

ABSTRACT

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Project Title : The mechanisms of hypoglycemic action of stevioside and aqueous extract of *Stevia rebaudiana* in diabetic rats.

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The present experiment was conducted to study the effect and mechanisms of action of stevioside (SVS) and *Stevia rebaudiana* (*Stevia*) on the plasma glucose level (P_G) in diabetic rats. Male Wistar rats weighting between 150-180 g were used. Six groups of rats were established. The first three groups were normal rats daily fed with distilled water, SVS (0.25 g/KgBW) or *Stevia* (4.66 g/KgBW) at the dose containing of SVS similar to that of rats fed with SVS. The other three groups were diabetic rats treated with the same manner as the normal rats. P_G and urinary glucose excretion (U_G) were determined once a week. After 8 weeks of feeding, serum insulin and plasma glucagon concentrations were evaluated. Diaphragm muscle was also isolated to determine glucose uptake using 2-deoxy-D-[3H]-glucose and [^{14}C]-manitol in the presence or absence of insulin in incubation medium. The results show that SVS significantly raised P_G during the 3-6 weeks ($P < 0.05$) in normal rats. After that, P_G was still high but the level was not significantly different from the normal control rats. There was no significant change of P_G in diabetic rats fed with SVS was apparent. *Stevia* had no effect on P_G in the normal rats whereas it reduced P_G in diabetic rats but the level was not significantly different from the normal diabetic rats. U_G was increased during 2-4 weeks of diabetic rats fed with SVS ($P < 0.05$) whereas it was not changed throughout 8 weeks in diabetic rats fed with *Stevia*. Serum insulin and plasma glucagon level were not significantly altered in normal rats fed with either SVS or *Stevia*. Serum insulin was potentiated in diabetic rats fed with SVS or *Stevia* ($P < 0.05$). *Stevia* normalized plasma glucagon level in diabetic rats ($P < 0.01$). In an absence of insulin in incubation medium, both SVS and *Stevia* had no effect on glucose uptake by isolated diaphragm of normal rats but SVS significantly raised glucose uptake in diabetic rats ($P < 0.01$). During the presence of insulin, glucose uptake by isolated diaphragm was significantly depressed in both normal ($P < 0.01$) and diabetic rats ($P < 0.05$) fed with SVS. *Stevia* feeding had no significant effect on glucose uptake by isolated diaphragm in both normal and diabetic rats. It can be concluded that SVS raised P_G whereas *Stevia* had no significant action on P_G in normal rats. In diabetic rats, SVS had no influence on P_G whereas *Stevia* slightly reduced P_G , indicating that the hypoglycemic effect of *Stevia* in diabetic rats is not due to the action of SVS. A decrease of insulin-induced glucose uptake seems to be an important factor to raise P_G in normal rats fed with SVS. Though SVS potentiated insulin released in diabetic rats fed with SVS, a depression of insulin-induced glucose uptake was also apparent, causing no significant change of P_G . Diabetic rats fed with *Stevia* showed an improvement of insulin release and normalization of the glucagon level without change of muscle response to insulin. However, P_G in diabetic rats fed with *Stevia* was slightly reduced.

Key words : stevioside, *Stevia rebaudiana*, diabetes mellitus, muscle glucose transporter