(구두-4)

The Inhibitory Effects of Korean Red Ginseng Saponins on 5-HT3AReceptor Channel Activity Are Coupled to Anti-Nausea and Anti-Vomiting Action

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Abstract: We performed *in vitro* and *in vivo* studies to know whether the inhibitory effects of ginsenosides on 5-HT3A receptor channel acctivity are coupled to anti-nausea and anti-vomiting action. *In vitro* study, we investigated the effect of compound K (CK) and M4, which are ginsenoside metabolites, on human 5-HT3A receptor channel activity expressed in *Xenopus* oocytes using two-electrode voltage clamp technique. Treatment of CK or M4 themselves had no effect in both oocytes injected with H2O and 5-HT3A receptor cRNA. In oocytes injected with 5-HT3A receptor cRNA, M4 treatment inhibited more potently 5-HT-induced inward peak current (*I*5-HT) than CK with dose-dependent and reversible manner. The half-inhibitory concentrations (IC50) of CK and M4 were 36.9 10.1 and 7.3 2.2 M, respectively. The inhibition of *I*5-HT by M4 was non-competitive and voltage-independent. These results indicate that M4 might regulate 5-HT3A receptors. *In vivo* experiments, first, injection of cisplatin (7.5 mg/kg, i.v.) induced both nausea and vomiting with 1 h latency in the cats (n=7~8). These episodes reached to peak after 2 h and persisted for 4 h. Pre-treatment of GTS (500 mg/kg, p.o.) significantly reduced cisplatin-induced nausea and vomiting by 51 8.4 and 48.8 6.4% during 4 h compared to GTS-untreated group, respectively. Second, we investigated the anti-emetic effect of Korean red ginseng total extract (KRGE) in cisplatin-induced nausea and vomiting using ferret (n= 6~7). Administration of cisplatin (7.5 mg/kg, i.p.) induced both nausea and vomiting with 1 h latency. The episodes on nausea and vomiting reached to peak after 1.5 h and persisted for 3 h. Treatment of KRGE via oral route significantly reduced cisplatin-induced nausea and vomiting with dose-dependent manner. Thus, anti-emetic effect was 12.7 ± 8.6, 31.8 ± 6.9 and 67.6 ± 4.0% at doses of 0.3, 1.0, and 3.0 g/kg of KRGE, respectively. Pretreatment of KRGE via oral route 1 and 2 but not 4 h before cisplatin administration also significantly attenuated cisplatin-induced nausea and vomiting. These results show the possibility that inhibition of 5-HT3A receptor channel activity by ginsenosides might be coupled to *in vivo*anti-emetic activity, and KRGE might be utilized as an anti-emetic agent against chemotherapy (i.e. cisplatin)-caused nausea and vomiting.

Key words: *Panax* ginseng; ginsenoside metabolites; KFGE, 5-HT3Areceptor; cisplatin; emesis