4-METHYLCOUMARINS PROTECT NEURONAL CELLS AGAINST OXIDATIVE STRESS

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The antioxidant activity of 4-methylcoumarins assessed by different methodologies has recently been reported by several investigators. Oxidative stress is involved in neurodegeneration and therefore antioxidants may have a role for treatment of disorders such as Alzheimer disease and Parkinson disease. We and other investigators have previously shown that 4-methylcoumarins containing catechol moiety exhibit strong antioxidant effect. In this study, we assessed the neuroprotective activity of several synthetic derivatives of 4-methylcoumarins containing 7,8-dihydroxy as well as 7-hydroxy and 5,7-dihydroxy moieties. We used hydrogen peroxide induced apoptosis in cultured neuronal PC12 cells as a cell model. This model closely mimics the oxidative stress induced damage in the central nervous system in neurodegenerative diseases. PC12 cells were preincubated with different concentrations of test compounds and then hydrogen peroxide was added to induce apoptosis. Cell viability was measured by the MTT assay and the capacity of the compound to prevent cell death was measured. Antioxidant activity of these compounds was also measured by DPPH radical scavenging and ferric reducing antioxidant power (FRAP) assays. 7,8-Dihydroxy-4-methylcoumarins with different substitutions at C3 position (including alkyl chains of different length) showed high antioxidant activity in FRAP and DPPH assays and most of them significantly inhibited PC12 cell damage at low micromolar concentrations. 7-Hydroxy and 5,7-dihydroxy derivatives generally showed much lower antioxidant and neuroprotective activities in comparison. In conclusion, these findings suggest that 4-methylcoumarins, especially catechol containing derivatives could be useful agents for prevention of oxidative stress-induced cell damage in neurodegenerative diseases.