HYPOGLYCEMIC COMPONENT IN GINSENG RADIX AND ITS INSULIN RELEASE

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Out of the blended therapeutics (Kanpō Hōzai) in traditional medicine expected for diabetic disease, some preparation containing ginseng radix (e.g., Byakko-ka-Ninjintō) were studied on hypoglycemic effect[1,2]. The analysis for combined effect in the diabetic model mice showed that ginseng played an important part, and the partially purified fraction of ginseng (DPG 3–2) was confirmed to be an active principle[3]. The DPG 3–2 fraction was observed to increase dose-dependently in blood insulin level of alloxan diabetic mice[4] and to enhance insulin release from pancreas perfusion system or isolated pancreatic islets[5,6]. The effect of DPG 3–2 on insulin release was observed more markedly in diabetic mice and its effect depended on the glucose concentration added. Glucose is reported to be one of the most important physiologic stimulus for insulin release and in diabetic disease its response to glucose may be impaired. The action of DPG 3–2 fraction, therefore, was studied to be related with glucose action on insulin release.

In isolated collagenase-treated rat islets, DPG 3–2 fraction dose-dependently (0.2–1 mg/ml) stimulated the insulin release in which effect there were two types, i.e., glucose-independent and glucose-potentiating type. These effects were not considered to depend on insulin biosynthesis because it was uninfluenced by protein synthesis inhibitor, cycloheximide. DPG 3–2-induced insulin release required above 1 mM Ca^{++}, and no more increase was observed at above 2.5 mM. The pancreatic islets of KK-CA^Y mice had a greater size and provoked to the basal and glucose-stimulated insulin release more markedly than those of control KK mice. DPG 3–2-induced insulin release was most markedly provoked under the condition of 16.7 mM glucose in islets of KK-CA^Y mice, which fact might coincide with the result of hypoglycemic effect of this fraction. Glucagon release from A cells which may closely interact with B cells in islets was also stimulated by DPG 3–2 fraction. But DPG 3–2-stimulated insulin release does not seem to depend on this glucagon release because the former was not preceded by the latter and there was different glucose dependency between both effects.

Results of experiments studying the facilitating effect of β-adrenergic agents suggest that cAMP system may play an important role in the regulation of insulin release and that glucose-induced insulin release could also been explained by this system mechanism. From this point of view, the effects of DPG 3–2 on total cAMP level (cAMP content of islets plus released cAMP level) were studied. In rat pancreatic islets, DPG 3–2 dose-dependently increased cAMP level under 2.8 mM glucose, and this effect was not inhibited by β-

adrenergic blocker (propranolol). The islet cAMP levels in KK-CA^Y mice were smaller than those in control KK mice in both conditions of with and without 10 mM theophylline treatment. Glucose (16.7 mM) and DPG 3–2 alone raised the cAMP level significantly, but did not in the presence of theophylline. In islets of diabetic KK-CA^Y mice, cAMP level was not increased by DPG 3–2 in the high concentration of glucose even without theophylline. These facts suggest that the site of action of DPG 3–2 may be phosphodiesterase of which activity masked in diabetic mice. A phosphodiesterase prepared from homogenate of rat islets was inhibited about 50% and 70% by DPG 3–2 at does of 5×10^{-4} g/ml and 2 mg/ml, respectively. Glucose in high concentration did not inhibit the activity of phosphodiesterase and uninfluenced the effect of DPG 3–2, indicating that DPG 3–2 directly inhibited phosphodiesterase without glucose. Cyclic AMP accumulation by the inhibition of phosphodiesterase is considered to enhance the cAMP-protein kinase system activated by glucose and also glucose-induced insulin release.

In conclusion, the site of action of DPG 3–2 fraction may be phosphodiesterase of which inhibitory effect seems to reflect the alone effect of DPG 3–2. On the other hand, the glucose-potentiating effect of DPG 3–2 is speculated by the possible mechanisms interacted with glucose through Ca^{++} which mediated the insulin release induced by DPG 3–2 and glucose.

References

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