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Search for natural compounds that promote CHOP-induced apoptosis

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The transcription factor CHOP, also known as GADD 153, increases expression level and induces apoptosis in response to endoplasmic reticulum stress caused by various factors including genetic mutation, pathogens and active oxygen. In order to search for natural compounds that induce CHOP expression, we screened about 6,000 kinds of methanol extracts from various higher plants and their different parts using a luciferase reporter gene assay with CHOP promoter in Mia PaCA-2 cells. In the first screening, 121 extracts showed induction of 2-fold or more luciferase activity compared to the control. By a second screening on the 121 extracts, 6 extracts showing 3-fold or more luciferase inducing activity were selected. Among them, the extract of *Macleaya cordata* (Willd.) was separated on silica gel column chromatography and then HPLC was done. Two compounds were thereby isolated, then identified as dihydrosanguinarine and 6-methoxydihydrosanguinarine based on NMR and MS spectral data. Both compounds were found to induce CHOP promoter-driven luciferase expression in the reporter gene assay, but did not significantly affect endogenous CHOP protein levels. Dihydrosanguinarine increased the levels of cleaved-PARP and cleaved-caspase-3 known as apoptosis markers. This suggests that dihydrosanguinarine may induce apoptosis not only through the ER stress pathway but also through other pathways. Although sanguinarine was reported to be a major compound of *M. cordata*, it was not isolated in this study. This may have been due to conversion of sanguinarine to 6-methoxysanguinarine during extraction with MeOH.

Biography

Young Sook Yun has completed her PhD from Tokyo University of Pharmacy and Life Sciences and Postdoctoral studies from Korea Institute Biosciences and Biotechnology and National Institute of Health Science in Japan. Recently, her researches have been focused on natural chemistry related to cancer and neurosciences.

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