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RESEARCH ARTICLE

Investigation of the Effect of Coconut Palm Sugar on Metabolic Disorders in Experimental Diabetic Rats

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Abstract

Diabetes is a metabolic disorder with many different underlying factors. Humans can develop Type 1 diabetes, which is brought on when the immune system assaults and destroys insulin, and Type 2 diabetes, which can be brought on by several variables, the most important of which is lifestyle, as well as by different genotypes. Due to the presence of polyphenols, which have high antioxidant qualities, Coconut Palm Sugar (CPS) is nutritious and has a good potential for managing diabetes. In this investigation, we took the STZ-Nicotinamide model for diabetes induction. In normal rats (Phase 1) and diabetes-induced rats (Phase 2), After exposure to table sugar and coconut palm sugar, we measured a variety of factors, including body weight, food intake, water consumption, blood sugar level, insulin level, insulin resistance, lipid profile, atherogenic index, and insulin resistance.

Keywords: Diabetes, Coconut Palm Sugar, Experimental Rats, Nicotinamide, Streptozotocin

1. Introduction

With the greatest impact on working-age adults in developing countries, diabetes is a serious hazard to global public health that is fast getting worse. At least 177 million people worldwide are affected by it, and by 2030, that number is predicted to nearly double, reaching 366 million[1]. There are two main forms of diabetes, with Type 2 being more prevalent in adults of all ages and Type 1 being more prevalent in adolescents and early children. According to the literature, Type 2 diabetes is now rising in youngsters all over the world, and it appears to have increased dramatically in the previous 15 years[2]. Additionally, Type 2 diabetes accounts for up to 45% of newly diagnosed cases in teenagers. Additionally, Type 2 diabetes accounts for 80% of new instances of paediatric diabetes in Japan and 70% of new cases among Native Americans[3,4]. An epidemiological study indicates that the number of diabetic patients in the Asia-Pacific area is significantly rising[5]. Furthermore, 3% of Europeans have Type 2 diabetes, and administrative expenditures associated with it make up about 5% of all healthcare spending[6]. Insulin resistance, a gradual reduction of insulin activity, and the inability of beta cells to make up for the diminished insulin activity are the hallmarks of Type 2 diabetes[7].

Coconut palm sugar is essentially a fairly pure form of sugar and like ordinary sugar it can contribute to obesity, diabetes and heart disease. Coconut sugar is healthier because fructose and glucose will be easily absorbed and converted into energy, while sucrose must be broken down first into monosaccharides. Palm sugar is more soluble in food additives. Consuming coconut palm sugar is healthier because it contains fructose and glucose will be easily absorbed. Coconut palm sugar also contains Fe, Zn and Cu which are important nutrients in small amounts for the biological function of the human body. CPS reduced calorific value, low glycemic index, and non-cariogenic properties Even though the CPS have less mineral content, the fat content is also smaller[8-12]. Consuming coconut sugar is healthier because fructose and glucose will be easily absorbed and converted into

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energy, while sucrose must be broken down first into monosaccharides. The complete metal content is in coconut sugar which contains Cu, Fe, Zn and Mn. Palm sugar contains Fe, Zn and Cu.

Rats are the most popular choice among the various animal species utilized in diabetes research. Nongenetic rat models are also often employed in diabetes research in addition to genetic models since they are easily available and affordable. Animals are given chemicals like streptozotocin (STZ) to create diabetes, and nicotinamide (NA)-STZ model for Type 2 diabetes has also been developed[13]. The quantity and diet of inducers significantly affect how diabetes develops in experimental animal models. Inducing diabetes requires higher doses of the inducer, which severely damages -cells at lower concentrations[14,15].

2. Materials and Methods

2.1 Experimental Materials

The local market was where the CPS formulation was purchased. It is produced by Chokanathapuram One Village, situated in Tamil Nadu. The powder was mixed with dissolved water to use it as a solvent.

2.2 Experimental Animals

The rats used in this study were male albino (SD) rats of the same age group and weight (250g-350g). 120 rats, all two-month-old, were present. Rats were procured from the SPARC research Vadodara, Gujarat, India, and kept in polypropylene cages at a constant temperature of 25 to 30 degrees Celsius and relative humidity of 45 to 55 per cent with a cycle of darkness and light lasting 12 hours each. The rats were given pelleted food and water ad libitum.

2.3 Ethics

IAEC of Parul University in Vadodara, Gujarat, India 390760, with the reference number PIPH-08/20, received ethics committee permission for the study.

2.4 Induction of Diabetes

The group of male rats only required one intraperitoneal injection of newly made nicotinamide (230 mg/kg) in saline (10 mg/100 ml) to develop diabetes. A group of rats were administered freshly generated streptozotocin (40 mg/kg) in 0.1 M citrate buffer (pH 4.5) after 15 minutes of fasting. After 72 hours, the rats' blood glucose levels were measured.

2.5 Experimental Procedure

The effects of different sweeteners on lipid and carbohydrate metabolism in healthy and diabetic people are examined in this study using in-vitro testing on healthy and diabetic rats. The main objective of this study on sweeteners is to offer secure substitutes for both healthy and diabetic people. Studies in Phases I and II are finished. The treatment lasted for around eight weeks. Phase I involved measuring the reaction while analyzing the impact of CPS on healthy male rates. We utilized SD rats, weighing 250g-350 g, aged 2–10 months. (Table 1).

In the Phase II investigation, we investigated the effects of intraperitoneal injections of 100–350 mg/kg Nicotinamide (NA) 15 minutes before intravenous administration of 40 mg/kg STZ in SD male rats with diabetes. The findings reveal that the most suitable NA dosage is 230 mg/kg (Table 2).

Eight weeks of treatment were given, and then the following parameters were evaluated: body weight,

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
Coconut palm sugar	Coconut palm sugar 500 mg/kg	Coconut palm sugar 500 mg/kg	8

Table 2. Induction of nicotinamide (NA) and streptozotocin (STZ) standards[16]

Strain	Fasting state before diabetes induction	Dose of NA (mg/kg)	Dose of STZ (mg/kg)	Time between STZ and NA injection (min)	Time of blood glucose test after diabetes induction/ fasted or non-fasted	Glucose levels (mg/dL) to be considered diabetic
SD	Overnight	230	40	15	72	> 250

food intake, water intake, BGL, insulin level, insulin resistance, lipid profile, atherogenic index, adiponectin, resistin, and TNF-α.

The experimental groups adhere to the experimental design in Table 2 once Type 2 diabetes is induced. The following parameters were assessed following the completion of the treatment for 8 weeks.

Parameters like body weight, food intake, water intake and BGL were measured weekly after completion of Phase 1 and Phase 2 study.

Insulin level, Lipid profile (including HDL, LDL, TG, TC), Serum Adiponectin level, Serum Resistin level, and Serum TNF-alpha level were measured at the end of the research study.

Atherogenic index = Log(TG/HDL) measured using this formula.

Additionally, the Coconut palm sugar toxicity investigation was performed. Three animals were employed for each stage of the procedure, with the beginning dose being 2000 mg/kg as advised by the daily human dose limit and calculated for animals. According to OECD TG 423, the Acute Toxicity investigation for "Coconut Palm Sugar" was used in this investigation. Information about the animals and their species is provided in detail in Table 3.

1. a. Animals were monitored individually after dosing for the first 30 minutes, then every hour for the following 4 hours, and then every 6 hours for the remaining 24 hours. Following that, the animals were monitored every day for a total of 14 days.
2. b. None of the animals displayed any toxicity-related symptoms or aberrant behaviour.
3. c. Each test animal's body weight was recorded weekly, as shown in Table 3. The body weight did not fluctuate in an unhealthy way.
4. d. After 14 days, a gross necropsy was performed on all test animals.

3. Result and Discussion

The results of the acute toxicity study of Coconut palm sugar are shown in Table 4.

3.1 Toxicity Study

Each animal had a toxicity test after dosing for the first 30 minutes, then every hour for the following 4, 6, and

Table 3. Dosage and groups for toxicity study of CPS

CPS level (mg/kg)	Animal No.	Body weight on Day 0 (gm)	Dose of CPS (mg)	Dose of CPS (mL)
2000 mg/kg	1	260	460	0.92
	2	220	480	0.96
	3	230	460	0.92
Repeat dose 2000 mg/kg	1	270	560	1.4
	2	250	540	1.08
	3	240	500	1.0

Table 4. Individual Animal Observations for 14 days

Dose Level	Animal No.	Body weight			Mortality	Signs of toxicity			Gross necropsy
		Day 0 (gm)	Day 7 (gm)	Day 14 (gm)		Nature	Severity	Duration	
2000 mg/kg	1	260	260	255	No	NAD	NAD	NAD	NAD
	2	220	225	225	No	NAD	NAD	NAD	NAD
	3	230	230	235	No	NAD	NAD	NAD	NAD
Repeat dose 2000 mg/kg	1	270	280	280	No	NAD	NAD	NAD	NAD
	2	250	260	265	No	NAD	NAD	NAD	NAD
	3	240	250	255	No	NAD	NAD	NAD	NAD

NAD: No abnormality detected

24 hours. The following 14 days saw daily observations of the animals. No animals displayed any toxicity-related symptoms or unusual behaviour. Each week, the test animals' body weights were recorded, and the results are shown in Table 5. The body weight didn't undergo any unusual modifications. After 14 days, a thorough necropsy was performed on all test animals. The table lists individual animal observations at a dose of 2000 mg/kg and the effects of repeated doses. (Table 5).

3.2 Results of Phase I (Normal Animals)

After eight weeks of therapy, Phase I investigations demonstrate the effects of various parameters on various groups as shown in Table 2. Weight measurements were taken before and after the course of treatment. Animals treated with CPS had 12% less body weight overall. White sugar treatment causes an increase in food intake, while CPS treatment causes a decrease. The water consumption of the CPS-treated rats was somewhat decreased, but it increased in the saline- and sugar-treated rats. Comparing CPS-treated rats to the other two categories, a decrease in BGL level was seen. However, there was an increase in insulin, HDL, and LDL. TG and TC were lower in rats fed with CPS than in those treated with saline or sugar. The atherogenic index didn't show any discernible difference. Additionally, rats given CPS had a modest increase in adiponectin levels. In rats treated with CPS, TNF- and resistin levels also rose (Table 6).

3.3 Results of Phase II (Diabetic Animals)

The effects of various factors on diverse groups are shown in Table 2 of Phase II investigations following eight weeks

Table 5. Individual Animal Cage Side Observations for dose level 2000 mg/kg

Animal ID	Observation parameters	Observation at Specific time Interval (hr)						
		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
	Diarrhea	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
	Diarrhea	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
	Diarrhea	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 6. Evaluation of biochemical parameters in Phase I trials

Parameter	Beginning of the study			End of the study		
	Saline	Sugar	CPS	Saline	Sugar	CPS
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-alpha	1.48±0.23	1.55±0.17	1.33±0.25	1±0.18	2±0.17	1±0.25

Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1)

of treatment. The body weight loss in diabetic rats was significantly different. Even diabetic and sugar-treated rats eat less, but CPS rodents eat more. In all circumstances, nevertheless, people drank more water. Rats given saline or sugar treatments had higher BGL levels than rats given CPS treatment, who had lower levels. When neither group showed any change, CPS-treated animals had higher insulin levels compared to sugar-treated rats and normal diabetic rats. In animals treated with CPS, the levels of HDL and LDL were greater. In animals treated with CPS, the TC levels were decreased. In rats treated with CPS, the atherogenic index, resistin, and TNF-levels all significantly increased. Rats treated with CPS had lower levels of adiponectin. (Table 7 and Figures 1-13).

4. Discussion

- The body weight of sugar-treated animals weight increases However, the body weight of CPS-treated animals significantly decreases in Phase 1 However in the Phase 2 study CPS treated animals were shown to increase body weight more than the diabetic and diabetic-sugar-treated animals.
- Food intake significantly increases in the sugar-treated group as compared to the saline and CPS-treated group in Phase 1. In Phase 2 study Food intake is better than diabetic and diabetic sugar-treated animals.
- In Blood glucose level: There were no significant changes in blood glucose level between the groups in the Phase 1 study. However, in the Phase 2 study, sugar control is better than the diabetic and diabetic sugar-treated animals.
- Differences were observed in lipid profile but they were non-significant were compared with saline in PHASE 1. In Phase 2 CPS treated animals have a better effect on lipid profile than the diabetic and diabetic sugar-treated animals.
- Atherogenic index: There were a decrease in the Atherogenic index in CPS treated group as compared to sugar treated group in both phase. (Phase 1 and Phase 2)
- There was an increase in the HDL level in CPS treated group as compared to sugar treated group in both Phase of the study.
- There was a decrease in the LDL level in Coconut palm sugar as compared to sugar-treated group in both phases of the study.
- In brief, CPS is better than sugar and has significant beneficial effects on Glucose, lipid profile and cytokines as compared to sugar-treated group.

Table 7. Evaluation of Biochemical parameters of Phase II trials

Parameters	Beginning of the study			End of the study		
	Saline	Sugar	CPS	Saline	Sugar	CPS
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	35±0.98	42±2.34	39±1.57	52±1.08	58±1.35	51±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±4.3 6	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±4.6 4***
Atherogenic index	0.12±0.04	0.30±0.07	0.09±0.06	0.31±0.03	0.40±0.22	0.36±0.0 3*
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-alpha	1.48±0.23	1.55±0.17	1.33±0.25	1.93±0.16	1.88±0.20	1.52±0.2 0*

Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the disease control group (Phase 2)

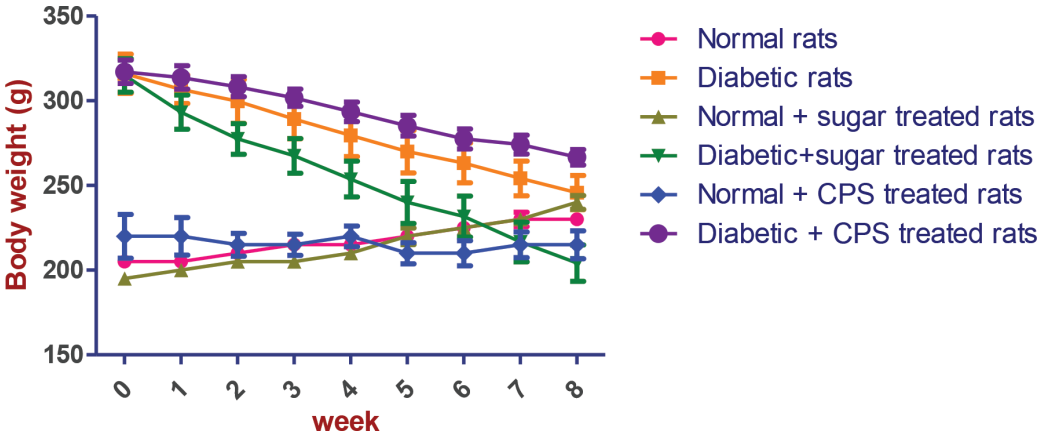


Figure 1. Effect of date palm sugar on body weight (g).

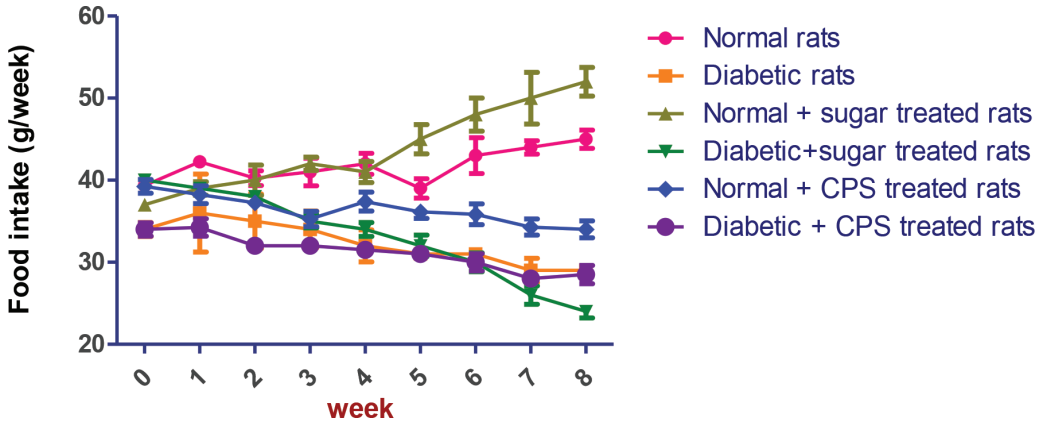


Figure 2. Effect of date palm sugar on food intake (g).

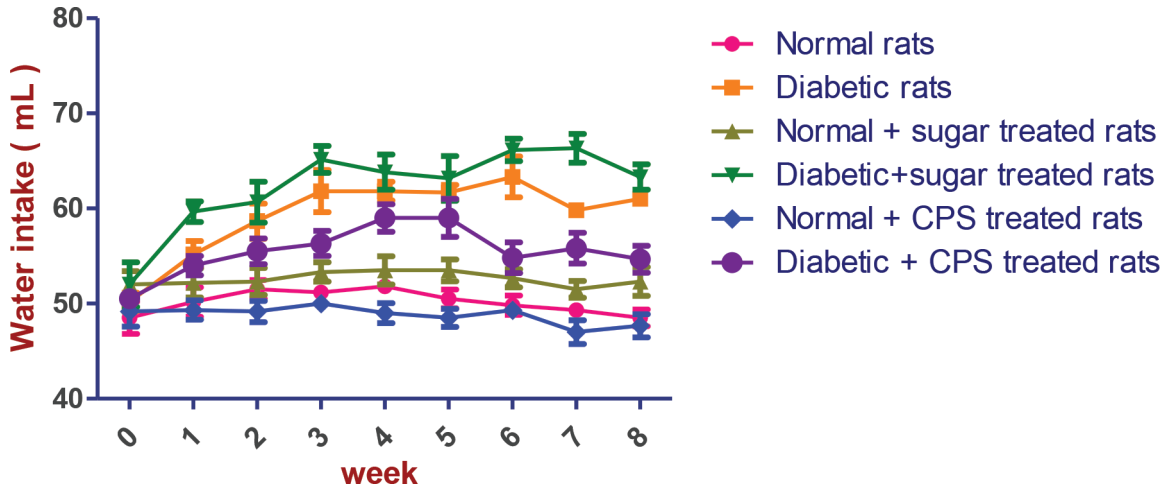


Figure 3. Effect of date palm sugar on water intake (ml).

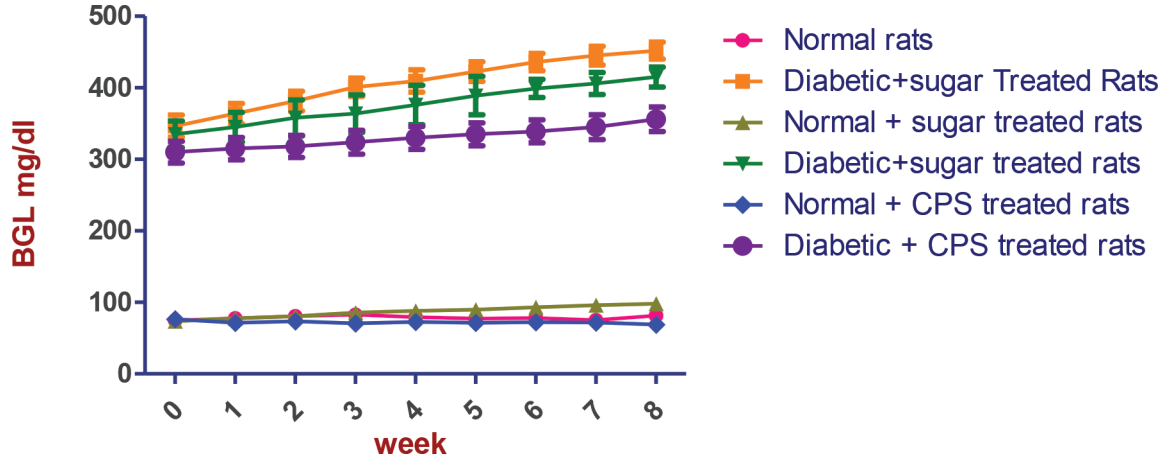
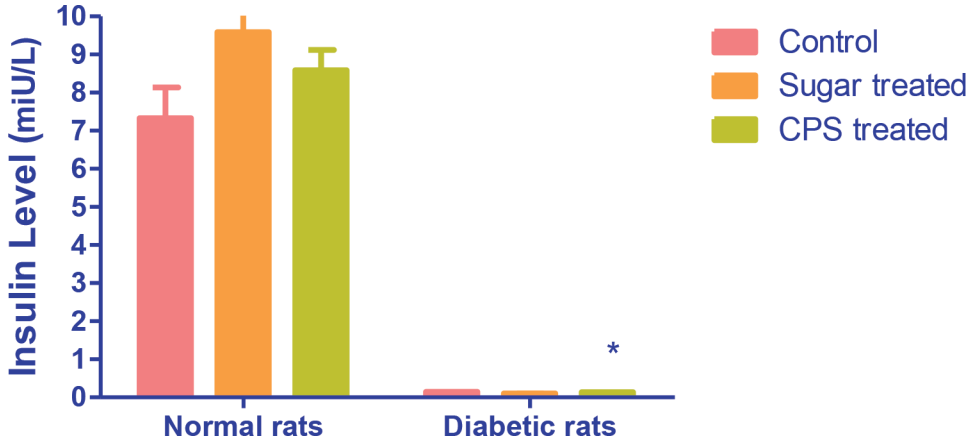
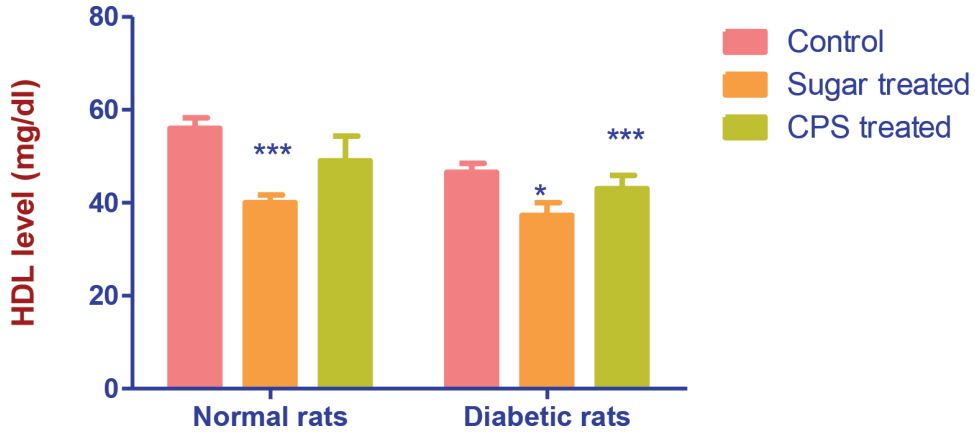


Figure 4. Effect of date palm sugar on blood glucose level (mg/dl).



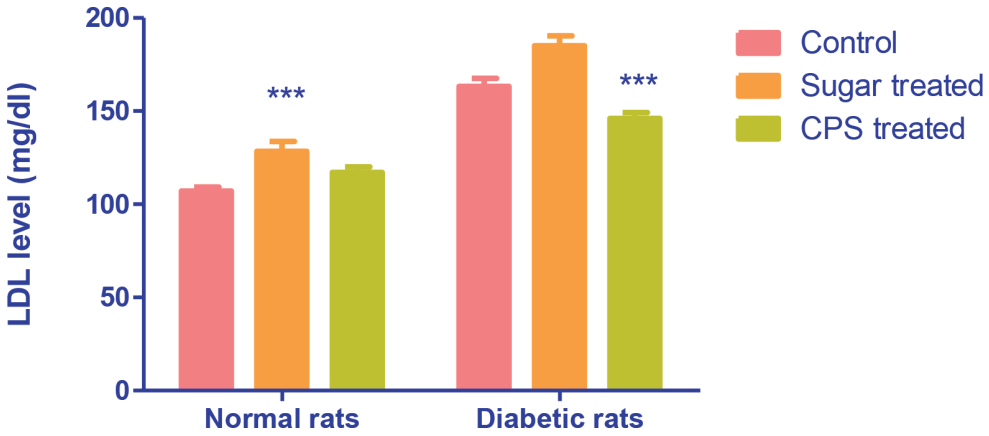
Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 5. Effect of date palm sugar on insulin level (miU/L).



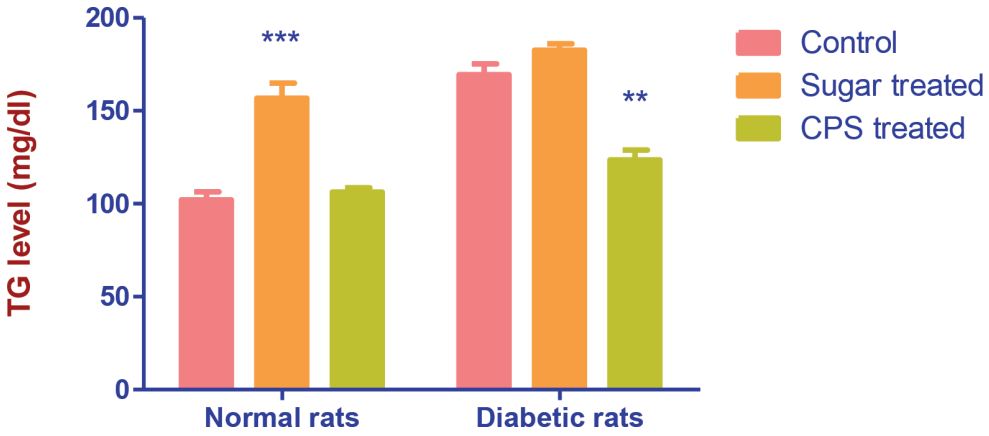
Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 6. Effect of date palm sugar on HDL level (mg/dl).



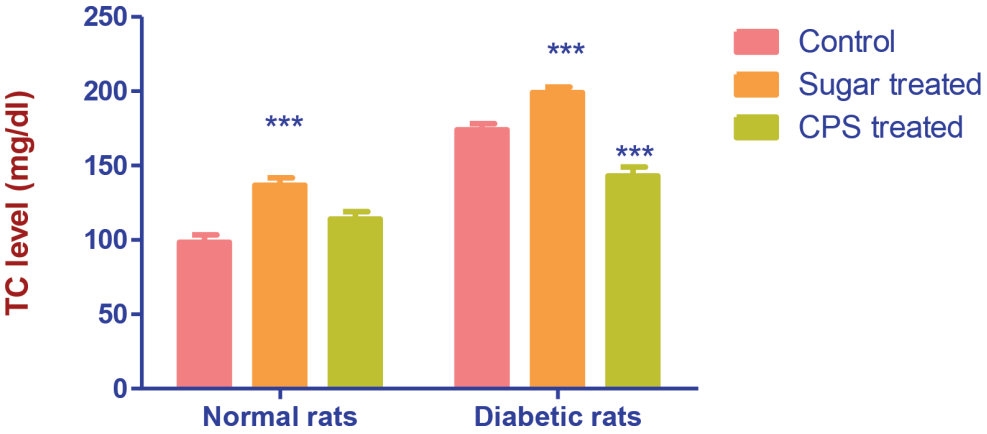
Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 7. Effect of date palm sugar on LDL level (mg/dl).



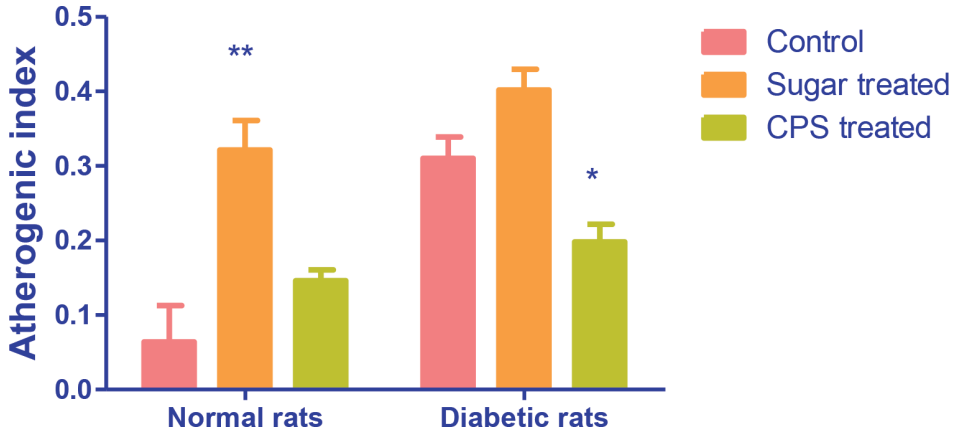
Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 8. Effect of date palm sugar on TG level (mg/dl).



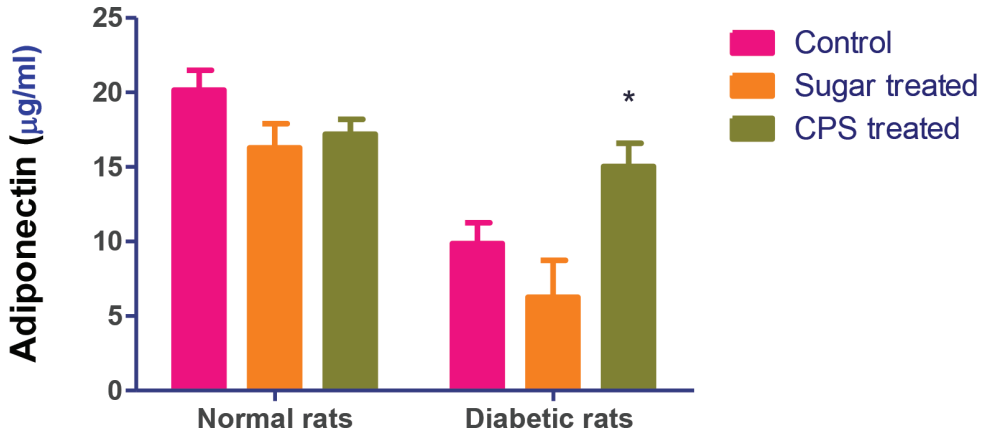
Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 9. Effect of date palm sugar on TC level (mg/dl).



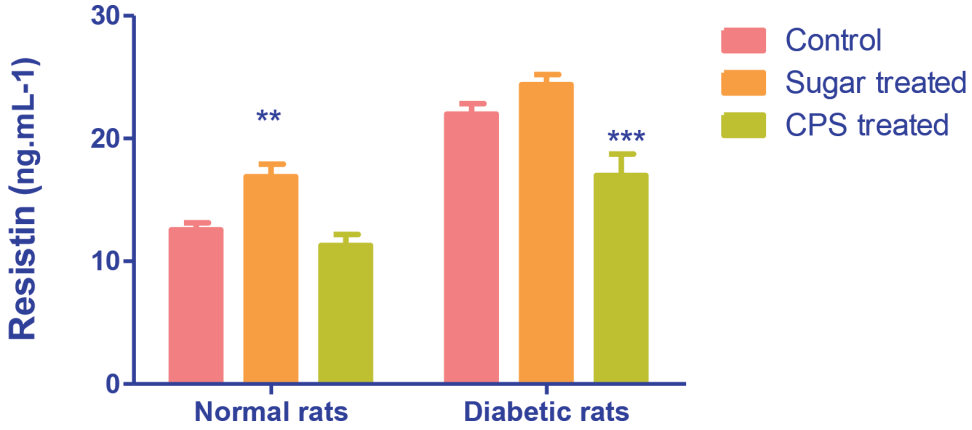
Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 10. Effect of date palm sugar on atherogenic index.



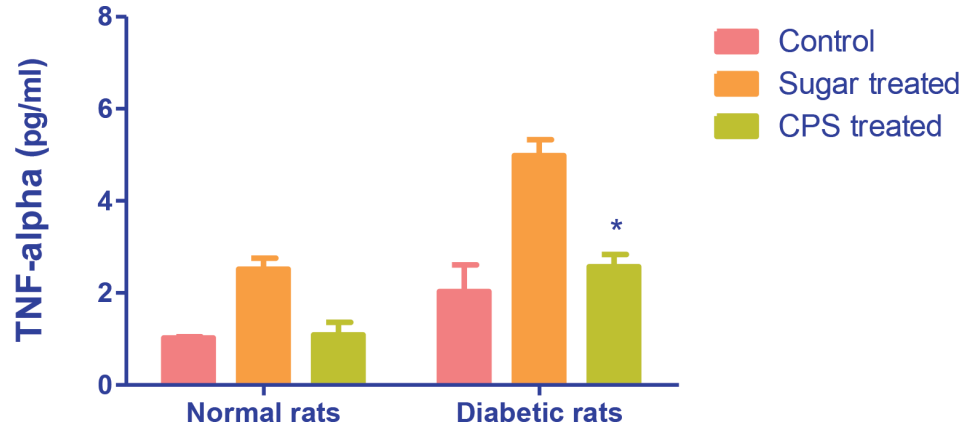
Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 11. Effect of date palm sugar on adiponectin level (µg/ml).



Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 12. Effect of date palm sugar on resistin level (ng.mL-1).



Values are Mean ± SEM (n=6), analysed by Two-way ANOVA followed by Bonferroni's test.
*denotes P < 0.05, when compared with the Normal control group (Phase 1) and disease control group (Phase 2)

Figure 13. Effect of date palm sugar on TNF-alpha level (pg/ml).

5. Conclusion

We discovered that diabetic rats significantly improved as a result of the CPS. The findings of this study show that eight weeks of CPS consumption can have positive impacts on body weight, food intake, water intake, BGL, insulin level, insulin resistance, lipid profile, atherogenic index, adiponectin, resistin, and TNF alpha in diabetic rats. Therefore, using CPS instead of other sugars is advantageous for those with diabetes.

6. References

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