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Neuroprotective effect of phospholipase A2 from Malaysian Naja sumatrana venom against H2O2-induced cell damage and apoptosis

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Abstract
Oxidative stress is one of the factors involved in the pathogenesis of several neurodegenerative diseases. It has been reported that a secretory phospholipase A2 known as A2-EPTX-NSm1a has lower cytotoxicity in neuronal cells compared to its crude Naja sumatrana venom. In this study, A2-EPTX-NSm1a was tested for its neuroprotective activity on human neuroblastoma cells (SH-SY5Y) differentiated into cholinergic neurons against oxidative stress induced by hydrogen peroxide (H2O2). H2O2 treatment alone increased the caspase-3 and caspase-8 activities, whereas pre-treatment with A2-EPTX-NSm1a reduced the activity of these apoptosis-associated proteins. Moreover, A2-EPTX-NSm1a protects the morphology and ultrastructure of differentiated SH-SY5Y cells in the presence of H2O2. Oxidative stress increased the number of small mitochondria. Further evaluation showed the size of mitochondria with a length below 0.25 μm in oxidative stress conditions is higher than the control group, suggesting mitochondria fragmentation. Pre-treatment with A2-EPTX-NSm1a attenuated the number of mitochondria in cells with H2O2 Furthermore, A2-EPTX-NSm1a altered the expression of several neuroprotein biomarkers of GDNF, IL-8, MCP-1, TIMP-1, and TNF-R1 in cells under oxidative stress induced by H2O2. These findings indicate that anti-apoptosis with mitochondria-related protection, anti-inflammatory effect, and promote expression of important markers for cell survival may underlie the neuroprotective effect of A2-EPTX-NSm1a in cholinergic rich human cells under oxidative stress, a vital role in the neuronal disorder. Copyright © 2022 Abdullah, Sainik, Esa, Muhamad Hendri, Ahmad Rusmili, Hodgson, Shaikh and Othman.

Author Keywords
apoptosis; inflammation; mitochondria; neurodegenerative disease; neuroprotection; snake venom phospholipase A2

Index Keywords
caspase 3, caspase 8, glial cell line derived neurotrophic factor, hydrogen peroxide, interleukin 8, monocyte chemotactic protein 1, secretory phospholipase A2, snake venom, tissue inhibitor of metalloproteinase 1, tumor necrosis factor receptor associated factor 1; antiinflammatory activity, apoptosis, Article, cell count, cell damage, cell differentiation, cell survival, cell ultrastructure, cholinergic nerve cell, controlled study, enzyme activity, human, human cell, mitochondrial dynamics, Naja, Naja sumatrana, neuroprotection, nonhuman, oxidative stress, protein expression, SH-SY5Y cell line

Chemicals/CAS
caspase 3, 169592-56-7; caspase 8; hydrogen peroxide, 7722-84-1; interleukin 8, 114308-91-7; snake venom, 55230-69-8; tissue inhibitor of metalloproteinase 1, 140208-24-8

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