Inhibitory Effects of Pasuchaca (Geranium dielsiaum) Extract on α-Glucosidase in Mouse

Mariko Karato,1 Kohji Yamaguchi,1 Shin Takei,2 Takao Kino,2 and Kazunaga Yazawa1,†

1Laboratory of Nutraceuticals and Functional Foods Science, Graduate School of Marine Science and Technology, Tokyo University of Marine Science and Technology, 4-5-7 Konan, Minato-ku, Tokyo 108-8477, Japan
2Technical Sourcing International, Inc., 2-3-7 Shintomi, Chuo-ku, Tokyo 104-0041, Japan

Received August 23, 2005; Accepted February 28, 2006; Online Publication, June 23, 2006 [doi:10.1271/bbb.50420]

The methanolic extract of pasuchaca (Geranium dielsiaum) (PsEx) was found to suppress blood glucose elevation after oral administration of sucrose, maltose, and starch, but not after oral administration of glucose, in the mouse. In vitro examination of the inhibitory effect of PsEx on maltase activity revealed that PsEx strongly inhibited mouse small intestine maltase activity. Taken together, these results suggest that the inhibitory effect of PsEx on α-glucosidase activity might contribute to delay in carbohydrate digestion and subsequent lowering of the blood glucose level, thereby leading to prevention and cure of diabetes.

Key words: pasuchaca; inhibitor; α-glucosidase; diabetes

Diabetes is one of the representative lifestyle-related metabolic disorders. Persistent hyperglycemia, the common characteristic of diabetes, can lead to various complications. This is including diabetic retinopathy,1) diabetic nephropathy,2) and diabetic neuropathy.3) Therefore, not only does diabetes harm the quality of life, it poses a threat to human lives as well.

The present study shows the effect of pasuchaca (Geranium dielsiaum) as an α-glucosidase inhibitor.4–7) Pasuchaca is a plant that thrives naturally in the Peruvian Andes, and it has been used as traditional medicine for the treatment of diabetes in South America, but scientific evaluation is still lacking. To clarify its mechanism of action, the inhibitory effect of pasuchaca methanolic extract (PsEx) on postprandial blood glucose elevation was evaluated in vivo. We examined the action of pasuchaca on carbohydrate digestion and glucose absorption, and found that the inhibitory effect of pasuchaca on α-glucosidase activity might contribute to a delay in carbohydrate digestion, which subsequently leads to suppressed blood glucose elevation.

Dried pasuchaca powder was extracted with 10 volumes of methanol for 24 h. After filtration and evaporation of the methanol, the recovered quantity was 12.2%.

Male ddY mice (8 to 10 weeks of age; Japan SLC, Inc.) were used. The room was maintained at 24 ± 1 °C and 50 ± 10% humidity under a 12 h light/dark cycle (lights on from 08:00 to 20:00), with free access to food and water. Animal studies were conducted according to the 1980 guidelines entitled “Notification No. 6 of the Prime Minister’s Office of Japan.”

For the oral carbohydrate tolerance test, the animals were deprived of food overnight and administered starch, maltose, or glucose orally at 1,000 mg/kg, or sucrose at 2,000 mg/kg, with or without PsEx at 1,400 mg/kg, dissolved in 1 ml of distilled water. Blood was sampled from the tail vein at 0, 30, and 60 min after carbohydrate administration to measure blood glucose levels. Blood glucose levels were determined with a Glucose C-II Test Wako Kit (Wako Pure Chemicals, Tokyo), based on the mutarotase-glucose oxidase method.

Figure 1 shows the effect of PsEx on blood glucose levels after oral administration of carbohydrates. Blood glucose levels in the control group (carbohydrates alone) showed a maximum value at 30 min after administration, and the value decreased with time thereafter. By contrast, PsEx suppressed postprandial blood glucose elevation 30 min after starch, maltose, and sucrose administration, but not after glucose administration. If PsEx inhibits glucose absorption in the small intestine, the postprandial blood glucose after glucose administration must be suppressed. In this study, however, we did not obtain such results. After glucose administration, blood glucose increases showed no differences compared with the control. For that reason, we suggest that PsEx has no inhibition on glucose absorption, but probably inhibits carbohydrate-hydrolyzing enzymes that are involved in the decomposition of disaccharide to monosaccharide. Hence, we investigated the inhibitory effect of PsEx on α-glucosidase activity.

In order to investigate the inhibitory effect of PsEx, an in vitro α-glucosidase inhibition test was performed. α-Glucosidase from yeast is used extensively as a screen-
ing material for α-glucosidase inhibitors, but the results do not always agree with those obtained in mammals. Therefore, we used the mouse small intestine homogenate as an α-glucosidase solution because we speculated that it would better reflect the in vivo state. The inhibitory effect was measured using a method slightly modified from Dahlqvist. After fasting for 20 h, the small intestine between the part immediately below the duodenum and the part immediately above the cecum was cut, rinsed with ice-cold saline, and homogenized with 12 ml of maleate buffer (100 mM, pH 6.0). The homogenate was used as the α-glucosidase solution. The assay mixture consisted of 100 mM maleate buffer (pH 6.0), 40 mM maltose (100 mM), and the sample extract (1–250 mg/ml). It was preincubated for 5 min at 37 °C, and the reaction was initiated by adding the crude α-glucosidase solution (50 µl) to it, followed by incubation for 10 min at 37 °C. The glucose released in the reaction mixture was determined with the kit described above.

PsEx inhibited maltase activity in a dose-dependent manner, as shown in Fig. 2. However, the inhibitory effect of PsEx was weaker than that of Morus sp. (kuwa), and as strong as that of Salacia oblonga (sarashia) and Psidium guajava (guava), which are well-known α-glucosidase inhibitors. In the experiment in vivo, the PsEx concentration in the intestines administrated at 1,400 mg/kg was 42 mg/ml, much higher than the in vitro maltase inhibitive activity test. It is expected that this PsEx concentration is sufficient for inhibition of maltase activity in the intestines. Although these results strongly suggest that PsEx inhibited blood glucose elevation by inhibiting α-glucosidase activity, it is able to take part in any other action mechanisms. It is necessary to investigate the action mechanism of PsEx on glucose transportation and insulin secretion.

It is essential for hyperglycemic patients that the intestinal absorption of dietary carbohydrates be suppressed by inhibiting the metabolic processes implicated in carbohydrate digestion and absorption. It is also generally recognized that carbohydrates are digested into oligosaccharides and then into disaccharides by enzymes secreted by the digestive tract, and that disaccharides like maltose, isomaltose, and sucrose are
converted into monosaccharides by α-glucosidase localized in the small intestinal mucosa.\(^4,6\)

α-Glucosidase inhibitors delay the digestion of oligosaccharide and disaccharide to monosaccharide, and reduce the rate of glucose absorption. As a result, they decrease the postprandial rise in blood glucose elevation, thereby stabilizing blood glucose levels. For diabetic patients, it is vital that they maintain their blood glucose levels to prevent hyperglycemia and the complications associated with diabetes. Moreover, there are many other lifestyle-related diseases caused by hyperglycemia.

To conclude, pasuchaca suppresses blood glucose elevation and this can be used as a preventive food for such metabolic disorders as diabetes.

References