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Neuroprotective effects of ginseng saponins against L-type Ca^{2+} channel-mediated cell death in rat cortical neurons

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Beneficial effects of ginseng on neuronal cell death associated with ischemia or excitotoxicity have been increasingly reported. In our previous study, we reported that ginseng inhibits NMDA receptor-mediated currents and that ginseng's active ingredient, ginsenoside Rg_3, significantly protects cultured hippocampal neurons against NMDA insults. Therefore, we further examined any possible involvement of L-type Ca^{2+} channels in ginseng-mediated neuroprotective actions because important roles of L-type Ca^{2+} channels in neuronal cell death have been increasingly reported. Exposure to a high concentration of KCl (high-K, 50 mM) produced neuronal cell death, which was blocked by a selective L-type Ca^{2+} channel blocker, nifedipine (10 μM), but not by an N-type blocker, ω-conotoxin MVIIA (10 μM), or a T-type Ca^{2+} channel blocker, mibefradil (1 μM), in cultured cortical neurons. When cultured cells were co-treated with ginseng total saponin (GTS) and high-K, GTS reduced high-K-induced neuronal death in a dose dependent manner with an IC_{50} of 12.5 μg/ml. Using fura-2-based digital imaging techniques, we found that GTS inhibited high-K-mediated acute and long-term $[Ca^{2+}]_i$ changes. These GTS-mediated $[Ca^{2+}]_i$ changes were diminished by nifedipine, but not by ω-conotoxin MVIIA or mibefradil. Furthermore, GTS-mediated effects were also diminished by a saturating concentration of Bay K (10 μM), an L-type Ca^{2+} channel activator. After confirming the protective effect of GTS using a TUNEL assay, we found that ginsenosides Rf and Rg_3 are active components in ginseng-mediated neuroprotection. These results suggest that inhibition of L-type Ca^{2+} channels by ginseng could be one of the mechanisms for ginseng-mediated neuroprotection in cultured rat cortical neurons.

Key words: Ginseng; Ginsenosides; L-type Ca^{2+} channel; Intracellular Ca^{2+}; Bay K; Fura-2/AM; Neuronal cell death; Cortical neurons