In conclusion, DT technology can revolutionize the traditional method of monitoring data on a 2D screen with an overwhelming number of data points, by having a 3D, interactive interface that focuses on selective data points that matter the most at any given time. In future, DT can be scaled up to all the complex engineering systems available at SAC ISRO to make data visualization accessible to all the concerned authorities in real time. Further, DT technology, along with IOT, can be extended to various domains and industries. Its implementation can also be used to analyse and optimize environmental impacts such as energy use, waste management or even water consumption. This will ultimately reduce the carbon footprint and support sustainability goals.

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Effect of date palm sugar on metabolic disorders in experimental diabetic rats

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Diabetes is a metabolic disease with multifactorial causes. There are two types of diabetes in humans: type-1 diabetes, which occurs when the immune system attacks and eliminates insulin secreting cells, and type-2 diabetes, which can be triggered by a variety of factors, the most important being lifestyle, but can also be caused by various genotypes. Date palm sugar (DPS) is nutritive with good potential in treating diabetes due to the presence of polyphenols that have strong antioxidant properties. We assess various parameters in normal rats, sugar-treated rats and diabetes-induced rats, including body weight, food intake, water intake, blood glucose level, insulin level, insulin resistance, lipid profile, atherogenic index, adiponectin, resistin and TNF-α. The study results reveal that DPS contributes to significant improvement in diabetic rats. Thus, DPS is a beneficial substitute compared to other sugars in treating diabetes.

Keywords: Date palm sugar, diabetes, experimental rats, nicotinamide, streptozotocin.

DIABETES is a significant threat to global public health that is rapidly worsening, with the maximum influence on working-age adults in developing nations. It affects at least 177 million individuals globally, and this figure is expected to nearly double by 2030, reaching 366 million[1]. There are two major types of diabetes, with type-2 being more common in adults of varying ages and constantly burgeoning in adolescents and young children. According to the literature, type-2 diabetes is currently increasing among children worldwide, and it seems to have risen significantly in the last 15 years[2]. Moreover, up to 45% of newly diagnosed cases of diabetes among adolescents are type-2. Also, type-2 diabetes accounts for 70% of new cases among native Americans and 80% of new paediatric diabetes cases in Japan[3,4]. According to an epidemiological study, the number of diabetic patients is significantly increasing in the Asia-Pacific region[5]. In addition, type-2 diabetes affects 3% of the population in Europe, and its administrative costs account for 5% of all healthcare spending[6]. When β-cells are unable to compensate for the lack of insulin action, type-2 diabetes is characterized by a progressive decrease of insulin action, also known as insulin resistance[7].

Date palm fruits have been found to have tremendous potential in treating diabetes due to the presence of polyphenols, which have high antioxidant properties. Date palm sugar (DPS) also displays similar properties. Other potential

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mode of action involves inhibiting enzymes like glucosidase and amylase by the polyphenolic compound. DPS also contains flavonoids that can increase the number of islets and β-cells, restore endocrine pancreatic tissues, reduce β-cell apoptosis, activate insulin receptors after an increase in insulin secretion and reduce complications associated with diabetes[8–12].

Animal models are frequently used in diabetes research, with rats being the most common choice. Due to their accessibility and affordability, rat models are also frequently used in diabetes research in addition to genetic models. Chemical inducers like streptozotocin (STZ) are used to cause type-1 diabetes in animals, and a nicotinamide (NA)-STZ model for type-2 diabetes has also been established[13]. In experimental animal models, the quantity and diet of inducers have a significant impact on how diabetes develops. Lower doses of the inducer are ineffectual at inducing diabetes, while higher doses cause severe β-cell damage[14,15].

The DPS formulation was purchased from the local market in Ekgaon, Tamil Nadu. The powder was dissolved in water as a solvent and used for experimental purposes. Following is the list for the composition of the selected DPS in 100 g: total fat, including saturated fat and trans fat (0%), cholesterol (0%), sodium (0%), potassium (0%), total carbohydrate, including dietary fibre and sugar (0%), protein (0%), vitamin C (13.33%), sucrose (30%) and iron (56.7%).

Albino (Sprague-Dawley (SD)) male rats of the same age group and body weight (250 g) were selected for all the experiments. The number of rats was 120, aged two months. Rats obtained from the National Institute of Communicable Diseases, New Delhi, India, were housed in polypropylene cages at an ambient temperature of 25°–30°C and relative humidity of 45–55% with 12 h each of dark and light cycles. The rats were given pelleted food and water ad libitum.

The Ethics Committee approval for the study was obtained from Institutional Animal Ethics Committee, Parul Institute of Pharmacy, Parul University.

Diabetes was induced by a single intraperitoneal injection of freshly prepared nicotinamide (230 mg/kg) in saline (10 mg/100 ml) in the group of male rats. After 15 min, freshly prepared STZ (40 mg/kg) in 0.1M citrate buffer (pH 4.5) was administered to a group of rats that had been fasted overnight. After 72 h, blood glucose levels were measured in the rats.

This study uses *in vivo* tests on healthy and diabetic rats to assess how various sweeteners affect lipid and carbohydrate metabolism in normal and diabetic individuals. The major goal of this study on sweeteners is to provide safe alternatives for both healthy and diabetic individuals. Phase I and Phase II studies have been completed. The timeline for the treatment was about eight weeks. In phase I, we studied the effect of DPS on healthy male rats and measured the response. SD rats aged 2–10 months weighing 180–250 g were used (Table 1).

In the phase II study, we examined the effects of 100–350 mg/kg NA injected intraperitoneally 15 min before intravenous administration of 40 mg/kg STZ in diabetes-induced SD male rats. The results suggest that the NA dosage of 230 mg/kg is the most appropriate (Table 2).

The treatment was continued for eight weeks. After that, the following parameters were checked: body weight, food intake, water intake, blood glucose level (BGL), insulin level, insulin resistance, lipid profile, atherogenic index, adiponectin, resistin and TNF-α.

Streptozotocin (40 mg/kg) and nicotinamide (230 mg/kg) were used to induce diabetes in rats. Overnight fasted animal were used in this study. Nicotinamide was injected into the rats via an IP route, and after a 15-minute interval, an appropriate dose of STZ was induced in the animals. The animals were then observed for 72 hours to induce diabetes. After 72 hours, the blood glucose levels (BGL) were checked, and if the BGL was found to be >250, the animal was considered diabetic. The appropriate dose of Nicotinamide is between 100–350 mg/kg, but 230 mg/kg is the recommended dose.

Additionally, the treatment was administered for eight weeks, following which the following parameters were evaluated on a weekly basis: body weight, food and water intake, and BGL. Insulin levels, lipid profiles, serum adiponectin levels, serum resistin levels, and serum TNF-a levels were measured at the end of the study. The atherogenic index was calculated using the formula log(TG/HDL).

The toxicity study was also carried out for DPS. Three animals were used for each stage in which the starting dose was 2000 mg/kg, and the upper dose limit was fixed at 5000 mg/kg, as recommended by the daily dose limit of humans and as per human calculation for animals. This study followed the acute toxicity study for DPS as per OECD TG 423. Table 2 provides detailed information about the animals and their respective dosage.

Animals were observed individually after dosing during the first 30 min, every hour for the next 4 h and every 6 h up to 24 h after dose administration. The animals were observed daily thereafter for a total of 14 days. No signs of toxicity or abnormal behaviour were observed in any of the animals. The body weights of the test animals were recorded every week for each animal (Table 3). There were no abnormal changes observed in body weight. All test animals were subjected to gross necropsy at the end of 14 days (Table 3).

The result shows the acute toxicity study of date palm sugar.

The toxicity test was conducted on each animal after dosing for the first 30 min every hour for the following 4, 6 and 24 h. The animals were observed daily thereafter for a total of 14 days. There were no signs of toxicity or abnormal behaviour observed in any of the animals. The body weight of the test animals was recorded every week. There were no abnormal changes observed in body weight. All test

Table 1. Experimental design

Name of group	PHASE 1 (normal animals)	PHASE 2 (diabetic animals)	Duration of study (week)
Control	Normal saline (0.2 ml, p.o.)	Normal saline (0.2 ml, p.o.)	8
Sugar	Sugar 500 mg/kg	Sugar 500 mg/kg	8
Date palm sugar	Date palm sugar 500 mg/kg	Date palm sugar 500 mg/kg	8

Table 2. Dosage and groups for toxicity study of DPS

DPS level (mg/kg)	Animal no.	Body weight on day 0 (g)	Dose of DPS (mg)	Dose of DPS (ml)
2000 mg/kg	1	230	460	0.92
	2	240	480	0.96
	3	230	460	0.92
Repeat dose 2000 mg/kg	1	280	560	1.4
	2	270	540	1.08
	3	250	500	1.0

Table 3. Individual animal observations for 14 days

		Body weight				Signs of toxicity			
Dose level	Animal no.	Day 0 (g)	Day 7 (g)	Day 14 (g)	Mortality	Nature	Severity	Duration	Gross necropsy
2000 mg/kg	1	230	240	235	No	NAD	NAD	NAD	NAD
	2	240	240	235	No	NAD	NAD	NAD	NAD
	3	230	240	240	No	NAD	NAD	NAD	NAD
Repeat dose	1	280	280	290	No	NAD	NAD	NAD	NAD
2000 mg/kg	2	270	280	275	No	NAD	NAD	NAD	NAD
	3	250	250	245	No	NAD	NAD	NAD	NAD

NAD, No abnormality detected.

Table 4. Individual animal cage side observations for dose level 2000 mg/kg

		Observation at specific time interval (h)						
Animal ID	Observation parameters	0	0.5	1	2	3	4	24
1	Fur	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Tremor	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Diarrhoea	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Lethargy	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Sleep	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Respiratory pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Behaviour	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Mortality	Nil	Nil	Nil	Nil	Nil	Nil	Nil
2	Fur	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Tremor	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Diarrhoea	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Lethargy	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Sleep	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Respiratory pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Behaviour	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Mortality	Nil	Nil	Nil	Nil	Nil	Nil	Nil
3	Fur	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Tremor	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Diarrhoea	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Lethargy	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Sleep	Nil	Nil	Nil	Nil	Nil	Nil	Nil
	Respiratory pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Behaviour	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Mortality	Nil	Nil	Nil	Nil	Nil	Nil	Nil

Table 5. Evaluation of biochemical parameters of phase I and phase II trials

Parameter	Beginning of the study			End of the study		
	Saline	Sugar	DPS	Saline	Sugar	DPS
Phase I						
Body weight	305 ± 1.89	301 ± 3.10	319 ± 6.87	339 ± 3.76	395 ± 2.89	281 ± 7.57
Food intake	55 ± 0.48	54 ± 0.71	59 ± 1.54	51 ± 2.09	78 ± 2.18	38 ± 0.68
Water intake	49 ± 1.67	52 ± 1.41	49 ± 1.58	50 ± 0.31	53 ± 0.61	46 ± 1.14
BGL	63 ± 8.85	74 ± 1.61	82 ± 4.99	84 ± 1.54	100 ± 0.61	70 ± 1.09
Insulin level	15.15 ± 0.8	14.95 ± 1.04	12.95 ± 1.15	14 ± 0.88	11 ± 1.61	13 ± 1.16
HDL	85.33 ± 3.06	79.13 ± 1.67	83.5 ± 2.09	85 ± 3.06	57 ± 2.78	87 ± 3.86
LDL	109.50 ± 4.1	127.66 ± 2.46	110.16 ± 2.42	117 ± 4.01	150 ± 3.15	121 ± 5.38
TG	113.50 ± 6.45	125.50 ± 3.72	111.17 ± 3.94	111 ± 6.45	139 ± 5.19	106 ± 2.56
TC	126.33 ± 5.60	168.33 ± 5.41	129.33 ± 6.59	135 ± 5.34	181 ± 3.71	122 ± 4.61
Atherogenic index	0.12 ± 0.04	0.30 ± 0.07	0.09 ± 0.06	0.115 ± 0.01	0.3 ± 0.013	0.09 ± 0.01
Adiponectin	14.98 ± 1.60	14.7 ± 1.88	12.86 ± 0.96	15 ± 1.34	10 ± 0.55	13 ± 0.96
Resistin	14.42 ± 1.16	15.15 ± 0.85	13.78 ± 1.20	12 ± 0.56	16 ± 1.02	11 ± 0.64
TNF-α	1.48 ± 0.23	1.55 ± 0.17	1.33 ± 0.25	1 ± 0.18	2 ± 0.17	1 ± 0.25
Phase II						
Body weight	316 ± 11.54	315 ± 9.92	319 ± 6.87	234 ± 11.58	292 ± 9.90	281 ± 7.57
Food intake	55 ± 0.85	54 ± 0.71	58 ± 1.54	33 ± 1.47	25 ± 0.61	65 ± 1.07
Water intake	50 ± 0.98	52 ± 2.34	49 ± 1.57	62 ± 1.08	63 ± 1.35	57 ± 1.70
BGL	346 ± 15.37	306 ± 18.51	342 ± 16.47	513 ± 12.15	540 ± 28.60	273 ± 16.30
Insulin level	15.15 ± 0.8	14.95 ± 1.04	12.95 ± 1.15	16.01 ± 0.38	14.95 ± 0.31	13.42 ± 0.59
HDL	85.33 ± 3.06	79.13 ± 1.67	83.5 ± 2.09	66 ± 2.31	58 ± 2.74	85 ± 3.15
LDL	109.50 ± 4.1	127.66 ± 2.46	110.16 ± 2.42	149 ± 4.36	159 ± 5.38	139 ± 3.84
TG	113.50 ± 6.45	125.50 ± 3.72	111.17 ± 3.94	106 ± 8.11	146 ± 6.13	102 ± 5.90
TC	126.33 ± 5.60	168.33 ± 5.41	129.33 ± 6.59	142 ± 4.25	165 ± 5.84	126 ± 4.64
Atherogenic index	0.12 ± 0.04	0.30 ± 0.07	0.09 ± 0.06	0.31 ± 0.03	0.40 ± 0.22	0.36 ± 0.03
Adiponectin	14.98 ± 1.60	14.7 ± 1.88	12.86 ± 0.96	11.86 ± 0.63	10.2 ± 0.62	10.87 ± 2.91
Resistin	14.42 ± 1.16	15.15 ± 0.85	13.78 ± 1.20	16.94 ± 0.85	18.72 ± 0.82	14.72 ± 1.42
TNF-α	1.48 ± 0.23	1.55 ± 0.17	1.33 ± 0.25	1.93 ± 0.16	1.88 ± 0.20	1.52 ± 0.20

BGL, Blood glucose level; HDL, High density lipoprotein; LDL, Low density lipoprotein; TG, Triglyceride; TC, Total cholesterol.

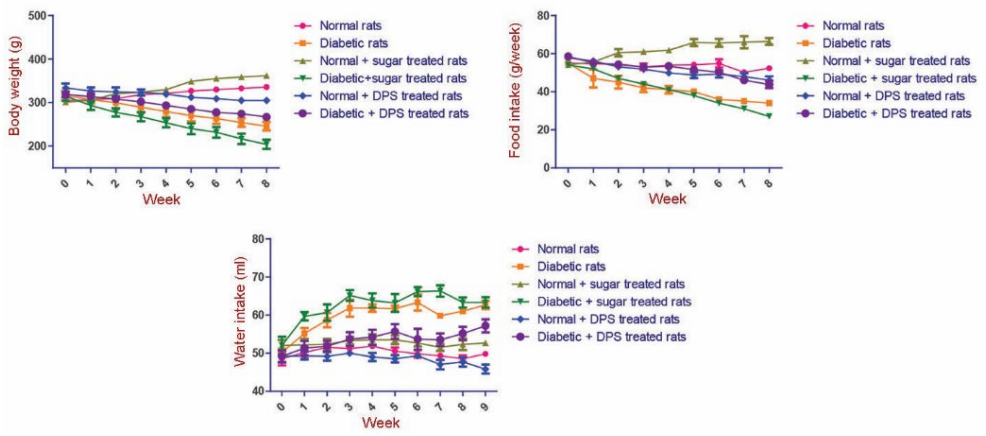

Figure 1. Effect of date palm sugar on body weight, food intake and water intake.

animals were subjected to gross necropsy at the end of 14 days. Table 4 lists individual animal observations at the dose of 2000 mg/kg and repeated dose effects.

The results provide the data on phase-I and phase-II research studies. Various factors such as body weight, food intake, water intake, BGL, insulin level, insulin resistance, lipid profile, atherogenic index, adiponectin, resistin, and TNF-α were evaluated.

Phase-I studies after eight weeks of treatment show the effects of different parameters on various groups as per Table 5. Body weight was determined at the beginning and end of the treatment. Body weight in DPS-treated animals decreased by 12%. The food intake of DPS-treated animals also decreased; white sugar-treated animals showed an increase. There was a minor reduction in the water intake of DPS-treated rats, which increased in saline and sugar-treated

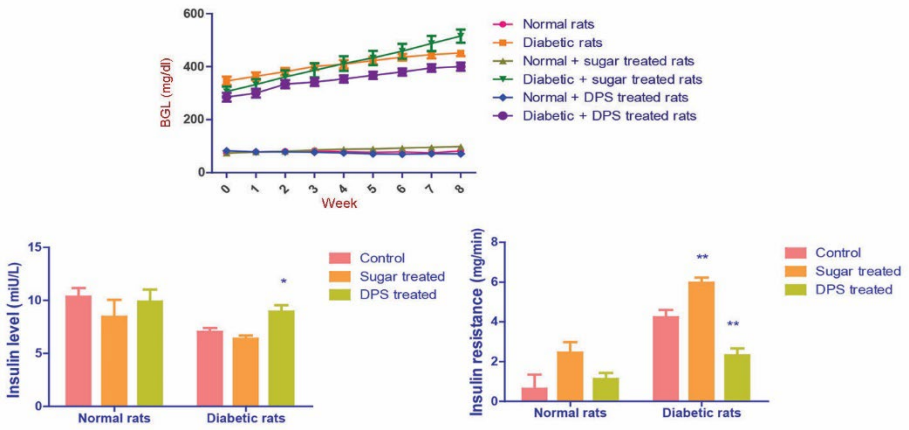

Figure 2. Effect of date palm sugar on blood glucose level, insulin level and insulin resistance.

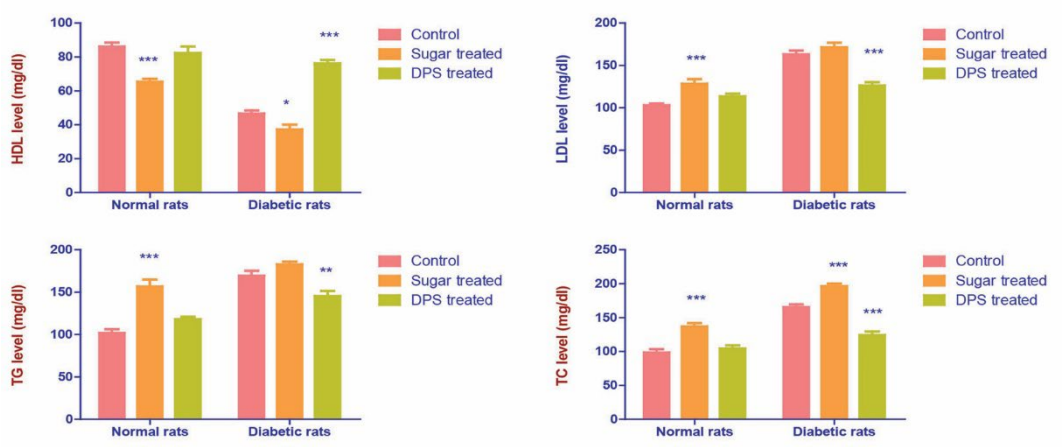

Figure 3. Effect of date palm sugar on HDL, LDL, TG and TC.

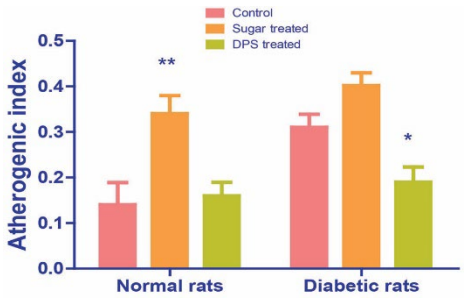

Figure 4. Effect of date palm sugar on atherogenic index.

rats. BGL level was observed to reduce in DPS treated rats compared to the other two categories. However, insulin, HDL and LDL were increased. TG and TC decreased in DPS-treated rats compared to saline and sugar-treated rats. There was no significant change observed in the atherogenic index. Moreover, the level of adiponectin was increased slightly in DPS-treated rats. The level of TNF-α and resistin also increased in DPS-treated rats (Table 5).

Phase-II studies after eight weeks of treatment show the effects of different parameters on various groups, as per Table 5. There was a significant change (decrease) in the body weight in diabetic rats. Food intake decreased in diabetic and sugar-treated rats but increased in DPS-treated rats. However, water intake increased for all conditions. In saline and sugar-treated rats, BGL levels increased, whereas in DPS rats, it showed a decrease. Contrary to sugar-treated and normal diabetic rats, the level of insulin increased in DPS-treated rats while there was no significant change in other groups. The HDL and LDL levels were higher in DPS-treated animals. The TC levels were reduced in DPS-treated

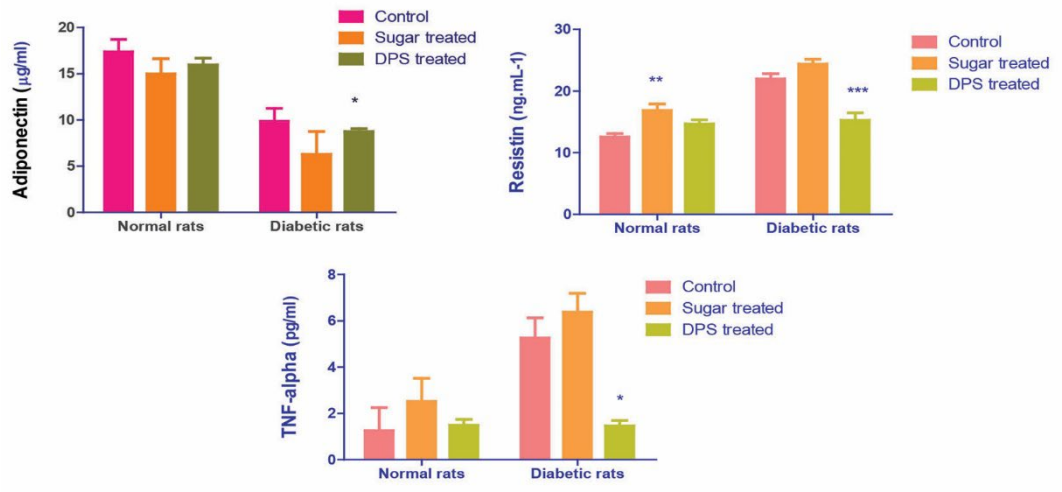

Figure 5. Effect of date palm sugar on adiponectin level, resistin and TNF-alpha.

animals. The atherogenic index, resistin and TNF-α showed a significant increase in their levels in DPS-treated rats. The adiponectin level had reduced in DPS-treated rats (Table 5).

Figures 1–5 show the results of phase-I and phase-II trials on the experimental rats.

We found that the DPS contributed to significant improvement in diabetic rats. The results of this study demonstrate that an eight-week consumption of DPS can provide advantageous effects on body weight, food intake, water intake, BGL, insulin level, insulin resistance, lipid profile, atherogenic index, adiponectin, resistin and TNF-α in diabetic rats. Thus, using DPS instead of other sugars is beneficial for diabetic individuals.

Conflict of interest: The authors declare that there is no conflict of interest.

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