J Nutr Sci Vitaminol, **54**, 511–514, 2008

Note

Acute D-Psicose Administration Decreases the Glycemic Responses to an Oral Maltodextrin Tolerance Test in Normal Adults

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(Received June 5, 2008)

Summary An examination was conducted to verify D-psicose suppressed the elevation of blood glucose and insulin concentration in a dose-dependent manner under the concurrent administration of maltodextrin and D-psicose to healthy humans. Twenty subjects aged 20–39 y, 11 males and 9 females were recruited. A load test of oral maltodextrin was conducted as a randomized single blind study. The subjects took one of five test beverages (7.5 g D-psicose alone, 75 g maltodextrin alone, 75 g maltodextrin +2.5, 5 or 7.5 g D-psicose). Blood was collected before an intake and at 30, 60, 90 and 120 min after an intake. Intervals of administration were at least 1 wk. The load test with 75 g maltodextrin showed significant suppressions of the elevation of blood glucose and insulin concentration under the doses of 5 g or more D-psicose with dose dependency. An independent administration of 7.5 g D-psicose had no influence on blood glucose or insulin concentration. D-Psicose is considered efficacious in the suppression of the elevation of blood glucose concentration after eating in humans.

Key Words D-psicose, insulin, sweetening agent, blood glucose, humans

The method of mass-producing D-psicose (D-ribo-2-hexulose; CAS registration number: 551–68–8; molecular formula: $C_6H_{12}O_6$; molecular weight: 180.156), which is a C-3 epimer of D-fructose, has recently been developed using D-tagatose 3-epimerase (*1*). This has enabled investigations of D-psicose to be conducted into various fields. With respect to safety from a clinical study, maximum non-effective levels of D-psicose in causing diarrhea in human subjects were estimated as 0.55 g per kg body weight (*2*). Looking at uses in food, D-psicose, corresponding to about 70% of the sweet taste of sucrose, was formed from fructose during cooking and was included in fruit juice, Worcestershire sauce and so on (*3*, *4*).

One of the effects D-psicose indicated is the suppression of the elevation of plasma glucose after feeding in rats (5), which fact is of assistance in reducing the risk of lifestyle-related diseases such as diabetes. In this study, we investigated the effect of D-psicose on postprandial plasma glucose concentration in healthy adults and confirmed the effective doses of an intake.

Materials and Methods

Subjects and study design. Table 1 summarizes the backgrounds of 20 healthy Japanese male and female volunteers, who were recruited from the employees of Matsutani Chemical Industry Co., Ltd. and the students of the Faculty of Agriculture, Kagawa University. The inclusion criteria were as follows: Volunteers were recruited if he or she was a healthy male or female adult showing a fasting plasma glucose concentration of 110 mg/100 mL or less as defined in the diabetes diagnosis standard prescribed by the Japan Diabetes Society. Volunteers were excluded if he or she was being treated for diabetes, had any notable systemic disease that was problematic in the performance of the study, had a hepatic function disorder or a renal function disorder or was judged as inappropriate by a physician.

A load test with oral maltodextrin was conducted under a randomized single blind study design. The experimental methods used in the current study have been referred to in a previous report (*6*). After over 12 h fasting, blood was first collected in the early morning. Soon after the first blood collection, subjects took D-psicose of differing doses including 75 g maltodextrin (300 mL) within 1 min. Blood (180 μL) was collected at 30, 60, 90 and 120 min after an intake. We set four doses of D-psicose (0, 2.5, 5 and 7.5 g). Administration was conducted at intervals of at least 1 wk. The intake order of the four beverages was randomly determined with respect to each subject. Life conditions for the subjects in the experimental period are indicated in Fig. 1.

As another experiment for examining the effect of D-psicose administration alone on plasma glucose and insulin concentration, a beverage (100 mL) containing 7.5 g D-psicose without containing maltodextrin was

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Table 1. Characteristics of the subjects in this clinical trial.

	Male (n=11)	Female (n=9)	Total (n=20)
Age (y)	29.8±6.9	26.1±4.8	28.2±6.2
Weight (kg)	64.3±5.3	50.1±3.7	57.9±8.6
BMI	21.5±1.7	19.9±1.6	20.7±1.8
Fasting plasma glucose (mg/100 mL)	92.3±8.6	91.7±6.2	92.1±7.4
Plasma glucose at 2 h after intake of carbohydrate (mg/100 mL)	104.3±24.8	119.0±15.3	110.9±21.9
Basal insulin (μU/mL)	3.2±1.7	3.1±1.5	3.1±1.6
HOMA-R	0.7±0.4	0.7±0.3	0.7±0.3

Values are expressed as means±SD. Blood for the measurement of fasting plasma glucose and basal insulin concentration was collected in the early morning after over 12 h fasting. Blood for the measurement of plasma glucose concentration at 2 h after an intake of carbohydrate was collected at 2 h after oral administration of 75 g maltodextrin. HOMA-R was calculated by the following equation: (fasting plasma glucose concentration×fasting plasma insulin concentration) /405.

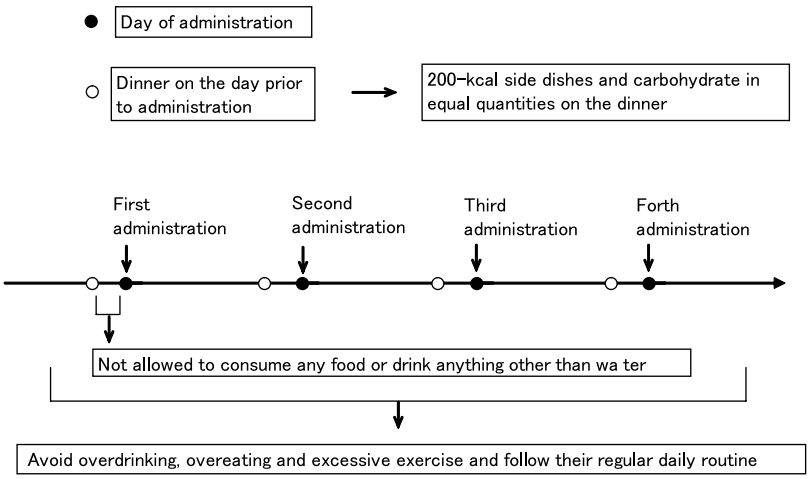

Fig. 1. Life conditions for the subjects in the experimental period.

independently administered to eight subjects.

Study beverage. D-Psicose (purity of over 98%) was provided by Rare Sugar Research Center, Kagawa University. The used maltodextrin manufactured by Matsutani Chemical Industry Co., Ltd., was composed of 2.5% D-glucose, 7.0% maltose and the rest dextrin. This maltodextrin has a sweet taste corresponding to about 16% of sucrose. Each beverage included small amounts of citric acid, carbonate and flavor to make it palatable for the subjects, and to mask differences in the sweetness of the four beverages. Intake intervals, masking effects of maltodextrin and these additives played a role in the blinding of this experiment.

Blood collection and measurements of plasma glucose and insulin concentration. Blood was collected in heparinized hematocrit tubes after a finger was pricked with a puncture device used in the testing of diabetes. The collected blood was centrifuged with a centrifuge (1,200 rpm) in a hematocrit tube for 5 min. The plasma was extracted and refrigerated or frozen until measurements. The plasma glucose concentration was determined in the glucose oxidase technique (Glucose C II-Test Wako; Wako Pure Chemical Industries, Ltd., Osaka, Japan). Insulin concentration was determined using the ELISA method (Human Insulin ELISA Kit EZHI-14K; LINCO Research, Missouri, United States).

Ethical committee. Volunteers were fully informed of the objective of the study, the test methods, expected adverse reactions and other related matters. Before the study started, written consent was obtained from the subjects. The study protocol and the implementation complied with the spirit of the Declaration of Helsinki in 1983 under the approval of the ethical committee of Matsutani Chemical Industry Co., Ltd. (Approval number: 060707), under the direction of which committee all operations of this trial was carried out.

Statistical analysis. Plasma glucose and insulin concentration were statistically analyzed. For these significant tests, male and female subject data were combined. The values for analysis were determined before the intake point as well as at the 30, 60, 90 and 120 min point after intakes for each dose and at the AUC (area under the curve), which was calculated by the trapezoidal method, for each dose. All measurements were expressed as average±standard deviation. To examine significant differences, repeated measures of ANOVA and Dunnett's multiple comparison tests as a post hoc analysis were employed with a level of significance of 5% or less. For software for statistical processing, we used SPSS 13.0 J (SPSS Inc.).

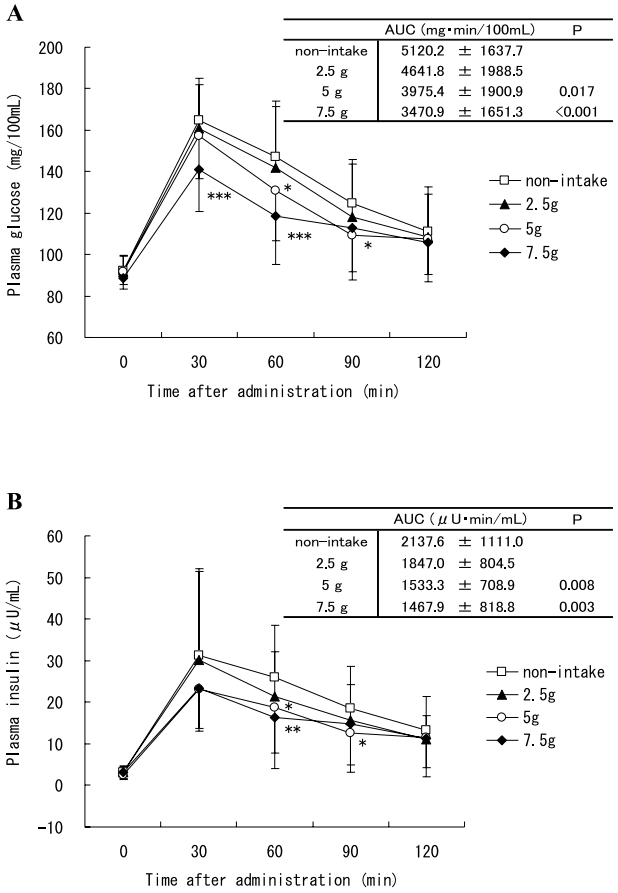

Fig. 2. Decreases of plasma glucose (a) and insulin (b) concentration after taking 5 g or more D-psicose in healthy adults during 2 h after 75 g oral maltodextrin tolerance tests. Values are expressed as average±SD. Significantly different from a non-intake of D-psicose at $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$ as determined by Dunnett's multiple comparison test for independent samples. □, non-intake of D-psicose ($n=20$); ▲, 2.5 g D-psicose intake ($n=20$); ○, 5 g D-psicose intake ($n=20$); ◆, 7.5 g D-psicose intake ($n=20$).

Results and Discussion

There were no dropouts among the 20 subjects participating in this trial.

The time course of plasma glucose and insulin concentration after an exclusive intake of D-psicose was not affected except the values declined within the range of physiological deviation. To ease the burden for the subjects in this experiment, the used beverage was prepared to only 100 mL, which was sufficient to solve 7.5 g D-psicose, and only eight subjects participated, which subjects were also sufficient to investigate the fluctuating trends of glucose and insulin concentration.

The effect of D-psicose intakes on plasma glucose concentration after maltodextrin loading is presented in Fig. 2a. The results of repeated measures of ANOVA among intake doses indicated significant differences at 30 min ($p<0.001$), 60 min ($p<0.001$), 90 min ($p=0.035$) and AUC ($p<0.001$). Increases of plasma glucose concentration after maltodextrin loading were significantly suppressed with 5 g or more D-psicose intake (Dunnett's multiple comparison tests). The lower values almost recovered to a concentration similar to the value in a non-intake of D-psicose at 120 min.

The effect of D-psicose intakes on plasma insulin concentration after maltodextrin loading is presented in Fig. 2b. The results of repeated measures of ANOVA among intake doses indicated significant differences at 60 min ($p=0.007$) and AUC ($p=0.004$). Increases of insulin concentration after maltodextrin loading were also significantly suppressed with 5 g or more D-psicose intake.

An animal study on the suppression of increase in plasma glucose concentration with D-psicose found significant drops in plasma glucose concentration when maltose and sucrose were used as substrates, but no significant drops when glucose and soluble starch were used as substrates (*5*). Another animal study proposed that D-psicose inhibited the hydrolysis of maltose with α-glucosidase, which was prepared from the membrane of rat small intestines (*7*). It follows from these facts that one of the suppressive mechanisms of D-psicose on the elevation of plasma glucose concentration of rats after carbohydrate administration is attributable to the inhibition of α-glucosidase. The suppression of the elevation of plasma glucose concentration in humans with D-psicose was accordingly expected when two or more types of sugars were used as a carbohydrate source. Moreover, maltodextrin, which is a starch hydrolysate, is used as the carbohydrate source in the oral glucose tolerance test for the diagnosis of diabetes in Japan. Not glucose, but maltodextrin, was hence used as a carbohydrate source in this study.

As another hypothetical mechanism for the suppression of increase in plasma glucose concentration, absorbed D-psicose in small intestine, in which D-psicose was estimated to absorb at about 25% (*8*, *9*), has the effect of promoting the uptake of glucose in the liver. It has been reported that fructose activated glucokinase and reduced plasma glucose concentration after being phosphorylated into fructose 1-phosphate by fructokinase in the liver (*10*, *11*). A similar mechanism of reducing plasma glucose concentration is also presumed for D-tagatose, an isometric form of D-psicose (*12*). The same biochemical path as fructose and tagatose could accordingly enhance glucose tolerance.

The doses of D-psicose at 5 g (around 1/15 of a carbohydrate intake) would be the minimum effective doses for suppressing the elevation of plasma glucose and insulin concentration for 75 g of maltodextrin. This suggests that about 5 g D-psicose, a practical amount for an intake, is suitable for suppressing the elevation of plasma glucose concentration from eating one meal such as a slice of toast (about 50 g carbohydrate).

As this study confirmed the improving effect of glucose tolerance, D-psicose is expected to serve as a food material with a low glycemic index. In the light of applications of D-psicose for food intended to prevent lifestyle-related diseases, this report is insufficient to elucidate D-psicose influences on glucose tolerance under a continued intake, eaten with many food materials and other hypoglycemic food materials such as L-arabinose,

which has substrate specificity for sucrose (*13*). Further research is thus required for the elucidation of these points.

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