

Poster Session

PS501 ATTENUATES PEROXYNITRITE-INDUCED OXIDATIVE DAMAGE AND APOPTOSIS IN NEURONAL CELLS

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Peroxynitrite, the anion formed by nitric oxide and superoxide, is a strong oxidant that reacts with a variety of biomolecules. It has been proposed that oxidative damage induced by peroxynitrite is involved in many neuronal diseases including Alzheimer's disease and Parkinson's disease. It has been reported that fermented papaya preparation could scavenge reactive oxygen species and regulate the synthesis of NO in RAW264.7 cells. However, the effects of papaya preparation on neuronal cells have not been studied yet. In the present investigation, we studied the protective effects of fermented papaya preparation PS501 (*Carica Celapi*, commercially available from Saido Corporation, Japan) on neuronal cell damage induced by peroxynitrite. Upon exposure to 1 mM of 3-morpholiniosydnonimine-*N*-ethylcarbamide (SIN-1), a peroxynitrite donor, primary cultured cerebellar granule cells underwent time-dependent cell apoptosis, which was characterized morphologically by nuclear fragmentation as observed by fluorescence microscopy. Peroxynitrite-induced neuronal apoptosis was further proved biochemically by DNA nucleosomal fragmentation (formation of DNA ladder) as observed by DNA agarose gel electrophoresis. Apoptotic cells were quantified by flow cytometry. In cells exposed to 1 mM of SIN-1 for 24 h, 40.6 % of total cells underwent apoptosis. Pretreatment with PS501 (1 mg/ml) effectively protected neuronal cells from apoptosis. In cells pretreated with PS501, only 14.4 % cells underwent apoptosis. Peroxynitrite treatment also triggered the decrease in the cellular GSH level (13.3 nmol/mg protein vs. 16.8 nmol/mg protein of normal cells) and the increase in the lipid peroxidation level (8.3 nmol/mg protein vs. 3.2 nmol/mg protein of normal cells). Pretreatment with PS501 also effectively prevented the depletion of GSH and inhibited lipid peroxidation. The efficacy of PS501 on protection from neuronal damage induced by peroxynitrite suggested that PS501 might be used as potential drugs for diseases associated with peroxynitrite.