Luteolin Counteracts ER Stress in PC12 Cells through Moderating ER Chaperones and Heat Shock Proteins

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Abstract
Luteolin, as a natural polyphenolic compound, has neuroprotective effect and exerts its function by attenuation of apoptosis and oxidative stress factors. Emerging evidences indicate that oxidative stress leads to neurodegeneration but is not the initial event and endoplasmic reticulum stress (ER) is often considered to be the stimulus event which is caused by accumulating of misfolded proteins. The activation of the unfolded protein response (UPR) outcrops as the one of early occurrence in brain injury when the agglomeration of mis- or unfolded proteins occur in the ER lumen. So, the present study try to define whether any neuroprotective effect is seen when Luteolin is administered in used \( \text{H}_2\text{O}_2 \)-injured PC12 cells. PC12 cells were cultured and exposed to different concentrations of \( \text{H}_2\text{O}_2 \) with different concentrations (10, 25, 50, 100 \( \mu \text{M} \)) of Luteolin for 2 hr prior to our experiments, then the cells were exposed with \( \text{H}_2\text{O}_2 \) (150 \( \mu \text{M} \)) for 24 hr. Western blot analysis was performed in PC12 cells to evaluate the levels of Heat shock proteins (Hsp70 and Hsp90) and ER stress chaperones such as GRP78/BiP and CHOP. Cell viability was evaluated by the conventional MTT reduction assay. Pretreatment of PC12 cells with different concentration (10, 25, 50, 100 \( \mu \text{M} \)) of Luteolin followed by exposure to \( \text{H}_2\text{O}_2 \) increased cell viability (about 46, 35, 78 and 80\%, respectively) relative to the \( \text{H}_2\text{O}_2 \)-treated cells. In the group that received (25 \( \mu \text{M} \)) concentration of Luteolin, ER stress chaperones such as GRP78/BiP and CHOP decreased compared to \( \text{H}_2\text{O}_2 \) treated cells, while HSP70 increased in Luteolin treatment of 25\( \mu \text{M} \). The level of hsp90 decreased in Luteolin (25\( \mu \text{M} \)) treatment. In conclusion, our data suggest that flavonoid has therapeutic potential following brain trauma.

Keywords: ER Stress, PC12 Cells, Heat Shock Proteins, Brain Trauma.

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