Effect of Corosolic Acid on the Hydrolysis of Disaccharides

Satoshi TAKAGI1, Toshihiro MIURA1, Chinami ISHBASHI1, Takanori KAWATA1, Eriko ISHIHARA1, Yeunhwa GU2 and Torao ISHIDA2

1Department of Clinical Nutrition, and 2Hi-tech Research Center, Suzuka University of Medical Science, 1001–1 Kishioka, Suzuka, Mie 510–0293, Japan
(Received October 10, 2007)

Summary The banaba leaf (Lagerstroemia speciosa L.) has been used in traditional Oriental medicine to treat diabetes in the Philippines. It contains corosolic acid (CA), a compound which has a hypoglycemic effect. We examined the effect of CA on blood glucose levels and the hydrolysis of disaccharides in the small intestine in mice. CA (10 mg/kg body weight) improved hyperglycemia after an oral administration of sucrose, and significantly reduced the hydrolysis of sucrose in the small intestine. These results suggest that the hypoglycemic activity of CA is derived, at least in part, due to the inhibition of the hydrolysis of sucrose.

Key Words corosolic acid, hydrolysis, sucrose

The banaba leaf (Lagerstroemia speciosa L.) has been used in traditional Oriental medicine to treat diabetes in the Philippines. It contains corosolic acid (CA) (Fig. 1), a compound which prevents oxidative stress, inflammation, hypertension and so on (1). The hypoglycemic effect of CA has been reported by various experiments (2–5). The decrease in insulin resistance due to the increase in GLUT4 translocation has been reported as a mechanism of action (6). On the other hand, there is no report that reviews brief direct action. Therefore we have hypothesized that CA inhibits the resolution of disaccharides in the small intestine. In the present study, we examined the specific direct action of CA on blood glucose levels and the hydrolysis of disaccharides in the small intestine.

Materials and methods

Materials CA was donated by Use Techno Corporation, Ltd. (Kyoto, Japan). CA was stored at room temperature until use. This agent was suspended in distilled water. Thirty minutes after oral administration of CA or distilled water, a sugar (sucrose, glucose and maltose, 1 g/kg body weight) solution was administered orally. Blood samples were collected before the administration of CA or distilled water and 30, 60 and 120 min after the administration of sugar.

Hydrolysis of disaccharides. After overnight (18 h) fasting, the mice were given CA (10 mg/kg body weight) orally. The control group received an equal volume of distilled water. Thirty minutes after oral administration of CA or distilled water, a sugar (sucrose, glucose and maltose, 1 g/kg body weight) solution was administered orally. Blood samples were collected before the administration of CA or distilled water and 30, 60 and 120 min after the administration of sugar.

Statistical analysis. All the data were expressed as mean±SE. A Student t-test and ANOVA were used for the statistical analysis. The values were considered to be significantly different when the p value was less than 0.05.

Results

Effect of CA on blood glucose levels

The mean blood glucose levels of ddY mice at various time intervals after an oral administration of CA and sucrose are shown in Fig. 2. These levels were compared with the values in the control mice. CA lowered blood
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The mean blood glucose levels of ddY mice at various time intervals after an oral administration of CA and glucose are shown in Fig. 3. CA had no effect on blood glucose levels.

The mean blood glucose levels of ddY mice at various time intervals after an oral administration of CA and maltose are shown in Fig. 4. No differences in blood glucose levels were observed when these values were compared with the values in the control mice.

In the case of lactose, CA also had no effect on blood glucose levels (data not shown). Effect of CA on the hydrolysis of disaccharides

Hydrolysis of disaccharides (sucrase, maltase and lactase) is shown in Fig. 5. These values were compared with those found when distilled water alone was administered (control group). CA (10 mg/kg) significantly inhibited the hydrolysis of sucrose by 57.4% (p<0.05). However, it exhibited no effect on the hydrolysis of maltose or lactose (sucrose, control 7.4±1.0 vs CA 4.3±0.56 (μmol/mg/h); maltose, control 29.4±3.6 vs CA 32.1±5.6 (μmol/mg/h); lactose, control 1.8±0.45 vs CA 1.7±0.27 (μmol/mg/h)).
Discussion

Increased glucose uptake in the small intestine has been known as one of the major pathogenic factors of type 2 diabetes mellitus, together with the insulin resistance in peripheral tissues and the impairment of glucose-induced insulin secretion from pancreatic beta cells. The extract from the banaba leaf contains polyphenol compounds. It has been reported that polyphenol shows glucose-lowering effects by inhibition of carbohydrate absorption (9), and decreases the uptake of glucose in the small intestine (10). However, because the structure of CA is different from polyphenol, its mechanism acts differently than that of polyphenol. So we studied the influence of CA on the hydrolysis of disaccharides in small intestine.

CA inhibited the hydrolysis of sucrose significantly. CA was effective for only sucrose; it was ineffective for maltose and lactose in the oral sugar tolerance test. Therefore it may be that CA acts selectively for the hydrolysis of sucrose.

Generally disaccharides are hydrolysed into monosaccharide in the small intestine by disaccharases, and absorbed after that. In the oral sucrose tolerance test, a significant difference was present 60 min after administration, though CA was ineffective for the glucose, which is a monosaccharide, hydrolysed from sucrose. Therefore we suggest that CA reaches the small intestine mucosmembrane 30 min after oral administration and then shows a direct action to inhibit the hydrolysis of sucrose in the small intestine. This may be like the inhibitor of the hydrolysis of sucrose, in parallel with the mechanism, considering that hypoglycemic activity of CA was shown after the metabolic process (6).

Alpha-glucosidase inhibitors restraining the action to hydrolyse disaccharides, such as acarbose or voglibose, are widely used for treatment of many type 2 diabetic patients in a clinical setting. Therefore further clinical studies of CA will be needed to use it the same as them, though it is sucrose limited. In this study, we have shown for the first time the brief direct action of CA in the small intestine.

REFERENCES