

Cinnamophilin 抑制腦血管內皮細胞凋亡之作用機轉探討 Inhibitory Mechanisms of Cinnamophilin in Cerebral Endothelial Cell Apoptosis

中文摘要

本論文主要探討由菲律賓樟樹 (*Cinnamomum philippines*) 中所分離出來的成分 cinnamophilin 抑制氧化態低密度脂蛋白 (oxidized low density lipoprotein; ox-LDL) 誘導小鼠腦血管內皮細胞 (cerebral endothelial cell; CEC) 死亡的機制研究。Cinnamophilin 以濃度相關方式抑制了 ox-LDL 所引發 CEC 的細胞凋亡現象以及 caspase-9 和 caspase-3 的活化。但是 cinnamophilin (10 μ M) 並無法抑制 cytochrome c 或 Smac 由粒線體中釋放到細胞質中，更進一步，cinnamophilin 並不影響 ox-LDL 所引起的粒線體膜電位的減少。此外，cinnamophilin 能抑制 ox-LDL 造成的活性氧分子 (reactive oxygen species; ROS) 增加。GRP78 蛋白的表現代表其內質網壓力增加。Ox-LDL 以時間相關增加內質網壓力。Cinnamophilin 以濃度相關方式明顯抑制 ox-LDL 所引發 GRP78 蛋白質表現量增加。綜合以上，cinnamophilin 抑制 ox-LDL 誘導腦血管內皮細胞凋亡的機制可能是經由抑制 ROS 的增加、內質網壓力、caspase-9 和 caspase-3 的活化。因此 cinnamophilin 可能具有發展成爲治療腦血管疾病的潛力。

英文摘要

In this study, we attempted to evaluate the inhibitory mechanism of cinnamophilin, isolates from *Cinnamomum philippinese*, on oxidized low density lipoprotein (ox-LDL)- induced cerebral endothelial cell (CEC) death. Cinnamophilin inhibited the ox-LDL-induced CEC apoptosis and the activation of caspase-9 and caspase-3 in a concentration-dependent manner. However, cinnamophilin did not affect the release of cytochrome c and second-mitochondria-derived activator of caspase (Smac) from the mitochondria to the cytoplasm. Furthermore, cinnamophilin (10 μ M) did not affect the ox-LDL-induced the loss of mitochondrial membrane potential. In addition, cinnamophilin concentration-dependently inhibited ox-LDL-induced production of reactive oxygen species (ROS). Ox-LDL increased endoplasmic reticulum (ER) stress, reflected by GRP78 expression, in a time-dependent manner. Cinnamophilin markedly inhibited ox-LDL-induced GRP78 expression in a concentration-dependent manner. Taken together, the inhibitory mechanism of cinnamophilin on ox-LDL-induced CEC apoptosis may be, at least in part, through suppression of ROS formation, ER stress, caspase-9, and caspase-3 activation. We conclude that cinnamophilin may have therapeutic potential in cerebrovascular diseases.