Dietary D-Psicose Reduced Visceral Fat Mass in High-Fat Diet-Induced Obese Rats

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Abstract: D-Psicose, a C-3 epimer of D-fructose, has shown promise in reducing body fat accumulation in normal rats and plasma glucose level in genetic diabetic mice. Effects of D-psicose on diet-induced obesity are not clearly elucidated, and we investigated food intake, body weight, and fat accumulation in rats fed high-fat (HF) diet. Sprague–Dawley rats became obese by feeding HF diet for 4 wk, and were assigned either to normal or HF diet supplemented with or without D-psicose, sucrose, or erythritol for 8 wk. Changing HF to normal diet gained less body weight and adipose tissue due to different energy intake. D-psicose-fed rats exhibited lower weight gain, food efficiency ratio, and fat accumulation than erythritol- and sucrose-fed rats. This effect was more prominent in D-psicose-fed rats with normal diet than with HF diet, suggesting combination of psicose and calorie restriction further reduced obesity. There was no difference in serum cholesterol/high-density lipoprotein (HDL)-C and low-density lipoprotein (LDL)-C/HDL-C ratios between D-psicose group and other groups. Liver weight in 5% psicose group with normal diet was higher than in other groups, but histopathological examination did not reveal any psicose-related change. D-Psicose inhibited the differentiation of mesenchymal stem cell (MSC) to adipose tissue in a concentration-dependent manner. These results demonstrate that D-psicose produces a marked decrease, greater than erythritol, in weight gain and visceral fat in an established obesity model by inhibiting MSC differentiation to adipocyte. Thus, D-psicose can be useful in preventing and reducing obesity as a sugar substitute and food ingredient.

Keywords: adipocyte differentiation, D-psicose, erythritol, obesity, sucrose

Practical Application: We can develop D-psicose as a sugar substitute and food ingredient since it can prevent obesity in normal people, but also suppress adiposity as a sugar substitute or food ingredients with antiobesity effect in obese people. D-psicose can be unique functional sweetener because of its function of reducing visceral fat mass and weight gain.

Introduction

Obesity is characterized at the cellular level by an increase in the number and size of adipocytes differentiated from preadipocytes in adipose tissue (Furuyashiki and others 2004). Differentiation from preadipocytes into adipocyte has highly relevance to induction of adipose tissue size and weight. During the differentiation process, the cells change both morphologically (for example, accumulation of lipid droplets) and biochemically (for example, upregulation of lipogenic enzymes such as fatty acid synthase, FAS, and acetyl-CoA-carboxylase, ACC). FAS and ACC generated signals may be essential to support preadipocyte differentiation (Schmida and others 2005). Recently, it was reported that previously uncharacterized differentiation route triggered by high glucose that drives not only resident stem cells of the adipose tissue but also uncommitted precursors present in muscle cells to form adipose depots. This process may represent a feed-forward cycle between the regional increase in adiposity and insulin resistance that plays a key role in the pathogenesis of diabetes mellitus (Aguiari and others 2008).

A correlation between intra-abdominal fat accumulation and abnormal lipoprotein metabolism has been reported in obese subjects (Rashid and Genest 2007). Moreover, abdominal fat accumulation is closely associated with metabolic disorders including hyperlipidemia, diabetes mellitus, and cardiovascular disease in normal weight subjects (Haslam and James 2005). Therefore, reduction of abdominal fat accumulation would be important for the control of geriatric-related diseases.

In particular, increases in the amount of fat in the diet have been shown to be associated with the risk of obesity and hyperlipidemia in human and rodents (Horton and others 1995; Nagai and others 2005). High sucrose intakes are shown to be another major factor contributing to the development of obesity and related diseases (Brenner and others 2003; Pagliassotti and others 1996; Malik and others 2010). Recently, various new sugars and sugar alcohols, including erythritol, have been developed for nutritional and therapeutic uses to manage the problems of overweight and diabetic complications. They are considered to be low-energy sweeteners, being less calorigenic than glucose or sucrose (Yokozawa and others 2002; Raben and others 2002).

D-Psicose, a C-3 epimer of D-fructose, is approximately 70% as sweet as sucrose. The method of mass-producing D-psicose (Oshima and others 2006; Granstrom and others 2004) has

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recently been developed, making it possible to conduct studies of bioactivity (Cree and Perlin 1968; Binkley 1963; Miller and Swain 1969). It has been reported that D-psicose decreased diurnal plasma glucose level and increased plasma insulin concentration in rats and suppressed postprandial plasma glucose and insulin concentration in human (Matsuo and Izumori 2006; Iida and others 2008).

Previous study reported that dietary D-psicose provides no energy and significantly lowered adipose tissue weight, not body weight in normal rats after 28 d treatment. This lower fat accumulation might result from the inhibitory action D-psicose on hepatic lipogenic enzymes including glucose 6-phosphate dehydrogenase and fatty acid synthase (Matsuo and others 2001). It was also reported that supplemental D-psicose reduced body weight gain and abdominal fat mass in normal rat for 8 wk (Matsuo and Izumori 2006). However, D-psicose supplementation did not show significant lowering effect on weight gain and abdominal fat mass in rats fed high fat diet for 16 wk (Matsuo and Izumori 2004). It seems that these inconsistent results were due to different experimental design and diet. Moreover, the effect of D-psicose in obese subjects has not been fully elucidated. In this study, we investigated antiobese effect of D-psicose on established diet-induced obesity in rats.

Table 1–Composition of experimental diets.

Ingredients (g/kg)	ND[a]	HF
Casein	140	174
Corn starch	465.692	271.192
Sucrose	100	100
Dextrose	155	155
Cellulose	50	50
Soybean oil	40	100
Lard	0	100
Vitamin mixture	35	35
Mineral mixture	10	10
TBHQ	0.008	0.008
L-cysteine	1.8	1.8
Choline bitartrate	2.5	2.5
Cholesterol	0	0.5
%Energy from protein	14.7	15.1
%Energy from fat	9.4	38.8
%Energy from carbohydrate	76.9	47.1
Energy (kcal/kg)	3.85	4.65

[a]Based on AIN-93M purified diet for the maintenance of adult rats (Reeves and others 1993).

Materials and Methods

Chemicals

D-Psicose, erythritol, and sucrose were provided by CJ Cheil-Jedang Food Research and Development Inst. (Seoul, Korea). All other chemicals were purchased from Sigma (St. Louis, Mo. U.S.A.)

Animals and experimental diet

All procedures involving animals were approved by the Experimental Animal Care Committee of CJ Corp., Seoul, Korea. Studies were performed in 7-wk-old male Sprague–Dawley (SD) rats (Orient, Inc., Seoul, Korea). Rats were singly housed at a temperature of 22 ± 2 °C, with a 12-h:12-h light–dark cycle (lights on at 7:00 a.m.), and were fed *ad libitum* standard laboratory chow and water for 1 wk. Then, rats were fed either normal diet (control, C) or HF diet (HF) based on AIN-93M diet (FeedLab, Seoul, Korea) (Table 1). After 4 wk, rats fed HF except C group were matched by weight and assigned to 1 of 2 studies. In study 1, 5 groups (50 male SD rats, $n = 10$) were switched from HF diet to normal diet (ND) or ND supplemented with 5% sucrose (SU-5), 5% erythritol (ES-5), and 2.5, 5% D-psicose (DP-2.5, DP-5) for 52 d. In study 2, 4 groups, 40 male SD rats ($n = 10$) also kept on HF with or without each supplement for 52 d (Table 2). The food intake (FI) and body weight (BW) were measured 3 times a week, respectively. Feeding efficiency ratio (FER) was calculated as follows: FER (%) = body weight gain (g/d)/food intake (g/d) × 100. The animals were killed and tissues (epididymal adipose tissue, perirenal adipose tissue, retroperitoneal adipose tissue, intersacpular brown adipose tissue, and liver) were removed, cleaned, weighed, and frozen at −70 °C until analysis.

Biochemical analysis

At the study endpoint, rats were previously fasted for 16 h and anesthetized with ether. Blood samples were obtained from the vein puncture of inferior vena cava. Serum samples were separated from blood by centrifugation and immediately frozen at −70 °C for measurement of biochemical parameters. Total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) were determined by Biochemical analyzer (AU 400, Olympus, Japan) from 200 μL serum.

Histopathological analysis of liver tissue

For histopathological evaluation of the liver morphology, the liver tissue was removed and fixed in a buffer solution of 10%

Table 2–Effects of D-psicose on body weight, and food efficiency.

Groups	Body weight (g)			Food intake (g/d)	Food efficiency ratio (FER)
	Initial (g)	Final (g)	Gain (g/d)		
Control	393.8 ± 5.99	534.9 ± 28.39	2.7 ± 0.47	18.8 ± 1.83	0.14 ± 0.01
Experiment 1					
ND	483.1 ± 25.57	605.3 ± 53.15	2.4 ± 0.67	20.1 ± 1.80	0.12 ± 0.02
ND-SU5	483.1 ± 25.35	606.7 ± 55.07	2.4 ± 0.61	20.9 ± 2.23	0.11 ± 0.02
ND-ER5	483.1 ± 25.05	589.0 ± 38.92	2.0 ± 0.45	19.3 ± 1.30	0.1 ± 0.02
ND-DP2.5	483.6 ± 24.81	573.0 ± 33.80	1.7 ± 0.35*	19.0 ± 1.33	0.09 ± 0.01
ND-DP5	483.6 ± 24.87	549.4 ± 29.97*	1.3 ± 0.27*,†	19.6 ± 0.83	0.06 ± 0.01*,†
Experiment 2					
HF	483.6 ± 24.92	648.5 ± 55.23	3.8 ± 0.70	21.5 ± 2.16	0.15 ± 0.02
HF-SU5	483.8 ± 24.79	633.4 ± 59.19	2.9 ± 0.69	19.9 ± 1.78	0.14 ± 0.02
HF-ER5	483.5 ± 25.24	634.8 ± 41.10	2.9 ± 0.45	22.2 ± 1.27	0.13 ± 0.01
HF-DP5	483.6 ± 25.61	580.8 ± 38.74*	1.9 ± 0.43*,†	20.1 ± 1.37	0.09 ± 0.01*,†

Data are mean ± S.D. from $N = 10$ rats/group.
*$P < 0.05$ compared to ND (experiment 1) or HF (experiment 2).
†$P < 0.05$ compared to ND-ER5 (experiment 1) or HF-ER5 (experiment 2).

formalin. Fixed tissues were processed routinely for paraffin embedding, and 4-m sections were prepared and dyed with hematoxylin–eosin (H&E); stained areas were viewed using an optical microscope at ×100 and ×400 (BX41TF, Olympus).

In vitro adipocyte differentiation and Oil Red O staining

Cell culture media and fetal calf serum were obtained from Gibco (Grand. Island, N.Y., U.S.A.). Mesenchymal stem cell (MSC) was isolated from C57BL/6 mice according to the method of Grimaldi and others (1997). For the differentiation into adipocytes, isolated MSC were cultivated in 6-well plates until confluence and incubated in Dulbecco's modified Eagle medium (DMEM) containing ascorbic acid, dexamethasone, and indomethacin for 7 d with medium changes every 3 d. To demonstrate the effect of D-psicose in adipocytes differentiation, MSC was maintained in medium containing the different D-psicose concentrations. Fully differentiated cells were stained with Oil Red O according to the method outlined here. Cells were washed with PBS, then fixed in 10% formaldehyde for 20 min, rinsed with water, and stained with 0.1% Oil Red O solution for 1 to 2 h. Cells were then washed 3 times with and maintained in H_2O. The phenotypic change of adipogenesis was observed under a microscope. For a quantitative assay, Oil Red O dye was extracted with isopropanol and the absorbance was measured at 510 nm with a spectrophotometer (Shimadzu UV-1601, Japan).

Statistical analysis

All data are presented as the mean ± S.D. The statistical analyses were performed using the statistical package for social science (SPSS) software program. Significant differences among groups were analyzed by one-way ANOVA followed by the Student's *t*-test. Statistical significance was accepted at $P < 0.05$.

Results and Discussion

Body weight, food intake, and food efficiency ratio

During the experimental period, feeding a high-fat (HF) diet for 4 wk produced significant increases in body weight as compared to control fed standard normal diet. Administration of the normal diet (ND) and HF diet supplemented with or without SU, ES, and DP started on Day 0 and ended Day 52. The average growth rate for 52 d is shown in Figure 1. Feeding a HF diet produced significant increases in body weight as compared to ND groups due to the difference of energy intake ($P < 0.05$). Overall, there were no significant intergroup differences on the initial body weight and the food intake per day except control group. In contrast, weight gain was significantly lower in the 5% DP group than in other groups ($P < 0.05$, Table 2).

In experiment 1, the administration of D-psicose significantly suppressed the increase of body weight in rats fed the high fat diet for 4 wk dose-dependently (2.5, 5%). This suppression was significant compared with ND-ER5 group as well as ND and ND-SU5 group, indicating D-psicose has a distinctive function differentiated from other zero-calorie sugar substitute. The calorie restriction by switching from high-fat diet (HFD) to ND reduced the body weight gain of all ND groups when compared to continuously HFD fed groups. It is obvious that calorie restriction is very important factor to control the body weight.

The increase of body weight was dramatically reduced by 41% in HF-DP5 group comparedwith HF group after 52 d in experiment 2, suggesting D-psicose would be helpful to prevent the obesity development in obese subjects. In contrast, HF-ER5 group did not show the significant decrease in body weight gain. The average food intake (g/d) was analyzed, and it was not significantly different among groups. Food efficiency ratio in the D-psicose group was significantly lower than other group including erythritol group (Table 2). In the current investigation, we were able to confirm that D-psicose has the potent effect of lowering body weight gain and FER in obese rats fed a HF diet. These effects were potentiated by diet switching from HF to ND, suggesting D-psicose supplementation combined by calorie restriction might exert the best antiobesity action in obese subjects.

Tissue weights

Total white adipose tissue mass including epididymal, perirenal, and retroperitoneal fat was significantly decreased by 38% in

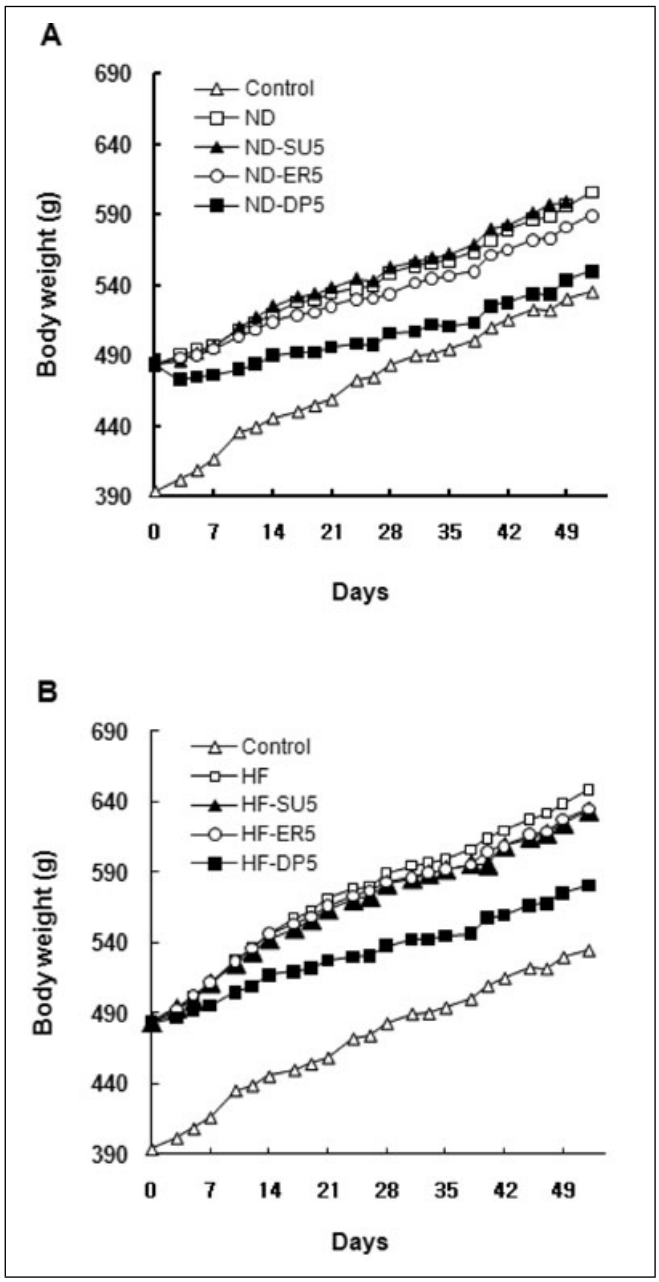

Figure 1–Effects of D-psicose supplements fed with normal diet (A) and with high fat diet (B) on body weight changes in high-fat diet-included obese rats.

ND-DP5 group in comparison to ND group in experiment 1. The pattern of decline in fat mass was observed in ND-ER5 group, however this difference was not significant. The epididymal, perirenal, and retroperitoneal fat pads were more significantly decreased by 38%, 41%, and 38%, respectively, in the rats fed the ND-DP5 than in rats fed ND ($P < 0.05$). The weight of the interscapular brown adipose tissue (IBAT) of the 5% DP group was markedly lower than that of ND (36%) and any other group including ND-ER5 ($P < 0.001$).

In experiment 2, there was also a prominent decrease of epididymal, perirenal fat, and IBAT weights in rats fed HF-DP5 compared with rats fed HF ($P < 0.05$). Those fat masses were significantly reduced by 19%, 27%, and 40%, respectively ($P < 0.05$). However, total white adipose tissue (WAT) and retroperitoneal were decreased by 17% and 13% in HF-DP5 compared with rats fed HF, but without significant differences (Table 3). HF-ER5 group failed to reduce fat mass in HF-diet. It seems that ER could not have much effect on extreme obesity induced by high fat diet. White adipose tissue is the primary site of energy storage and of release of hormones and cytokines that modulate whole-body metabolism and insulin resistance. Brown adipose tissue, on the other hand, is important for both basal and inducible energy expenditure in the form of thermogenesis (Rosen and Spiegelman 2000; Giacobino and Casteilla 2010). Interestingly, D-psicose reduced both types of adipose tissue. Despite the reduction of BAT, the reduced weight gain and WAT weight were observed. It suggested that D-psicose might have some effect on the fat accumulation in WAT, and lead a decrease of excess fat storage regardless of BAT size. Further experimental studies would be helpful in the elucidation of the effect of D-psicose on WAT.

A previous study demonstrated that some portion of D-psicose absorbed is excreted in urine or feces, and other portion remains in the body and is fermented by bacteria in the caecum or large intestine (Matsuo and others 2003). Therefore, antiobesity effect of D-psicose in this study can also be attributed to the possibility that a large part of D-psicose absorbed in the small intestine is excreted without metabolizing into energy or fermented in large intestine providing no energy.

Serum biochemical analysis

Serum CHO, LDL-C, and HDL-C levels were significantly higher in the ND-DP5 group than in ND group in experiment 1. ER group did not affect serum lipid profile. There were no significant changes in other groups. However, TC/HDL-C, LDL-C/HDL-C ratio in DP5 group showed no difference with any of other group, because HDL-C, cholesterol, and LDL-C level were increased together (Table 4). The TC/HDL-C ratio known as the atherogenic or Castelli index and the LDL-C/HDL-C are 2 important indicators of vascular risk with greater predictive value than the isolated parameters (Millán and others 2009). Therefore, we can predict the risk of cardiovascular disease of psicose group would not be different with that of control group. In experiment 2, there were no significant differences between the groups indicating no alteration in lipid profile by psicose in rats fed continuous HFD.

Table 3–Effects of D-psicose on adipose tissue and liver weights.

	Adipose tissue weight (g)					
Groups	**Epidodymal**	**Perirenal**	**Retroperitoneal**	**Total WAT (g)**	**Interscapular BAT (g)**	**Liver (g)**
Control	10.98 ± 2.09	4.72 ± 1.01	13.75 ± 2.94	29.46 ± 5.69	0.52 ± 0.11	12.17 ± 1.61
Experiment 1						
ND	16.35 ± 7.23	5.30 ± 1.83	17.93 ± 4.71	39.58 ± 6.65	0.69 ± 0.12	13.44 ± 2.43
ND-SU5	15.28 ± 2.96	4.86 ± 1.02	16.25 ± 5.44	36.39 ± 6.18	0.75 ± 0.12	14.64 ± 2.20
ND-ER5	12.93 ± 3.46	4.08 ± 1.49	13.55 ± 4.35*	30.57 ± 5.37	0.68 ± 0.16	14.21 ± 2.16
ND-DP2.5	12.84 ± 3.63	3.85 ± 0.99*	14.15 ± 3.81	30.84 ± 5.59	0.52 ± 0.18*,†	15.56 ± 2.14
ND-DP5	10.19 ± 1.65*,†	3.13 ± 0.89*	11.10 ± 1.68*	24.41 ± 4.64*	0.44 ± 0.09*,†	18.18 ± 2.68*,†
Experiment 2						
HF	21.54 ± 4.77	6.81 ± 2.35	22.28 ± 5.53	50.63 ± 8.10	0.80 ± 0.36	16.29 ± 2.79
HF-SU5	19.14 ± 4.81	6.04 ± 0.92	22.18 ± 5.51	47.36 ± 7.64	0.72 ± 0.18	14.96 ± 2.65
HF-ER5	17.82 ± 5.04	5.86 ± 1.95	21.84 ± 5.99	45.53 ± 7.41	0.83 ± 0.65	14.69 ± 2.03
HF-DP5	17.36 ± 3.22*	4.97 ± 1.44*	19.48 ± 4.30	41.81 ± 7.39	0.48 ± 0.16*,†	16.76 ± 3.15

Data are mean ± S.D. from $N = 10$ rats/group.
*$P < 0.05$ compared to ND (experiment 1) or HF (experiment 2).
†$P < 0.05$ compared to ND-ER5 (experiment 1) or HF-ER5 (experiment 2).

Table 4–Effects of D-psicose on serum cholesterol, triglyceride, LDL-C, and HDL-C.

Groups	**TC**	**TG**	**LDL-C**	**HDL-C**	**TC/HDL-C**	**LDL-C/HDL-C**
Control	63.4 ± 16.4	95.4 ± 51.6	14.3 ± 3.7	36.7 ± 9.1	1.73 ± 0.21	0.39 ± 0.07
Experiment 1						
ND	68.9 ± 25.3	98.7 ± 35.3	13.1 ± 5.1	40.5 ± 13.5	1.69 ± 0.10	0.32 ± 0.04
ND-SU5	79.6 ± 17.9	110.7 ± 34.3	16.2 ± 2.8	45.7 ± 10.9	1.75 ± 0.13	0.36 ± 0.05
ND-ER5	59.9 ± 25.0	106.4 ± 43.0	12.9 ± 5.4	33.7 ± 14.2	1.79 ± 0.13	0.39 ± 0.04
ND-DP2.5	76.2 ± 17.5	130.5 ± 39.7	14.6 ± 3.6	40.3 ± 8.8	1.90 ± 0.21	0.37 ± 0.06
ND-DP5	110.8 ± 30.9*,†	132.7 ± 77.0	22.6 ± 6.5*,‡	58.2 ± 13.2*,†	1.89 ± 0.19	0.39 ± 0.06
Experiment 2						
HF	76.6 ± 26.3	113.0 ± 41.3	15.8 ± 4.1	41.1 ± 12.5	1.84 ± 0.12	0.39 ± 0.05
HF-SU5	63.6 ± 16.0	88.1 ± 26.4	13.5 ± 3.3	35.8 ± 8.7	1.77 ± 0.15	0.38 ± 0.05
HF-ER5	72.8 ± 15.6	81.9 ± 18.9	15.1 ± 3.6	42.0 ± 8.2	1.73 ± 0.11	0.36 ± 0.05
HF-DP5	74.9 ± 14.2	103.3 ± 54.5	15.9 ± 3.2	38.5 ± 7.9	1.96 ± 0.20	0.42 ± 0.05

Data are mean ± S.D. from $N = 10$ rats/group.
*$P < 0.05$ compared to ND (experiment 1) or HF (experiment 2).
†$P < 0.05$ compared to ND-ER5 (experiment 1) or HF-ER5 (experiment 2).

An alteration in lipid composition in ND-DP5 group might be magnified by diet switching.

The pathological changes in liver tissue

Relative weights of liver (mg/g BW) were comparable for all groups except ND-DP5 group. Liver weights were significantly higher in ND-DP5 group than in other group (Table 3). However, there were no significant differences in the pathological data and H&E staining between the groups ($P < 0.05$). Figure 2 shows microscopic observation of liver tissues in each group. In hematological parameter examination, aspartate aminotransferase (AST) was increased in ND-DP5 group (data not shown) and other parameters (alanine aminotransferase [ALT] and billirubin [BIL]) are comparable with other groups. Histopathological examination of liver did not reveal any psicose-related changes and we concluded that 5% psicose did not induce the liver toxicity.

Matsuo and Izumori (2004) proposed that D-psicose induced higher glycogen deposition and liver enlargement. Liver enlargement occurs in animals and humans under a variety of conditions and can be the result of a physiological adaptation to an enhanced workload or metabolic demand, a toxic effect, an inflammatory process, or a proliferative disease (Bar and others 1999). Our results also showed that ND-DP group tended to induce liver enlargement suggesting increased glycogen deposition in liver as extra-energy storage of D-psicose. However, HF-DP group did not show any difference compared to HF group. It is possible that HF diets containing relatively low carbohydrates made rats use its endogenous proteins to support the level of blood glucose, and induced lower liver glycogen level masking the effects of D-psicose. According to the recent studies on long-term toxicity of D-psicose in rats, long-term administration of 3% D-psicose for 12 to 18 mo rats leads to increase liver and kidney weights with no gross

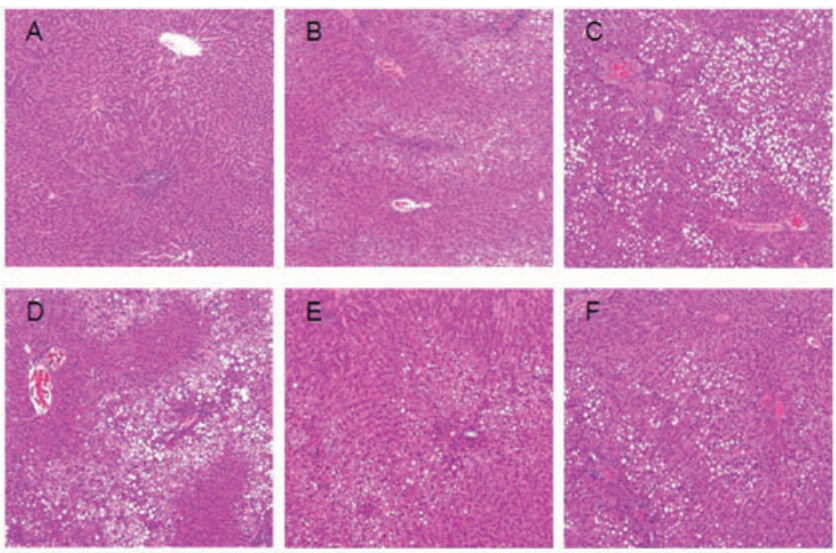

Figure 2–Representative microscopic appearance of live tissues (H&E stain, ×100). Light image of liver tissue section from each treatment group shown in (A) to (F). (A) Section of control group. (B) Section of ND group. (C) Section of ND-SU5 group. (D) Section of ND-ER5 group. (E) Section of ND-DP2.5 group. (F) Section of ND-DP5 group.

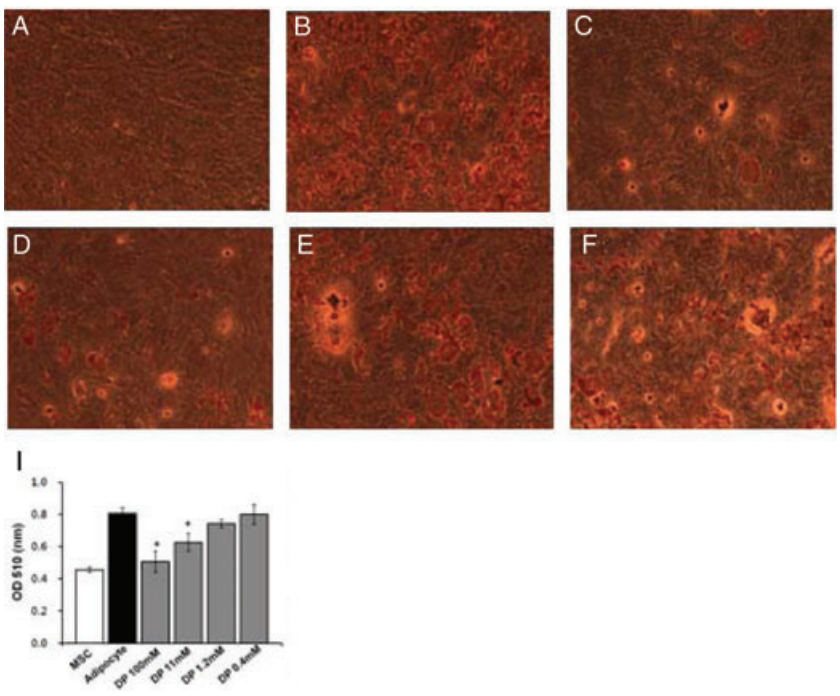

Figure 3–Differentiated adipocytes were monitored by microscopic pictures with Oil Red O staining. (A) Representative picture of MSC. (B) Adipocytes. (C) DP 0.4 mM. (D) DP 1.2 mM. (E) DP 11 mM. (F) DP 100 mM treatment group. (I) Quantification of Oil Red O staining measured at 510 nm. (*$P < 0.05$ compared with adipocyte).

pathological findings correlated with the hypertrophy. There was a report that no adverse effects were observed at low-dose of D-psicose in the diet (Yagi and Matsuo 2009). These previous reports are consistent with our current results reducing weight gain and fat accumulation without D-psicose-induced liver toxicity.

The effect of D-psicose on preadipocytes differentiation in mouse MSC

Mesenchymal stromal cells (MSCs) can be isolated from various tissues such as bone marrow aspirates, fat, or umbilical cord blood, and have the ability to proliferate *in vitro* and differentiate into several types of cells such as osteoblasts, adipocytes, myocytes, and vascular cells (Aguiari and others, 2008; Schmida and others, 2005). To investigate the effect of D-psicose on preadipocyte differentiation, MSC isolated from C57BL/6 mouse was induced using some stimuli and treated with D-psicose for 7 d. Oil Red O staining was used to confirm MSC differentiation within 7 d (Figure 3A and B). Quantification of Oil Red O staining demonstrated that D-psicose inhibits the differentiation from MSC into adipocyte in a dose-dependent manner with IC_{50} value around 11 mM (Figure 3C to H).

Conclusions

This study suggested that dietary D-psicose is effective in lowering weight gain and visceral fat mass in established obesity model. These antiobese effects of D-psicose were differentiated from the existing sugar substitutes. Consequently, D-psicose can lower body weight gain and visceral fat mass as regulation of inhibition of adipocyte differentiation as well as hepatic lipogenic enzymes. Therefore, D-psicose can be useful not only to prevent obesity in normal people, but also to suppress adiposity as a sugar substitute or food ingredients with antiobesity effect in obese people.

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