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Thevetiaflavone Protects PC12 Cells Against Neurotoxicity Induced by $A\beta_{1-42}$ Through Inhibiting Oxidative Stress and Activating Nrf2/HO-1 Pathway

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***SUMMARY*. Thevetiaflavone is a flavonoid possessing neuroprotective effects on PC12 cells injured by oxygen and glucose deprivation and restoration or H2O2, which inspires us to elucidate if it protects PC12 cells against the neurotoxicity induced by amyloid β. As a result, thevetiaflavone can improve the survival of PC12 cells injured by $A\beta_{1-42}$ through increasing the viability and blocking intracellular LDH release. Further investigation revealed thevetiaflavone can ameliorated the neurotoxicity in PC12 cells induced by $A\beta_{1-42}$ via inhibiting oxidative stress and preventing apoptosis. The excessive ROS was reduced and the activity of SOD and CAT was elevated. Meanwhile, the activity of caspase-3 and -9 was suppressed as well as up-regulation of Bcl-2 and down-regulation of Bax were observed. Additionally, Nrf2/HO-1 pathway was found to be involved in this protection. These findings gave evidences for the discovery of neuroprotective agents for Alzheimer's disease.**

RESUMEN. Tevetiaflavona es un flavonoide que posee efectos neuroprotectores en las células PC12 lesionadas por el oxígeno y la privación y restauración de glucosa o H2O2, lo que nos inspira a dilucidar si protege las células PC12 contra la neurotoxicidad inducida por β amiloide. Como resultado, tevetiaflavonae puede mejorar la supervivencia de las células PC12 lesionadas por $A\beta_{1-42}$ al aumentar la viabilidad y bloquear la liberación de LDH intracelular. La investigación adicional reveló que tevetiaflavona puede mejorar la neurotoxicidad en las células PC12 inducidas por $A\beta_{1-42}$ mediante la inhibición del estrés oxidativo y la prevención de la apoptosis. El exceso de ROS se redujo y la actividad de SOD y CAT fue elevada. Mientras tanto, se suprimió la actividad de caspasa-3 y -9, así como la regulación positiva de Bcl-2 y la regulación negativa de Bax. Además, se encontró que la vía Nrf2/HO-1 estaba involucrada en esta protección. Estos hallazgos dieron evidencias para el descubrimiento de agentes neuroprotectores para la enfermedad de Alzheimer.

KEY WORDS: thevetiaflavone, neurotoxicity, amyloid β, oxidative stress, Nrf2/HO-1 pathway, PC12 cells.

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