

**The influence of flavonoids from Georgian endemic grape species “Saperavi”
on brain disfunction induced by kainic acid-status epilepticus in rats.**

Mariam Kurasbediani

Supervisor: Nanuli Doreulee

Epilepsy is a chronic neurological disease affecting roughly 1% of the human population. The progressive spontaneous recurrent seizures (SRS) induces hippocampal neuronal loss, cognitive impairment and psychiatric comorbidities. Regular treatment with the antiepileptic drugs (AED) is useful for controlling seizures. However, more than 35% of people with temporal lobe epilepsy (TLE) have chronic seizures that are resistant to AEDs. Thereby new approaches in therapies for easing the frequency and intensity of SRS, learning and memory impairments, and depression in TLE are needed.

The evidence indicates that Glutamate excitotoxicity is involved in a pathophysiology of Epilepsy. It has been also proposed that activation of the innate immunity, i.e. inflammation is contributed to nerve cell damage after seizures or an excitotoxic insult. Considering the importance of oxidative stress in epilepsy disorders antioxidant and anti-inflammatory treatments may attenuate or prevent the neurodegenerative disorders involved in glutamate excitotoxicity.

The aim of the present work was to investigate the effects of active flavonoids from Georgian endemic grapes species Saperavi on behavioral and morphological alterations induced by Status Epilepticus. Kainic Acid temporal lobe epilepsy animal model was used to define antiepileptic and neuroprotective potency of flavonoids from Saperavi. Effectiveness of Saperavi flavonoids were assessed in comparison of the effects of early-described flavonoid quercetin.

To define the mechanisms of action of flavonoids from Saperavi on structural and functional abnormalities of rat brain induced by KA-SE behavioural experiments – the open field, T-maze and passive avoidance tests were carried out. In different series of experiments were defined strength of disorders in motor activity, emotional state and in learning/memory ability induced by KA-SE and influence of 8 days supplementation (feeding) of flavonoids from Saferavi (25mg/kg) on KA (15mg/kg, single administration) induced epileptogeneses was investigated. KA-SE induced structural changes in hippocampal CA1/CA3 fields and Dentate gyrus were studied in morphological experiments and effects of Saperavi flavonoids feedings were defined.

Neuroprotective effects of Saperavi flavonoids against epilepsy induced destruction were first investigated in our experiments and suggestion is that Saperavi flavonoids protect rat brain from KA induced neuronal injury and memory disruption associated with it.