seizures were monitored during open field and T-maze laboratory tests.

Our experiments revealed that behavioral alterations induced by KA-SE are abolished by administration of SF. The frequency and duration of behavioral seizures in KA-SE rats statistically decreased and correction in learning/memory ability were detected. The efficiency of quercetin on epilepsy induced cognitive impairment compare to the SF was less pronounced. L-NAME effectively blocked the KA-SE-induced seizure frequency and duration, but exacerbate memory deficit induced by epilepsy.

The work is supported by Rustaveli foundation, grant FR/617/7-270/13.

References

[1] J. Jr. Engel, M.D. Philadelphia, F.A., Davis: Seizures and epilepsy. (1989), 536p.

[2]A. Pitkänen, K. Lukasiuk Mechanisms of epileptogenesis and potential treatment targets. Lancet Neurol., (2011), 10(2): 173-186.

[3]H.Prast and A.Philippu, Nitric oxide as modulator of neuronal function. Progress in Neurobiology, (2001), 64(1): 51–68.