Effects of Fructose and Xylitol on the Urinary Excretion of Adenosine, Uridine, and Purine Bases

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To examine whether fructose and xylitol increase the plasma concentration and urinary excretion of adenosine, as well as uridine and purine bases (hypoxanthine, xanthine, and uric acid), we intravenously administered xylitol and, 2 weeks later, fructose, to five healthy subjects. Analyses of blood and urine samples obtained during these infusion studies demonstrated that fructose increased the urinary excretion of adenosine and uridine 11.9- and 105.5-fold, respectively, and caused only a small increase in the plasma concentrations of uridine and purine bases. It was further demonstrated that xylitol increased the urinary excretion of uridine 58.4-fold, with a marked increase in the plasma concentrations of purine bases and uridine but without an increase in the urinary excretion of adenosine. However, neither infusion increased the plasma concentration of adenosine. These results suggest that in addition to many organs, including the liver, fructose is significantly metabolized by an abrupt adenosine triphosphate (ATP) consumption in the kidney, leading to an increase in the urinary excretion of adenosine and uridine. They also suggest that xylitol is not significantly metabolized in the kidney.

XYLITOL AND FRUCTOSE are used as a supplemental energy source and are administered intravenously, especially in patients with diabetes mellitus. When these substances are administered, they transiently and rapidly consume adenosine triphosphate (ATP) via their respective metabolism in the body.[1-6] Rapid ATP consumption enhances purine degradation. Namely, ATP is dephosphorylated via adenosine diphosphate to adenosine monophosphate (AMP), which is deaminated to inosine monophosphate (IMP) by AMP deaminase. IMP is then converted to inosine by 5′-nucleotidase, inosine to hypoxanthine by purine nucleoside phosphorylase, and hypoxanthine to uric acid (the final product in humans) via xanthine by xanthine oxidase. As a result, purine bases (uric acid, hypoxanthine, and xanthine) are excessively produced, resulting in an increase in the plasma concentration and urinary excretion of purine bases. In addition, ATP consumption induces the degradation of pyrimidine,[4,5,7] leading to an increased plasma concentration and urinary excretion of uridine. Further, since AMP may be dephosphorylated to adenosine by AMP-specific 5′-nucleotidase, an increase in adenosine production may be concomitant with adenine nucleotide degradation.

There is no known previous study in which xylitol and fructose are reported to increase the plasma concentration and urinary excretion of adenosine, although ischemia-induced adenine nucleotide degradation has been found to increase the tissue concentration of adenosine in the heart.[8] Since adenosine may play a physiological role in many tissues, including the kidney,[8-14] it is important to determine whether xylitol and fructose enhance the production of adenosine. Therefore, we conducted the present study to determine whether these substances increase the plasma concentration and urinary excretion of adenosine concomitantly with purine and pyrimidine degradation.

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SUBJECTS AND METHODS

Subjects and Protocol

Five men aged 32 to 50 years (body weight, 49 to 73 kg) participated in the study after provision of informed consent. Each subject had normal laboratory data including liver function, renal function, and blood glucose (Table 1). After an overnight fast except for water, the urine was completely voided, followed by collection of the first urine sample 1 hour later. The first blood sample was drawn with a heparinized syringe 30 minutes before the first urine collection. After the first urine sample, xylitol (0.7 g/kg weight) was infused over a 1-hour period as a 10% solution. The second urine sample was collected at the end of the infusion, and the second and third blood samples were drawn 30 minutes before and at the end of the infusion, respectively. Two weeks later, a fructose study was performed with intravenous administration of fructose (0.7 g/kg weight) as a 10% solution using the same protocol except with infusion of fructose instead of xylitol. In the present study, xylitol and fructose were infused at a higher rate than is recommended for intravenous administration in Japan (<0.3 g/kg weight/h for xylitol and <0.5 g/kg weight/h for fructose) to determine whether these substances increase the plasma concentration and urinary excretion of adenosine.

Blood and Urine Analyses

Hypoxanthine, xanthine, and uridine concentrations in plasma and urine and adenosine in plasma were determined using high-performance liquid chromatography (HPLC) as described previously.[15] In brief, the column was a Wakosil 5C-18 (4.6 × 250 mm; Wako Pure Chemicals, Osaka, Japan). The flow rate was 1 mL/min, and the mobile phase was 0.02 mol/L KH_2PO_4 (pH 2.2). To measure the plasma concentration of hypoxanthine, xanthine, and uridine, the plasma was separated after blood sampling with a heparinized syringe as described previously.[15] However, to prevent a decrease in the plasma concentration of adenosine, we added 620 μL physiological saline containing 2′-deoxycoformycin (16 μg/mL final concentration), EDTA (16 mmol/L final concentration), and dipyridamole (0.48 μmol/L final concentration) to 1 mL blood immediately after blood sampling as described previously.[16] Then, the plasma was immediately separated after centrifugation at 4°C and used to measure the concentration of adenosine. The urinary concentration of adenosine was determined as follows. The chromatograph consisted of two CCPM pumps, an SC-8020 system controller, two spectrophotometric detectors (UV-8010 and UV-8020), and a VC-8020 column-switching valve (all from Tosoh, Tokyo, Japan). The chromatographic columns were a Wakosil 5C18-200 (4.6 × 250 mm; Wako Pure Chemicals, Osaka, Japan) as the first column and a Tosoh TSK Gel (ODS-120A, 4.6 × 250 mm) as the second column. In both columns, the mobile phase was 0.02 mol/L KH_2PO_4 (pH 2.2), the

Table 1. Laboratory Data of the Subjects (N = 5)

AST (IU/L)	ALT (IU/L)	Albumin (g/L)	Globulin (g/L)	RBC ($\times 10^4/\mu L$)	WBC ($\times 10^2/\mu L$)	Platelets ($\times 10^4/\mu L$)	Creatinine (μmol/L)	BUN (mmol/L)	FBG (mmol/L)	HbA_{1c} (%)
19 ± 3	24 ± 4	44 ± 1	28 ± 3	488 ± 13	67 ± 5	23.0 ± 3.0	72 ± 5	5.0 ± 0.5	5.47 ± 0.26	5.0 ± 0.2

Abbreviations: RBC, red blood cells; WBC, white blood cells; FBG, fasting blood glucose; AST, aspartate transaminase; ALT, alanine transaminase; BUN, blood urea nitrogen; HbA_{1c}, hemoglobin A_{1c}.

flow rate was 1 mL/min, and the detection wavelength was 254 nm. Twenty microliters of the urine sample was injected into the first column. At the fraction time at which adenosine was eluted via the first column, the two columns were connected and the eluate from the second column was monitored at 254 nm. The urinary concentration of uridine was also measured by HPLC with column-switching. The HPLC method was the same as already described, except that the pH of the mobile phase was 4.7 instead of 2.2. The concentration of uric acid and creatinine in plasma and urine was measured by the uricase method using a Wako Uric Acid B Test kit and by the enzymatic method using a Diacolor Liquid CRE kit (Toyobo, Osaka, Japan), respectively. The concentration of fructose and xylitol in plasma was determined as described previously.[3,5] Lactic acid and pyruvic acid levels in blood and inorganic phosphate levels in plasma were also determined as described previously.[3,5] Plasma renin activity and the plasma concentration of aldosterone and angiotensin were measured by Shionogi Biomedical Laboratories (Osaka, Japan). The other parameters were measured in our hospital laboratory.

Chemicals

Adenosine was obtained from Boehringer (Mannheim, Germany). Fructose and xylitol were purchased from Otsuka Pharmaceuticals (Tokyo, Japan) and Fuso Pharmaceuticals (Osaka, Japan), respectively. Other chemicals were purchased from Wako.

Statistical Analysis

The data are presented as the mean ± SD. The significance of differences between variables was analyzed by a two-tailed paired *t* test.

RESULTS

Effect of Fructose and Xylitol on the Plasma Concentration of Purine Bases, Uridine, and Adenosine

Fructose infusion increased the plasma concentration of hypoxanthine, xanthine, uric acid, and uridine 1.39-, 1.28-, 1.03-, and 1.28-fold, respectively, 30 minutes after starting the infusion and 1.59-, 1.50-, 1.03-, and 1.34-fold, respectively, 1 hour after beginning the infusion. Xylitol infusion also increased the plasma concentration of hypoxanthine, xanthine, uric acid, and uridine 10.89-, 6.77-, 1.29-, and 3.15-fold, respectively, after starting the infusion and xanthine, uric acid, and uridine 5.62-, 1.35-, and 4.46-fold, respectively, 1 hour after beginning the infusion. However, neither fructose nor xylitol infusion increased the plasma concentration of adenosine. The increases in the plasma concentration of purine bases and uridine were greater for xylitol infusion versus fructose infusion (Tables 2 and 3).

Effect of Fructose and Xylitol on the Urinary Excretion of Purine Bases, Uridine, and Adenosine

Fructose infusion did not increase the urinary excretion of hypoxanthine, xanthine, or uric acid, but it did increase the urinary excretion of uridine and adenosine 105.5- and 11.93-fold, respectively. In contrast, xylitol infusion increased the urinary excretion of hypoxanthine, xanthine, uric acid, and uridine 13.55-, 5.18-, 1.46-, and 58.4-fold, respectively, but it did not affect the urinary excretion of adenosine (Tables 4 and 5).

Plasma Concentration of Fructose and Xylitol

Fructose infusion increased the plasma concentration of fructose from an undetectable level at 30 minutes before beginning the infusion to 0.53 ± 0.08 mg/mL at 30 minutes after and then to 0.54 ± 0.12 mg/mL at 1 hour after beginning the infusion. Xylitol infusion also increased the plasma concentration of xylitol from an undetectable level at 30 minutes before beginning the infusion to 0.99 ± 0.18 mg/mL at 30 minutes after and then to 1.10 ± 0.18 mg/mL at 1 hour after beginning the infusion (Table 6).

Blood Concentration of Lactic Acid and Pyruvic Acid

The blood concentration of lactic acid increased 2.71-fold at 30 minutes and then 2.62-fold at 1 hour after beginning the fructose infusion, and pyruvic acid also increased 2.21-fold at 30 minutes and then 2.21-fold at 1 hour after beginning the infusion. On the other hand, while the blood concentration of lactic acid increased 1.44-fold at 30 minutes and then 1.72-fold at 1 hour after beginning the xylitol infusion, pyruvic acid decreased 45% at 30 minutes and then 48% at 1 hour after beginning the infusion (Table 6).

Effect of Fructose and Xylitol on the Plasma Concentration and Urinary Excretion of Inorganic Phosphate, Sodium, Potassium, and Chloride

The plasma concentration of inorganic phosphate decreased 7% at 30 minutes and then 10% at 1 hour after beginning the fructose infusion, but the 1-hour urinary excretion of inorganic phosphate did not decrease during the infusion, whereas the

Table 2. Effect of Fructose on the Plasma Concentration of Purine Bases, Uridine, and Adenosine (N = 5)

Parameter	Period 1	Period 2	Period 3
Hypoxanthine (μmol/L)	1.36 ± 0.40	1.90 ± 1.14*	2.12 ± 1.20
Xanthine (μmol/L)	0.80 ± 0.40	1.02 ± 0.61*	1.20 ± 0.62*
Uric acid (μmol/L)	351 ± 41	363 ± 27†	363 ± 33†
Uridine (μmol/L)	4.14 ± 0.46	5.30 ± 1.10†	5.56 ± 1.02†
Adenosine (nmol/L)	68.2 ± 19.6	69.0 ± 17 3	66.6 ± 18.5

NOTE. Values are the mean ± SD. *P* values refer to the difference *v* control. Periods: 1, 30 minutes before beginning fructose infusion; 2, 30 minutes after beginning fructose infusion; 3, 1 hour after beginning fructose infusion.

*$P < .05$.

†$P < .01$.

Table 3. Effect of Xylitol on the Plasma Concentration of Purine Bases, Uridine, and Adenosine (N = 5)

Parameter	Period 1	Period 2	Period 3
Hypoxanthine (μmol/L)	1.20 ± 0.60	13.04 ± 5.94*	8.34 ± 6.46
Xanthine (μmol/L)	0.78 ± 0.19	5.28 ± 2.40*	4.38 ± 2.24*
Uric acid (μmol/L)	345 ± 29	446 ± 42†	464 ± 43†
Uridine (μmol/L)	4.02 ± 0.50	12.67 ± 3.90†	17.93 ± 5.32†
Adenosine (nmol/L)	59.0 ± 20.0	63.4 ± 14.6	59.4 ± 17.8

NOTE. Values are the mean ± SD. *P* values refer to the difference *v* control. Periods: 1, 30 minutes before beginning xylitol infusion; 2, 30 minutes after beginning xylitol infusion; 3, 1 hour after beginning xylitol infusion.

*$P < .05$.

†$P < .01$.

plasma concentration of inorganic phosphate decreased 22% at 30 minutes and then 34% at 1 hour after beginning the xylitol infusion. The 1-hour urinary excretion of inorganic phosphate also decreased 43% after beginning the infusion. The plasma concentration and urinary excretion of sodium, potassium, and chloride did not change significantly during fructose or xylitol infusion (Tables 7 and 8).

Effect of Fructose on Creatinine Clearance and Plasma Renin, Angiotensin, and Aldosterone

Fructose infusion did not affect plasma aldosterone, renin, or angiotensin I or II or creatinine clearance (Table 9).

DISCUSSION

The present study demonstrates that fructose increased the concentration of purine bases (hypoxanthine, xanthine, and uric acid) in plasma and lactic acid and pyruvic acid in blood, but decreased the plasma concentration and urinary excretion of inorganic phosphate (Table 2). However, it did not increase the urinary excretion of purine bases or decrease the urinary excretion of inorganic phosphate significantly (Table 4). These results show that fructose was metabolized using ATP as a phosphate donor, leading to enhanced purine degradation, but it was also shown that the enhanced purine degradation was not sufficient to increase the urinary excretion of oxypurines, since lactic acid in blood does not inhibit the urinary excretion of oxypurines differently from uric acid.[17] On the other hand, xylitol increased the urinary excretion and plasma concentration of purine bases (Tables 3 and 5) and the blood concentration of

Table 4. Effect of Fructose on the Urinary Excretion of Purine Bases, Uridine, and Adenosine (N = 5)

Parameter	1-Hour Urinary Excretion (μmol/h) A	B
Hypoxanthine	6.48 ± 2.99	22.80 ± 13.01
Xanthine	3.91 ± 1.55	6.94 ± 2.75
Uric acid	174 ± 54	161 ± 36
Uridine	0.12 ± 0.02	12.66 ± 8.2*
Adenosine	0.14 ± 0.06	1.67 ± 0.84*

NOTE. Values are the mean ± SD. *P* values refer to the difference *v* control. Periods: A, before beginning fructose infusion; B, after beginning fructose infusion.

*$P < .01$.

Table 5. Effect of Xylitol on the Urinary Excretion of Purine Bases, Uridine, and Adenosine (N = 5)

Parameter	1-Hour Urinary Excretion (μmol/h) A	B
Hypoxanthine	5.18 ± 1.53	70.19 ± 33.19*
Xanthine	3.60 ± 1.32	18.63 ± 7.73†
Uric acid	189 ± 76	276 ± 104*
Uridine	0.12 ± 0.02	7.01 ± 4.62†
Adenosine	0.14 ± 0.09	0.12 ± 0.07

NOTE. Values are the mean ± SD. *P* values refer to the difference *v* control. Periods: A, before beginning xylitol infusion; B, after beginning xylitol infusion.

*$P < .05$.

†$P < .01$.

lactic acid, while it decreased the concentration of inorganic phosphate in plasma and pyruvic acid in blood. These results also show that xylitol was converted to xylulose together with an abrupt reduction of NAD to NADH in cytosol, as shown by the increase in the ratio of lactic acid to pyruvic acid in blood, and also that xylulose was then phosphorylated using ATP as a phosphate donor, leading to the enhanced purine degradation. Further, it was demonstrated that the enhanced purine degradation was sufficient to increase the urinary excretion of uric acid, since the urinary excretion and plasma concentration of uric acid increased despite the inhibition of xanthine dehydrogenase activity via an increase in the cytosol concentration of NADH.[2,18] Although fructose and xylitol enhance purine and pyrimidine degradation in many organs, including the liver, the plasma concentration of purine bases and uridine were increased less by fructose versus xylitol, indicating that fructose-induced purine and pyrimidine degradation is of lesser magnitude than xylitol-induced degradation. Although enhanced purine degradation may have increased the concentration of adenosine in plasma during both infusions, especially with xylitol, the plasma concentration of adenosine did not increase during either infusion. A previous study[19] demonstrated a higher activity of AMP deaminase in comparison to AMP-specific 5′-nucleotidase, and that a decrease in the concentration of ATP in liver cells

Table 6. Concentration of Fructose and Xylitol in Plasma and Lactic Acid and Pyruvic Acid in Blood (N = 5)

Parameter	Period 1	Period 2	Period 3
Fructose infusion			
Fructose (mg/mL)	ND	0.53 ± 0.08†	0.54 ± 0.12†
Lactic acid (mmol/L)	0.85 ± 0.35	2.30 ± 0.69†	2.23 ± 0.56†
Pyruvic acid (mmol/L)	0.063 ± 0.019	0.139 ± 0.031†	0.139 ± 0.035†
Xylitol infusion			
Xylitol (mg/mL)	ND	0.99 ± 0.18†	1.10 ± 0.18†
Lactic acid (mmol/L)	0.72 ± 0.24	1.04 ± 0.27†	1.24 ± 0.12†
Pyruvic acid (mmol/L)	0.067 ± 0.020	0.037 ± 0.005*	0 035 ± 0.008*

NOTE. Values are the mean ± SD. *P* values refer to the difference *v* control. Periods: 1, 30 minutes before beginning fructose or xylitol; 2, 30 minutes after beginning fructose or xylitol; 3, 1 hour after beginning fructose or xylitol.

Abbreviation: ND, below the detection limit (fructose 0.05 mg/mL and xylitol 0.02 mg/mL).

*$P < .05$.

†$P < .01$.

Table 7. Plasma Concentration of Na, Cl, K, and Inorganic Phosphate (N = 5)

Parameter	Period 1	Period 2	Period 3
Fructose infusion			
Na (mEq/L)	142 ± 2	141 ± 2	141 ± 2
Cl (mEq/L)	104 ± 1	104 ± 1	104 ± 2
K (mEq/L)	3.9 ± 0.3	3.9 ± 0.3	4.0 ± 0.4
Inorganic phosphate (mmol/L)	1.10 ± 0.05	1.02 ± 0.08*	0.99 ± 0.07*
Xylitol infusion			
Na (mEq/L)	142 ± 1	141 ± 2	143 ± 2
Cl (mEq/L)	103 ± 1	103 ± 1	104 ± 2
K (mEq/L)	4.1 ± 0.1	4.0 ± 0.2	4.1 ± 0.2
Inorganic phosphate (mmol/L)	1.09 ± 0.07	0.85 ± 0.08*	0.72 ± 0.07*

NOTE. Values are the mean ± SD. *P* values refer to the difference *v* control. Periods: 1, 30 minutes before beginning fructose or xylitol; 2, 30 minutes after beginning fructose or xylitol; 3, 1 hour after beginning fructose or xylitol.

*$P < .01$.

inhibited AMP-specific 5′-nucleotidase. In addition, another study[20] demonstrated that with the induction of ATP catabolism by the addition of fructose to isolated hepatocytes, the dephosphorylation of AMP was almost completely suppressed. These results suggest that adenosine may not be converted from AMP in the liver in quantities large enough to increase the plasma concentration of adenosine significantly, although fructose and xylitol did enhance purine degradation.

The concentration of adenosine in plasma did not change during fructose infusion. Nevertheless, fructose increased the urinary excretion of adenosine. Further, the increased urinary excretion of uridine induced by fructose was comparable to that induced by xylitol, although the increase in the plasma concentration of uridine was smaller with fructose versus xylitol. Therefore, plasma adenosine and uridine concentrations do not seem to reflect increases in the urinary excretion of adenosine and uridine. A previous study[21] demonstrated that AMP-specific 5′-nucleotidase activity is markedly high in membrane fractions of rat kidney cortical tubules, suggesting that AMP can be converted preferentially to adenosine in the cortical tubules. In addition, other studies[13,14] have demonstrated that the urinary excretion of adenosine reflects the concentration of adenosine produced in the kidney, and also that fructose is metabolized in the kidney in rats.[22] These studies suggest that in the renal cortical tubules, fructose is metabolized via ATP consumption, leading to purine and pyrimidine degradation, which increases the urinary excretion of adenosine and uridine.

Table 8. Urinary Excretion of Na, Cl, K, and Inorganic Phosphate (N = 5)

Parameter	Fructose Infusion Before	Fructose Infusion During	Xylitol Infusion Before	Xylitol Infusion During
Na (mmol/h)	8.5 ± 4.9	11.7 ± 4.5	9.8 ± 6.3	13.3 ± 9.3
Cl (mmol/h)	10.3 ± 4.9	8.0 ± 3.5	11.6 ± 5.9	20.1 ± 11.9
K (mmol/h)	4.6 ± 1.6	3.5 ± 1.0	4.3 ± 1.0	4.6 ± 1.9
Inorganic phosphate (mmol/h)	1.0 ± 0.2	1.0 ± 0.2	0.7 ± 0.3	0.4 ± 0.2*
Urine flow (mL/h)	235 ± 175	329 ± 239	183 ± 111	402 ± 283

NOTE. Values are the mean ± SD. *P* values refer to the difference *v* control.

*$P < .05$.

Table 9. Effect of Fructose on the Plasma Concentration of Aldosterone, Plasma Renin Activity, Angiotensin I and II, and Creatinine Clearance (N = 5)

Parameter	Period 1	Period 2	Period 3
Aldosterone (pg/mL)	86.6 ± 28.4	74.4 ± 33.5	80.4 ± 39.0
PRA (ng/mL/h)	1.6 ± 0.8	1.7 ± 0.8	1.5 ± 0.8
Angiotensin I (pg/mL)	450 ± 55	438 ± 88	452 ± 85
Angiotensin II (pg/mL)	13.7 ± 9.3	13.1 ± 10.8	13.3 ± 10.2
Creatinine clearance (mL/min)	105.0 ± 11.5	106.3 ± 6.7	

NOTE. Values are the mean ± SD. Periods 1, 2, and 3 are the same as in Table 2. Creatinine clearance was calculated using the plasma concentration of creatinine 30 minutes before and after beginning the infusion.

Abbreviation: PRA, plasma renin activity.

On the other hand, although it was previously shown that small amounts of xylitol are metabolized in the rat kidney,[23] the present study suggests that xylitol is not significantly metabolized in the human kidney, since xylitol did not affect the urinary excretion of adenosine. However, the plasma concentration and urinary excretion of purine bases and uridine were increased by xylitol infusion, indicating that xylitol enhances purine and pyrimidine degradation in many organs, especially the liver. These increases in the plasma levels seem to lead to increased urinary excretion of purine bases and uridine. Therefore, although xylitol and fructose enhance purine and pyrimidine degradation in many organs, it is suggested that the organ(s) in which enhanced pyrimidine degradation occurs, leading to the urinary excretion of uridine, may differ for xylitol versus fructose. Namely, the xylitol-induced increase in the urinary excretion of uridine seems ascribable to a marked enhancement of pyrimidine degradation, mainly in the liver, while the fructose-induced increase in the urinary excretion of uridine seems ascribable to an enhancement of pyrimidine degradation in the kidney.

In previous studies,[10-14] it has been demonstrated that adenosine has several actions in the kidney, such as a decrease in the glomerular filtration rate (GFR), an alteration in the cortical distribution of blood flow, and a decrease in renin release. It has been further demonstrated that intrarenally produced adenosine plays a role in the intrinsic control of GFR; namely, an increased production of adenosine in the kidney constricts the afferent arteriole and dilates the efferent arteriole, thereby reducing the glomerular capillary hydrostatic pressure and GFR. Therefore, adenosine in the kidney seems clinically important. Since adenosine excreted in the urine may reflect adenosine produced by the kidney,[13,14] fructose may affect renal hemodynamics and natriuresis. Since fructose is abundant in many kinds of fruit, adenosine produced by ingestion of a large quantity of fruit may be clinically important in the kidney. However, the present study shows that fructose did not affect creatinine clearance, urinary excretion of sodium, chloride, and potassium, plasma renin activity, or the plasma concentration of aldosterone, angiotensin I, and angiotensin II, suggesting that a fructose (40

to 50 g)-induced production of adenosine does not significantly affect renal physiological function. Since the recommended rate of intravenous infusion of xylitol and fructose is less than 0.3 g/kg weight/h and less than 0.5 g/kg weight/h, respectively, in Japan, the plasma concentrations of xylitol and fructose seem to be lower with the recommended doses versus the doses used in the present study. Therefore, clinically, xylitol and fructose infusions do not seem to affect the plasma concentration of adenosine or the renal physiological function. Furthermore, since fructose and xylitol were intravenously administered in the present study, and since it was previously demonstrated that a large amount of fructose incorporated into meals (60 to 90 g/d) had no deleterious effects, including the serum uric acid level, on human subjects over a 2-week period,[24] the present results may not reflect the effect of either fructose or xylitol administered orally over a more prolonged time course.

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