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Harnessing phytochemicals to protect neuronal and glial cells from oxidative stress

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Oxidative stress and amyloid beta toxicity are involved in the pathogenesis of Alzheimer's diseases. We have previously demonstrated that an extract prepared of the plant *Achillea fragrantissima* (*Af)* protected cultured brain astrocytes from oxidative stress-induced cell death and down regulated microglial activation. Using activity guided fractionation, we have purified from Af an active flavonoid named 3,5,4-trihydroxy-6,7,3-trimethoxyflavone (TTF). TTF protected cultured astrocytes from H_2O_2–induced cell death via interference with cell signaling (inhibition of SAPK/JNK, ERK 1/2, and MEK1 phosphorylation) and by reducing the levels of oxidative stress-induced intracellular reactive oxygen species (ROS). The mechanism of the protective effect of TTF against H_2O_2-cytotoxicity could not be attributed to a direct H_2O_2 scavenging but rather to the scavenging of free radicals as was shown in cell free systems. In addition, TTF protected cultured neuronal cells from amyloid beta cytotoxicity via interference with cell signaling events and by reducing the amyloid beta - induced levels of intracellular ROS. Moreover, TTF exhibited anti-inflammatory activities and inhibited the LPS-elicited secretion of the proinflammatory cytokines Interleukin 6 (IL-6) and IL-1beta from microglial cells. Our results suggest that TTF might be a therapeutic candidate for the treatment of Alzheimer's disease as well as other neurodegenerative diseases where oxidative stress, neuroinflammation and amyloid beta toxicity are part of the pathophysiology.

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