Neuroprotective and antioxidant effects of Esculetin against Amyloid Beta Peptide-Induced Toxicity in SH-SY5Y cells

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Alzheimer's disease (AD) is a chronic neurodegenerative disease characterized by a progressive neuronal loss, particularly in hippocampus and cortex, associated with abnormal accumulation of extracellular amyloid-beta (Abeta) protein and intracellular tau tangles. Several studies also suggest that the reactive oxygen species mediated-neuronal injury can increase the severity and the progression of AD. Recent studies show that several coumarins with pharmacological properties such as anti-inflammatory, antioxidant and neuroprotective properties might be future drugs for the treatment of neurodegenerative disorders including AD. Among the coumarins, esculetin shows an interesting ability to cross the blood-brain barrier and counteract the oxidative stress at system nervous central level in a in vivo model of Parkinson's disease. In this study, we found that esculetin (6,7-dihydroxycoumarin, ESC) possess both direct and indirect antioxidant activities against oxidative stress elicited by tert-butyl hydroperoxide and Abeta peptides in human neuroblastoma (SH-SY5Y) cells. In particular, the indirect antioxidant activity of ESC could be ascribed to its ability to active Nrf2 at nucleus level and increase the antioxidant activity and glutathione levels at cytosolic level. In addition, ESC counteracted the early and late neurotoxic events, in terms of formazan exocytosis and necrosis, respectively, evoked by Abeta peptides. ESC also exerted the interesting ability to prevent the early events leading to neuronal death such as the Abeta peptide binding to plasma membrane and the subsequent membrane integrity loss. In conclusion, these results encourage further preclinical studies to explore the potential profile of ESC as novel neuroprotective agent in AD. *Supported by MIUR-FIRB project RBAP11HSZS (2011) and Fondazione del Monte di Bologna e Ravenna (Italy)*

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