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## Investigation of the Role of Oxidative Stress and Endoplasmic Stress Pathway in the Protective Effect of Quercetin on 4-aminopyridine-Induced Neuronal Damage

Ahmet Sevki Taskiran, Ayse Topcu

Departments of Physiology, School of Medicine, Sivas Cumhuriyet University, Sivas, Türkiye

### Abstract

Quercetin (QU) is a subtype of flavonoid that can be found in different fruits and vegetables. Many studies report that QU may have positive effects on neurological diseases. However, the effect and possible mechanisms of QU on 4-AP-induced neuronal damage remain unclear. In the present study, therefore, it was aimed to reveal the effects of QU on the hippocampal neuronal damage induced by 4-aminopyridine (4-AP) and the possible roles of oxidative stress and endoplasmic reticulum stress in this effect. The study was carried out using the HT-22 hippocampal neuronal cell line. The effect of pre-treatment with QU on cell viability after 4-AP-induced neuronal damage was determined by the XTT test. Cells were evaluated histopathologically for apoptotic nuclear change (ANC) using DAPI stain. The effects of QU on oxidative stress markers (total oxidant status (TOS) and total antioxidant status (TAS)) and endoplasmic reticulum stress markers (activating transcription factor 4 (ATF-4) and C/EBP homologous protein (CHOP)) were measured using colorimetric commercial kits and ELISA kits after neuronal damage. Treatment of hippocampal cells with 4-AP alone reduced cell viability, while pre-treatment with QU reversed this effect of 4-AP. In respect of histopathologically, treatment with 4-AP alone increased the number of ANCs, while pre-treatment of QU decreased the ANCs. In addition, in terms of biochemical evaluations, TOS, ATF-4, and CHOP increased after 4-AP in neuronal cells and QU suppressed this increase after neuronal damage. In addition, QU normalized the decreased TAS levels following 4-AP administration. As a result, it was found that QU prevents 4-AP-induced neuronal damage in hippocampal neuronal cells. It is thought that the neuroprotective effects of QU may be mediated by its suppressive properties on oxidative stress and endoplasmic reticulum stress. The use of QU supplementation may be beneficial in reducing the risks of diseases associated with neuronal damage.

**Key Words:** Quercetin, 4-aminopyridine, Neuronal Damage, Oxidative stress, Endoplasmic reticulum stress

