Effects of ginsenosides and their metabolites on voltage-dependent Ca^{2+} channel subtypes

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In previous reports we have demonstrated that ginsenosides, active ingredients of *Panax* ginseng, regulate some subsets of voltage-dependent Ca^{2+} channel in neuronal cells and expressed in *Xenopus laevis* oocytes. However, no previous reports have identified the major component(s) regulating the cloned Ca^{2+} channel subtypes such as L-, N-, P/Q-, R- and T-types from ginsenosides or ginsenoside metabolites. Here, we used the two-microelectrode voltage clamp technique and further characterized the effect of ginsenosides and ginsenoside metabolites on Ca^{2+} currents (I_{Ca}) in *Xenopus* oocytes expressing five different Ca^{2+} channel subtypes. Ginseng total saponins (GTS) treatment induced voltage-dependent, dose-dependent and reversible inhibitions in five different Ca^{2+} channel subtypes, specially with more potent inhibition of T-type, an IC_{50} value of 31 ± 2 μM. Among various ginsenosides such as Rb_1, Rc, Re, Rf, Rg_1, Rg_3, Rh_2, ginsenoside Rg_3 also inhibited all five different Ca^{2+} channel subtypes and ginsenoside Rh_2 inhibited more potently L- and R-type Ca^{2+} channels than other types. Compound K (CK), a protopanaxadiol ginsenoside metabolite, strongly inhibited only T-types of Ca^{2+} channel, whereas M4, a protopanaxatriol ginsenoside metabolite, almost had no effect on all Ca^{2+} channel subtypes examined. Ginsenoside Rg_3 treatment shifted the steady-state activation but not inactivation curve to depolarizing direction in N- and P/Q types. These results reveal that GTS, ginsenoside Rg_3, Rh_2 and CK are the main Ca^{2+} channel regulators, with some Ca^{2+} channel selectivity, capable of inhibiting Ca^{2+} channels in *Panax* ginseng.

Keywords: Ginseng; Ginsenosides; L-, N-, P/Q-, R- and T-type Ca^{2+} Channel subtypes; *Xenopus* Oocytes.

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