

## **Rutin protects mitochondria, increases glutamine synthetase expression and protects neurons against glutamate excitotoxicity**

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**INTRODUCTION:** Rutin is a glycosylate flavonoid that has various biological functions, including anti-inflammatory action, antioxidant, antitumoral and promising pharmacological effects on CNS. Neuronal death by glutamate excitotoxicity is present in several diseases and involves various cellular dysfunction, including mitochondrial damage. To prevent excitotoxicity, glutamate is removed by astrocytes and converted to L-glutamine through the action of glutamine synthetase (GS), which is released to the extracellular fluid taken up by neurons. **OBJECTIVES:** The aim of this study was to evaluate the neuroprotective effects of rutin with a focus on mitochondrial protection and GS expression. **MATERIAL AND METHODS:** Neuronal viability was performed by Fluoro-Jade B staining on cerebellar primary cultures from P8 Wistar rats (P8). Modulation of GS expression levels on rats cortical organotypic culture (P8) was assessed by Western blot. Mitochondrial protection by rutin was evaluated by membrane potential and ROS production analysis, using safranin O and amplex red as probe, respectively, in mitochondria isolated from cortex of adults rats. **RESULTS AND DISCUSSION:** Our results demonstrated that glutamate (1mM) induced increase of 1.7 times on rate of fluorescent intensity of Fluoro-Jade B/DAPI and rutin (10 and 50  $\mu$ M for 24h) reduced cell death induced by glutamate in cerebellar primary cultures. We also observed that rutin inhibited 44.6% of membrane potential increase and inhibited 30.5% of ROS production in isolated mitochondria. Moreover, we observed that rutin (10  $\mu$ M for 24h) induced increase of 9.8% in the expression of GS in cortical organotypic culture. **CONCLUSION:** We conclude that rutin is a potential neuroprotective agent against excitotoxicity and suggested that this protective effect involves mitochondrial protection and modulation of GS expression. However, more studies are crucial in order to elucidate the molecular mechanism of neuroprotection induced by rutin against damage by glutamate, and understand the role of glial cells, especially astrocytes on bioactivity of rutin.

**Keywords:** Rutin; Neuroprotection; Glutamate excitotoxicity

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