ABSTRACT 179

Gamma-tocotrienol protects human neuroblastoma SH-SY5Y cells against buthionine sulfoximine-induced cell death.

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Background: Vitamin E analogs are potent antioxidants that modulate aging and aging related cognitive diseases. Besides acting as an antioxidant, vitamin E was also shown to be involved in the apoptosis process. The mechanism and protective effects of gammatocotrienol (γT3) against apoptosis in neuronal cells are yet to be fully elucidated as compared to the widely studied analog, alpha-tocopherol (αT).

Objective: Therefore, we examined the regulatory role of γT3 against buthionine sulfoximine (BSO)-induced apoptosis in undifferentiated human neuroblastoma SH-SY5Y cells.

Methods: The SH-SY5Y cells were divided into six groups of treatment: untreated control, BSO, γT3 + BSO, γT3 only, αT + BSO and αT only. The treatments were assessed by MTS and LDH release assay. Apoptosis was estimated by single-stranded DNA (ssDNA) apoptosis ELISA assay. The generation of reactive oxygen species (ROS) was estimated by confocal microscopy. Gene expressions of p53, Bcl-2, Bax, Bid, ERK1/2, p38 MAPK and PKC-□ were quantified by RT-qPCR to elucidate genes that are involved in γT3-mediated neuroprotection against BSO-induced apoptosis.

Results & Discussion: γT3 effectively protected neuronal cells against BSO-induced apoptosis. γT3 neither reduced nor increased cellular reactive oxygen species (ROS) when added with BSO or treated alone. This suggested that □T3 does not act as a free radical scavenger to protect the cells. However, co-treatment of γT3 and BSO was found to increase p53 gene expression as compared to BSO-treated only cells. Interestingly, when γT3 was added alone, Bcl-2 mRNA expression decreased as compared to the untreated control.

Conclusions: Our results showed that γT3 acts as a strong neuroprotectant against BSO induced apoptosis in undifferentiated SH-SY5Y cells. The molecular mechanism regulated by γT3 is not directly mediated by ROS. The p53 gene might play an important role in γT3-mediated neuroprotection. The regulation of Bcl-2 gene expression by γT3 in neuronal cells suggests the involvement of the vitamin E analog in Bcl-2-mediated cell signaling.