

Ginseng Saponins Induce Store-Operated Calcium Entry in *Xenopus* Oocytes

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We investigated the effect of ginsenosides, the active ingredients of *Panax ginseng*, on store-operated Ca^{2+} entry (SOCE) using the two-electrode voltage clamp technique in *Xenopus* oocytes where SOCE is monitored through the Ca^{2+} -activated Cl^- currents. Under hyperpolarizing voltage clamp conditions, treatment of ginsenosides produced a biphasic Ca^{2+} -activated Cl^- current; a rapid transient inward current and a slowly developing secondary sustained inward current. The transient inward current inactivated rapidly, whereas the sustained inward current persisted near 10 min. The effect of ginsenosides on the biphasic current was dose-dependent and reversible. The EC_{50} was 42.8 ± 11.6 and 46.6 ± 7.1 $\mu\text{g/ml}$ for transient and sustained inward current, respectively. Ginsenosides induced only transient inward current in the absence of extracellular Ca^{2+} , whereas ginsenosides induced the biphasic current in the presence of extracellular Ca^{2+} . The magnitudes of sustained currents were dependent on extracellular Ca^{2+} concentration. Ginsenoside-induced sustained but not transient inward current and ginsenoside-induced store-operated Ca^{2+} (SOC) currents (I_{SOC}) were blocked by La^{3+} , Ca^{2+} channel blocker, suggesting that the sustained inward current and I_{SOC} was derived from influx of extracellular Ca^{2+} . Treatment of 2-APB and heparin, which are IP_3 receptor antagonists, inhibited ginsenoside-induced biphasic current. Treatment of PLC inhibitor, U73122 inhibited ginsenoside-induced biphasic current. Intraoocyte injection of ATP- γS but not adenylyl AMP-PCP induced a persistent activation of ginsenoside-induced sustained but not transient current. In rat hippocampal neurons, ginsenosides inhibited both carbachol-stimulated intracellular Ca^{2+} release and intracellular Ca^{2+} depletion-activated SOCE. These results indicate that ginsenosides might act as a differential regulator on intracellular Ca^{2+} level between neurons and *Xenopus* oocytes.

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