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A functional Role of Carbohydrate Portion of Ginsenoside Rg_3 in Brain Na^+ Channel Regulation

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Recently, we demonstrated that ginsenosides regulate various types of ion channel activity. However, it is not yet precisely determined on the role of sugar moiety attached to ginsenosides. Here, we investigated the role of the carbohydrate component of ginsenoside Rg_3 in regulation of Na+ channels expressed in *Xenopus* oocytes after injection of cRNAs encoding rat brain Nav1.2 α and β1 subunits using two-electrode voltage clamp technique. Treatment of ginsenoside Rg_3 inhibited inward Na^+ peak current (I_{Na}) reversibly. The inhibition of I_{Na} by ginsenoside Rg_3 was a voltage- and dose-dependent manner. The IC_{50} of ginsenoside-Rg_3 on I_{Na} was 32.2 ± 4.5 μM. To confirm the role of the sugar moiety of ginsenoside Rg_3, we prepared a straight chain form of second glucose of ginsenoside Rg_3 and a conjugate of the second glucose of ginsenoside Rg_3 with 3-(4-Hydroxyphenyl) propionic acid hydrazide (HPPH). We tested the effect of these ginsenoside Rg_3 derivatives on I_{Na}. We found that both ginsenoside Rg_3 derivatives had no effect on I_{Na}. Moreover, treatment of the carbohydrate portion of ginsenoside Rg_3, sophorose (β-D-glucopyranosyl (1→2)-β-glucopyranoside), aglycone (protopanaxadiol) itself or the combination of two components of ginsenoside-Rg_3 had no effect on I_{Na}. These results indicate that the carbohydrate portion of ginsenoside Rg_3 might play an important role in the Na^+ channel regulation induced by ginsenoside Rg_3.