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Hypoglycemic and antioxidant effects of Opuntia streptacantha cladodes juice in alloxan-induced diabetic rats

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ABSTRACT

We assessed the hypoglycemic, hypolipidemic as well as the antioxidant potential effects of the *Opuntia streptacantha* cladodes juice (OSCJ) in alloxan-induced diabetic rats (140 mg/kg of body weight (bw)). The results evidenced that alloxan-induced diabete, caused weight loss, polyphagia, hyperglycemia, hyperlipidemia and the disturbance of enzymatic and non-enzymatic antioxidant systems. The daily oral administration of OSCJ (30 g/kg of b.w during 4 weeks) to diabetic rats clearly improved the antioxidant status in liver and kidney. Such fact is materialized by a decrease in the lipid peroxidation product, thiobarbituric acid-reacting substances (TBARS) level and an increase in glutathione peroxidase (GPX), superoxide dismutase (SOD) and catalase (CAT) activities. Histopathological investigation of the pancreatic tissue of alloxan-diabetic rats indicated the presence of necrosis in the islets of Langerhans cells. The curative effect of OSCJ was well evidenced by normal islets of Langerhans cells, which explain its antidiabetic effect.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder which may be suspected or recognized clinically by one or more of the characteristic symptoms such as polyuria, polyphagia and unsolved weight loss (Eliza et al. 2009). A worldwide survey reported that the estimated incidence of diabetes and projection for year 2030 is 350 million (Qiao et al. 2011). Because of the complex mechanism involved in DM, many of the current anti-diabetic chemical agents have some limitations and even some severe adverse-effects (May et al. 2002). Insulin therapy is used for the management of diabetes mellitus, but there are several drawbacks including insulin resistance and fatty liver after long-term treatment (Yaryura-Tobias et al. 2001). In recent years, there has been renewed interest in plant medicine for the treatment of different diseases. The search for effective and safer antidiabetic plant drugs is, thus, of great importance. Some studies have demonstrated the hypoglycemic activity of the prickly pear cactus extract on non-diabetics and diabetes-induced rats or diabetic humans. The hypoglycemic activity of a purified extract from stems of *Opuntia fuliginosa* Griffiths was evaluated on streptozotocin-induced diabetic rats. (Trejo-González et al. 1996). Plasma glucose concentrations in streptozotocin-induced diabetic and non-diabetic rats were reduced by the oral administration of *Opuntia megacantha* leaf extracts (20 mg/100 g b.wt.) (Bwiti et al. 2000). Recently, Lopez-Romero et al. (2014) reported that consumption of *Opuntia ficus-indica* could reduce postprandial blood glucose, serum insulin, and plasma glucose-dependent insulinotropic peptide peaks, as well as increase antioxidant activity in healthy people and patients with type 2 diabetes…..The cladode of *O. streptacantha Lem.* is traditionally used to treat gastritis, intestinal colic and ulcers (Argueta 1994). Also, other studies have examined inhibition of replication of DNA and RNA viruses by extracts of *O. streptacantha* (Ahamd et al. 1996). To accomplish this, we evaluated the effect of *O. streptacantha Lem.* on blood glucose and lipid levels in alloxan–induced diabetic rats, we also analyzed the levels of TBARS, CAT in kidney and liver tissues, as well as the activities of SOD and GPx. The present investigation was designed to evaluate the hypoglycemic effect of *O. streptacantha Lem.* cladode juice (OSCJ) by using in vivo model, with a view to establish the pharmacological basis for its hypoglycemic use in folk medicine.

Materials and methods

O. streptacantha stem preparation

Fresh cladodes from *O. streptacantha* were collected from municipal areas of Gafsa (Tunisia) in Mai 2015. Cactus cladodes were washed and ground. 30 g of the crushed cladodes were mixed with 100 ml of distilled water, agitated for 15 min at room temperature and then centrifuged at 4000 rpm for 15 min. The sample was filtered then collected and stored at -20°C until use (Galati et al. 2001).

Test animals

Two month adult male Wistar rats (n=30), weighting about 130–140 g, purchased from Pasteur Institute (Tunisia), were housed and kept under a controlled environment: temperature (22 ± 1 °C), relative humidity (70 ± 4%) with a 12 h light/dark cycle (Alimi et al. 2010). The rats were fed with a commercial pellet diet then acclimatized for these conditions before starting the experiment. Animals were cared according to the guidelines and Tunisian code of practice for the Care and Use of Animals for Scientific Purposes.

Induction of experimental diabetes mellitus

The rats were fasted overnight before induction of diabetes with alloxan (Sigma, St. Louis, MO, USA; 140 mg kg^{-1}, IP). Alloxan was freshly dissolved in NaCl buffer (0.01 mol/l, pH 4.5) (Matteucci et al. 2008), and maintained on ice

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before use. Diabetes was confirmed in the Alloxan-treated rats by measuring the fasting blood glucose concentration 72 h after injecting Alloxan. The rats with blood glucose levels more than 250 mg/dl were considered to be diabetic and were used in the experiment (Eidi et al. 2009). Hyperglycaemia was confirmed by using a commercial glucometer (Acku-Check Active - Roche Diagnostics, Germany).

Experimental procedure

After the induction of diabetes, the rats were divided into 5 groups (n=6):

NC, normal control group: rats receiving distilled water; NOS, normal group treated daily by OSCJ; DC, rats with alloxan-induced diabetes mellitus served as diabetic control; DOS, diabetic rats treated daily with OSCJ and DINS, diabetic rats treated daily by insulin.

The OSCJ was suspended in distilled water and administered orally through the sonde once daily. The treatment was continued for 4 weeks, and the body weight of each animal was measured weekly. In addition, food and water intakes were measured daily. At the end of the 4th week trial, the animals were anesthetized with diethyl ether, and the blood was collected via abdominal aorta puncture. The blood samples were centrifuged at 2500 rpm for 15 min to obtain the serum, which was kept at −70°C until analysis.

Testing of fasting blood glucose levels (FBG) and oral glucose tolerance (OGTT)

The FBG levels were measured weekly. Blood was collected from the tail vein, and the FBG level was measured using a commercial glucometer (Acku-Check Active, Roche, Mannheim, Germany). After 4 weeks of animal treatments, rats were fasted for 12 h and then subjected to OGTT. Rats were loaded with glucose (Sigma; 1 g/kg bw) by oral sonde, and blood was drawn from the tail vein before glucose solution administration (time 0) at 30, 60, 90, and 120 min after glucose load. Blood glucose levels were measured using a commercial glucometer (Acku-Check Active) according to (Hahm et al. 2011).

Biochemical analysis of serum

Concentrations of total cholesterol (TC), triglycerides (TGs), creatinine and urea in the serum were measured using commercially available kits (Biomaghreb, Tunisia). The lipid peroxidation in the liver and kidneys of control and all treated groups of animals was measured by the quantification of TBARS determined by the method of Buege and Aust (1984).

The activity of SOD was assayed by the spectrophotometric method of Marklund and Marklund (1975). The activities of GPX and CAT were measured by the method of Suzuka et al. (1989) and Aebi (1984), respectively. The level of total protein was determined by the method of (Bradford 1976).

Histological

The pancreatic tissues was harvested from the sacrificed animals, fragments from tissues were fixed in a 4% paraformaldehyde solution, embedded in paraffin and stained with Hematoxylin and Eosin (H&E). Tissue preparations were observed and examined microscopically.

Statistical analysis

Results were expressed as mean±SEM. Data were statistically analyzed for variance using one-way analysis variance (ANOVA) according to Dunnett's. The differences were considered significant at P≤0.01.

Results and Discussion

Body weight, water and food intake

As can be seen in Table 1, NC group was found to be stable in its body weight, while NOS group showed a negligible increase in the body weight. DOS rats showed an increase in body weight compared to that of DC rats (P<0.01). Table 1 illustrates also, the food and the water intake. Results showed that the induction of diabetes was accompanied by polyphagia in DC rats. In fact, the rate of daily food consumption and water intake in DC rats significantly increased compared to NC rats (P<0.01). While, the treatment of diabetic rats by the OSCJ decreased the rate of daily food consumption compared to DC group (P<0.01). The high rate of food and water intake and the severe loss of body weight are among the characteristics associated with diabetes mellitus (Maiti et al. 2004). Indeed, the weight loss was associated with a correction in abnormalities due to osmotic diuresis and glucose intolerance, resulting from inadequate insulin secretion or hyperlipidemia in diabetes mellitus (Yang et al. 2008). The administration of the OSCJ for 30 days was shown to be able to protect diabetic rats from the massive loss of body weight and significantly attenuate the polyphagia. This curative effect given by the cladode juice of *O. streptacantha* could be explained by the dietary and medicinal qualities of this medicinal plant. In fact, it was reported that the high content of flavonoids, polyphenols and carotenoids within *O.*

Table 1.Food intake, water intake and body weight gain of nondiabetic control and diabetic rats treated.

	NC	NOS	DC	DOS	DINS
Food intake (g/d)	50±2.4	49.13±2.1	80±3.2[a]	61.33±2.9[b]	59.80±3.01[b]
Water intake (ml/d)	220±4.2	200±4.6	500±5.1[a]	350±4.9[b]	300±5.12[b]
Body weight gain (g)*	4.24±0.70	12.01±1.66[a]	-24.21±4.22 [a]	4.28±0.99[b]	11.24±2.45[b]

Values are expressed as means ± SE (n = 6). Data were statistically analyzed for variance using one-way analysis variance (ANOVA) according to Dunnett's. The differences were considered significant at P≤0.01. Abbreviations: NC, normal control; NOS, normal rats treated by OSCJ; DC, rats with alloxan-induced diabetes mellitus (DM) served asdiabetic control; DOS, diabetic rats treated by OSCJ; DINS, diabetic rats treated by insulin.

*Body weight gain was calculated as final body weight−initial body weight.

[a]significantly different from the normal control group (P<0.01).

[b]significantly different from the diabetic control group (P<0.01).

Table 2. Change of fasting glucose level in rats with alloxan-induced diabetes over 4 weeks.

Groups	Day 0	Day 7	Day 14	Day 21	Day 30
NC	115.99±2.14	116.44±2.19	117.36± 3.11	119.47±3.89	122.41±2.77
NOS	115.02±2.20	114.31±2.16	112.68± 2.54	110.11± 1.99	100.45±1.10
DC	261.22±9.11[a]	275.33±9.78[a]	280.64±9.85[a]	290.24±9.92[a]	314.36±10.22[a]
DOS	262.37±7.88	197.22±7.01[b]	195.11±6.55[b]	190.02±6.12[b]	170.32±5.43[b]
DINS	265.40±8.01	189.34±6.51[b]	179.23±5.12[b]	170.17±4.63[b]	161.22± 3.22[b]

Values are expressed as means ± SE (n = 6). Data were statistically analyzed for variance using one-way analysis variance (ANOVA) according to Dunnett's. The differences were considered significant at P≤0.01. Abbreviations: NC, normal control; NOS, normal rats treated by OSCJ; DC, rats with alloxan-induced diabetes mellitus (DM) served asdiabetic control; DOS, diabetic rats treated by OSCJ; DINS, diabetic rats treated by insulin.

Values are expressed in mg⁄dl.

[a]significantly different from the normal control group (P<0.01).

[b]significantly different from the diabetic control group (P<0.01).

Table 3.Effect of OSCJ on serum urea and creatinineprofiles in nondiabetic control and diabetic.

	NC	NOS	DC	DOS	DINS
Urea (µmol/l)	6±0.54	6.2±0.66	12.5±0.79[a]	7±0.65[b]	6.7±0.59 [b]
Creatinine (µmol/l)	34±1.2	33.95±1.5	49±1.1[a]	36±1.2[b]	35.01±0.9 [b]

Values are expressed as means ± SE (n = 6). Data were statistically analyzed for variance using one-way analysis variance (ANOVA) according to Dunnett's. The differences were considered significant at P≤0.01. Abbreviations: NC, normal control; NOS, normal rats treated by OSCJ; DC, rats with alloxan-induced diabetes mellitus (DM) served asdiabetic control; DOS, diabetic rats treated by OSCJ; DINS, diabetic rats treated by insulin.

[a]significantly different from the normal control group (P<0.01).

[b]significantly different from the diabetic control group (P<0.01).

Table 4. Blood glucose changes in rats with alloxan-induced diabetes by OGTT.

Groups	0 min	30min	60min	90min	120min
NC	122.41±2.77	139.21±3.89	130.56±3.78	125.76±3.50	123.50±3.69
NOS	100.45±1.10	130.36±2.87	120.48±1.80	114.33±1.76	99.72±2.17
DC	314.36±10.22[a]	339.19±7.89[a]	350.24±11.01[a]	331.19±10.43[a]	320.21±13.01[a]
DOS	170.32±5.43[b]	198.15±7.13[b]	185.23±6.49[b]	177.44±6.32 [b]	171.21±5.65[b]
DINS	161.22±3.92[b]	190.54±5.32[b]	180.72±5.17[b]	171.09±6.44[b]	165.62± 3.89[b]

Values are expressed as means ± SE (n = 6). Data were statistically analyzed for variance using one-way analysis variance (ANOVA) according to Dunnett's. The differences were considered significant at P≤0.01. Abbreviations: NC, normal control; NOS, normal rats treated by OSCJ; DC, rats with alloxan-induced diabetes mellitus (DM) served asdiabetic control; DOS, diabetic rats treated by OSCJ; DINS, diabetic rats treated by insulin.

Values are expressed in mg⁄dl.

[a]significantly different from the normal control group (P<0.01).

[b]significantly different from the diabetic control group (P<0.01).

Streptacantha may play a crucial role in the recovery of the body weight, food and water intake (Hahm et al. 2011).

Fasting blood glucose levels and oral glucose tolerance test The effects of OSCJ on FBG levels in diabetic rats are shown in Table 2. The FBG levels significantly decreased from the first week in DOS rats compared with DC group (P<0.01). The administration of the OSCJ for 4 weeks revealed a significant improvement in the blood glucose levels of DOS rats compared with DC group. The blood glucose levels of NC and NOS groups reached a peak, 30 min after the oral administration of glucose and gradually decreased to the preglucose load level (Table 3). The blood glucose levels of the DC group reached a peak, 60 min after the oral administration of glucose, however the FBG levels of DOS group attained a peak, 30 min after the oral administration of glucose and then showed a significant decrease (P<0.01). This finding is in line with the results of Hahm et al. (2011), who reported the significant decrease in serum glucose levels in rats with STZ-induced diabetes when treated with *Opuntia humifusa* stem (OHSt). Due to its richness in bioactive molecules, the cladodes juice of *O. streptacantha* could increase the secretion of insulin by its antioxidant activity (El-Alfy et al. 2005). However, according to Kuti (2004), the *O. streptacantha* contained a high level of quercetin which appears as the major flavonoid. The work of Knishinsky (2004) could explain further the hypoglycemic effect of *O. Streptacantha*, where some enzymes being part of this plant were shown to act like natural insulin. Elsewhere, Andrade-Cettoa and Wiedenfeld (2011) attributed this hypoglycemic effect to the control of blood glucose levels which is manifested by a blocking of the hepatic glucose exit.

Serum Total cholesterol and Triglycerides levels

The serum lipid profiles are shown in Table 4. There was a significant increase in TC and TGs of DC rats compared to the NC (P<0.01). In addition, DOS group had a significant lower serum levels of TC and LDL cholesterol compared with DC group (P<0.01). However, the HDL cholesterol levels was increased in DOS group compared to DC group (0.60 mmol/l, 0.40 mmol/l respectively) (P<0.01). The administration of OSCJ also had a significant effect on the levels of TGs. In fact, DOS rats showed a considerable decrease in serum TGs concentration compared to DC rats (1.30 mmol/l, 3.12 mmol/l respectively) (P<0.01).

Our results are in agreement with those of Gupta et al. (2009), who suggest that in DM, hyperglycemia was accompanied with dyslipidemia, which is characterized by significant higher values of serum TC, LDL-C, TGs and significant lower values of HDL-C compared to NC rats. Several mechanisms may explain the alteration of the serum lipid profile. There is evidence that insulin plays an important role in lipid metabolism. Hyperinsulinemia has been documented to enhance hepatic VLDL synthesis, and thus may directly contribute to the increased plasma TG and LDL cholesterol levels observed in obese adolescents (Steinberger et al. 1995). Resistance to the action of insulin on lipoprotein lipase in peripheral tissues may also contribute to elevated TG and LDL cholesterol levels (Sadur et al. 1984). While, decreasing serum HDL-C level in STZ-induced diabetic rats, may be attributed to the decrease of lecithin-cholesterol acetyl transferase (LCAT), which is responsible of the estrification of cholesterol in HDL (Abdallah 2008).

The drop of HMG CoA (Hydroxy-méthyl-glutaryl-coenzyme A) reductase activity resulted in reduced hepatic cholesterol synthesis and theoretically lowered blood cholesterol concentrations (Groff and Gropper 2000). On the other hand, soluble fibers were usually fermented by colonic microflora producing short chain fatty acids (SCFA), which reduced serum and liver cholesterol concentrations. SCFA inhibit the synthesis of hepatic triacylglycerols and therefore reduce serum lipids (Suzuki and Kajuu 1983; Hara et al. 1999).

Serum urea and creatinine profiles

Changes of serum urea and creatinine profiles are shown in Table 5. Higher serum urea and creatinine profiles were observed in DC group compared to NC group (12.5 µmol/l, 6.0 µmol/l and 49.0 µmol/l, 34.0 µmol/l, respectively) (P<0.01). Serum urea and creatinine profiles were decreased in DOS group compared to DC group (7.0 µmol/l, 12.5 µmol/l and 36.0 µmol/l, 49.0 µmol/l, respectively) (P<0.01).

Table 5. Effect of OSCJ on serum lipid profiles in nondiabetic control and diabetic rats.

	NC	NOS	DC	DOS	DINS
TC (mmol/l)	1.09±0.06	0.89± 0.05	2.95±0.34[a]	1.91±0.16[b]	1.30±0.05[b]
HDL-C(mmol/l)	0.50±0.03	0.58±0.04	0.40±0.02[a]	0.60±0.03[b]	0.66±0.04[b]
LDL(mmol/l)	0.17±0.01	0.14±0.01	0.20±0.04[a]	0.11±0.02[b]	0.13±0.01[b]
TG (mmol/l)	1.07±0.09	0.95±0.09	3.12±0.27[a]	1.30±0.27[b]	1.10±0.11[b]

Values are expressed as means ± SE (n = 6). Data were statistically analyzed for variance using one-way analysis variance (ANOVA) according to Dunnett's. The differences were considered significant at P≤0.01. Abbreviations: NC, normal control; NOS, normal rats treated by OSCJ; DC,rats with alloxan-induced diabetes mellitus (DM) served asdiabetic control; DOS, diabetic rats treated by OSCJ; DINS, diabetic rats treated by insulin; TC, Total cholesterol; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; TG, Triglycerides.

[a]significantly different from the normal control group (P<0.01).

[b]significantly different from the diabetic control group (P<0.01).

Table6.TBARS (nM/mg protein) levels, GPX (U/mg protein/min) activities and enzyme activities of SOD (U/mg) and CAT (U/mg), in liver and kidney after4weeks of treatment in all groups.

	TBARS		GPX		SOD		CAT	
Groups	Liver	Kidney	Liver	Kidney	Liver	Kidney	Liver	Kidney
NC	0.53±0.2	1.1±0.38	11.26±0.7	5.01±0.2	13±0.5	16.2±0.41	60.12±2.8	66.02±2.4
NOS	0.5±0.18	1.12±0.36	11.23±0.6	6.12±0.32	12.6±0.6	15.8±0.3	62.14±2.5	65.13±2.1
DC	1.02±0.35[a]	1.8±0.48[a]	3.5±0.11[a]	2.30±0.21[a]	7.5±0.31[a]	10±0.22[a]	34.01±1.5[a]	35.16±2.5[a]
DOS	0.65±0.26[b]	1.25±0.5[b]	9.5±0.43[b]	4.2±0.1[b]	11.5±0.62[b]	14.5±0.5[b]	55.15±2[b]	60.07±2.8[b]
DINS	0.57±0.24[b]	1.14±0.52[b]	11.09±0.37[b]	4.7±0.15[b]	12.21±0.58[b]	15.3±0.47[b]	58.19±1.8[b]	63.11±2.6[b]

Values are expressed as means ± SE (n = 6). Data were statistically analyzed for variance using one-way analysis variance (ANOVA) according to Dunnett's. The differences were considered significant at P≤0.01. Abbreviations: NC, normal control; NOS, normal rats treated by OSCJ; DC,rats with alloxan-induced diabetes mellitus (DM) served as diabetic control; DOS, diabetic rats treated by OSCJ; DINS, diabetic rats treated by insulin; TBARS, thiobarbituric acid-reacting substances; GPX, glutathione peroxidase; SOD, superoxide dismutase and CAT, catalase.

[a]significantly different from the normal control group (P<0.01).

[b]significantly different from the diabetic control group (P<0.01).

In this regards, Kondeti et al. (2010) have reported that STZ-induced diabetic rats account for the observed decrease in the total protein content. Increased urea production in diabetes could be associated to enhanced catabolism of both liver and plasma proteins. The treatment by *O. streptacantha* appreciably normalized the content of urea (Kondeti et al. 2010). During diabetes, creatinine was increased in the serum, suggesting an impairment of kidney functions. *O.streptacantha* showed a clear improvement in kidney functions, perhaps due to their antioxidant properties (Hassan et al. 2009).

Antioxidant levels

Changes of TBARS, GPX, SOD and CAT activities in liver and kidney are summarized in Table 6. The administration of insulin significantly regulated the level of antioxidant activities and corrected the oxidative damages in the liver and kidney of the DC rats

O. streptacantha treatment decreased significantly TBARS concentrations in liver by 36.27% and in kidney by 30.55% in DOS rats compared to DC rats (P<0.01). However, the treatment of NOS rats with the cladodes juice showed no significant difference in liver or in kidney TBARS values compared to NC rats. In diabetes, hypoinsulinaemia increased the activity of enzyme fatty acyl-coenzyme A oxidase, which initiates β oxidation of fatty acids, resulting in lipid peroxidation (Saumya and Basha 2011).

The GPX levels were significantly decreased in liver and kidney of DC group than NC group (P<0.01). Decreased glutathione in diabetes could be the result of the low synthesis or the high degradation of GPX by increased oxidative stress (Matkovies et al. 1998). *O. streptacantha* treatment enhanced GPX in DOS group compared to DC group. In fact, the level of GPX was (9.5±0.43 U/mg protein/min) against (3.5±0.11 U/mg protein/min) and (4.2±0.1 U/mg protein/min) against (2.30±0.21 U/mg protein/min) in liver and kidney, respectively (P<0.01).

Daily treatment of DOS rats by OSCJ significantly increased SOD and CAT activities when compared to DC rats (P<0.01). Hence, the SOD activity increased from 7.5±0.31 U/mg (in DC) to 11.5±0.62 U/mg (in DOS) in liver. The same activity also increased from 10±0.22 U/mg (in DC) to 14.5±0.5 U/mg (in DOS) in kidney. We encountered the same behavior for CAT activity (Table 6). Within NOS group, there is no significant change in liver or in kidney antioxidant enzymes activities, as compared to NC rats (Table 6).

Cactus ability to prevent and protect against oxidative damage is due to the presence of several antioxidants compounds as ascorbic acid, vitamin E, carotenoids, reduced glutathione, flavonoids and phenolic acids actually detected in fruits and vegetables of different varieties of cactus (Kuti 2004; Tesoriere et al. 2005; Shim et al. 2006).

Histological studies

The results of histopathological alterations in the pancreatic islet tissues of experimental rats are depicted in Fig. 1. Histopathological examinations showed that in DC group, alloxan administration elicited severe injury of pancreatic β-cells, such as a decrease in islets cell numbers, cell damage and death (Fig. 1C), as compared to the NC group (Fig. 1A). In NOS group, the administration of OSCJ did not show effects on pancreas (Fig. 1B) compared with NC group. Treatment of DOS rats with *O. streptacantha* showed a significant restoration in the pancreatic histology (Fig. 1D) compared to DC rats. Pancreatic β-cells loss in diabetes is probably due to an autoimmune response. In fact, ROS produced during inflammation are considered as a predisposing factors and increased mitochondrial ROS production during hyperglycemia may be central too much of the pathology of diabetes (Kowluru et al. 2006). Atangwho et al. (2007) have reported that flavonoids of plants can exert a protective effect against oxidative stress damage in organs.

From this study, we can conclude that OSCJ displayed significant hypoglycemic effects. The cladodes juice also showed an improvement in lipid profile and body weights. On the other hand, OSCJ presented a good antioxidant property, as evidenced by an increase in antioxidants status and a decrease in lipid peroxidation, which may protect from the risk of diabetic complications. The mechanism of action of the active components of cladodes juice is presently unknown.

While it is not possible to identify the active principle in the *O. streptacantha* or its relationship with other recognized hypoglycemic components until it has been isolated and characterized. It is intended to thoroughly characterize the hypoglycemic component by biochemical analysis.

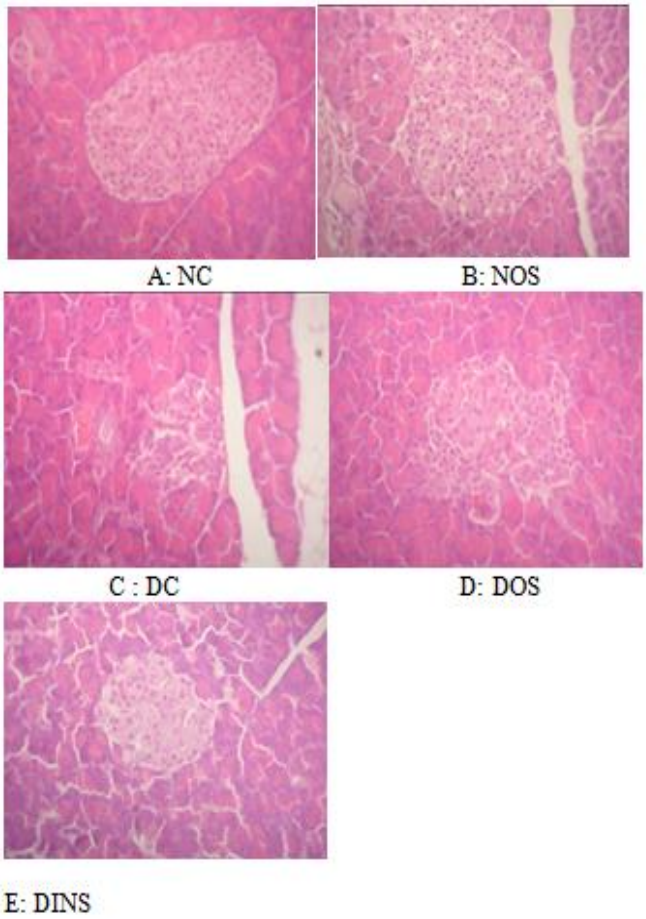

Figure 1.Histologic findings with H&E staining of Langerhans islets of alloxan-treated rat pancreas.Abbreviations: NC, normal control; NOS, normal rats treated by OSCJ; DC,rats with alloxan-induced diabetes mellitus (DM) served as diabetic control; DOS, diabetic rats treated by OSCJ; DINS, diabetic rats treated by insulin.

References

Abdallah I. (2008):Evaluation of Hypoglycemic Activity of *Opuntiadillenii*Haw Fruit Juice in Streptozotocin-Induced Diabetic Rats. E. J. H. M. 33,544–558

AebiH. (1984): Catalase in vitro. Method.Enzymol.105, 121-6

Ahmad A., Davies J., Randall S., Skinner G. R. (1996): Antiviral properties of extract of *Opuntiastreptacantha*. Antiviral Res. 30, 75-85

Alimi M., HfaiedhaN., Bouoni Z., Hfaiedha M., Saklyb M., Zourgui L., Ben Rhoumab K. (2010): Antioxidant and antiulcerogenic activities of *Opuntiaficusindica f. inermis*root extract in rats. Phytomedicine. 17,1220-1226

Andrade-Cettoa A., Wiedenfeld H. (2011):Anti-hyperglycaemic effect of *OpuntiastreptacanthaLem*. J. Ethnopharmacol. 133,940-943

ArguetaV.(1994): Atlas of the Traditional Mexican Medicinal Plants. National Indigenous Institute, Mexico, pp. 1051-1052

Atangwho I. J., Ebong P. E., Egbung G. E., EtengM. U., Eyong E. U. (2007): Effect of *Vernoniaamygdalina* Del. on liver function in alloxan-induced hyper glycemic rats. J. Pharm. Bioresour. 4,25–31

BradfordM. (1976): A rapid and sensitive methodfor the quantitation of microgram quantities of proteinutilizing the principle of protein-dye binding. Anal.Biochem.72,248-254

BuegeJ. A., AustS. D. (1984): Microsomal lipid peroxidation. Method.Enzymol.105, 302-10

BwitiP., MusabayaneC. T., NhachiC. F. (2000): Effects of *Opuntiamegacantha* on blood glucose and kidney function in streptozotocin diabetic rats. J. Ethnopharmacol. 69, 247-52

Eidi A., Maryam E. (2009): Antidiabetic effects of sage (*Salvia officinalis L.)*leaves in normal and streptozotocin-induced diabetic rats. Diabetes.Metab.Syndr. 3,40-4

El-AlfyA., Ahmed A., Fatani A. (2005): Protective effect of red grape seeds proanthocyanidins against induction of diabetes by alloxan in rats. Pharmacol.Res. 52, 264-270

Eliza J., Daisy P., Ignacimuthu S., Duraipandiyan V. (2009): Normo-glycemic and hypolipidemic effects of costunolide isolated from *Costusspeciosus (Koen ex. Retz.)Sm*. in streptozotocin-induced diabetic rats. Chem. Biol. Interact. 179,329-334

Galati E., Monforte M., Tripodo M., Aquino A., Mondello M. (2001) :Anti-ulcer activity of *Opuntiaficus-indica (L.) Mill.* (Cactaceae): ultrastructural study. J. Ethnopharmacol. 76,1-9

Groff J. L., Gropper S. S. (2000): Advanced nutrition and human metabolism. Belmont, CA Wadsworth.

Gupta S., Sharma S. B., BansalS. K., PrabhuK. M. (2009): Antihyperglycemic and hypolipidemic activity of aqueous extract of *Cassia auriculata L*. leaves in experimental diabetes. J. Ethnopharmacol. 123,499-503

Hahm S. W., Park J., Son Y. S. (2011): *Opuntiahumifusa stems* lower blood glucose and cholesterol levels in streptozotocine-induced diabetic rats. Nutr. Res. 31, 479–487

Hamden K., Boujbiha M. A., Masmoudi H., Makni-Ayadi F., Jamoussi K., Elfeki A. (2009): Combined vitamins (C and E) and insulin improve oxidative stress and pancreatic and hepatic injury in alloxan diabetic rats. Biomed.Pharmacother. 63, 95-99

Hara H., HagaS., Aoyama Y., Kiriyama S. (1999):Short chain fatty acids suppress cholesterol synthesis in rat liver and intestine. J.Nutr. 129,942-948

Hassan H. A., El-Agmy S. M., Gaur R. L., Fernando A., Raj M. H. G., Ouhtit A. (2009): *In vivo* evidence of hepato and reno-protective effects of garlic oil against sodium nitrite-induced oxidative stress. Int. J. Biol. Sci. 5, 249-255

Knishinsky R. (2004): Prickly Pear Cactus Medecine; Treatments for Diabetes, Cholesterol and the Immune System. 1. Prickly pear – Therapeutic use. I. Title. Healing Arts Press Rochester, Vermont, 50, 44-48.

KondetiV. K., BadriK. R., MaddiralaD.R., ThurS.K. M., FatimaS. S., KasettiR. B. (2010): Effect of *Pterocarpussantalinus* bark, on blood glucose, serum lipids, plasma insulin and hepatic carbohydrate metabolic enzymes in streptozotocin induced diabetic rats. Food Chem. Toxicol.48,1281-1287

KowluruR. A, Kowluru V, Xiong Y, Ho Y. S. (2006): Overexpression of mitochondrial superoxide dismutase in mice protects the retina from diabetes-induced oxidative stress. *Free Radical Bio. Med*.41,1191–1196

Kuti J. O. (2004): Antioxidant compounds from four *Opuntia*cactus pear fruit varieties. Food Chem. 85, 527-533

López-Romero P., Pichardo-Ontiveros E., Avila-Nava A., Vázquez-Manjarrez N., Tovar A. R., Pedraza-Chaverri J., Torres N. (2014): The Effect of Nopal (*OpuntiaFicusIndica*) on Postprandial Blood Glucose, Incretins, and Antioxidant

Activity in Mexican Patients with Type 2 Diabetes after Consumption of Two Different Composition Breakfasts. J. Acad. Nutr. Diet.114, 1811-8

Maiti R., Jana D., Das U. K., Ghosh D. (2004): Antidiabetic effect of aqueousextract of seed of*Tamarindusindica*in streptozotocin-induceddiabetic rats. J. Ethnopharmacol. 92, 85-91

MarklundS., MarklundG. (1975): Involvement of the superoxide anion radical in the autoxidation of pyrogallol and convenient assay for superoxide dismutase. Eur. J. Biochem. 47, 469-474

Matkovies B., KotoromanM., VargaI. S., HaiD. Q., Varga C. (1998): Oxidative stress in experimental diabetes induced by streptozotocin. Acta Physiol. Hung. 85, 29-38

Matteucci E., Giampietro O. (2008): Proposal open for discussion: defining agreed diagnostic procedures in experimental diabetes research. J. Ethnopharmacol. 115,163–72

May L. D., LefkowitchJ. H., KramM. T., Rubin D. E. (2002): Mixed hepatocellularch-olestatic liver injury after pioglitazone therapy. Ann. Intern. Med. 136,449–452

Mohamed A. K., Bierhaus A., Schiekofer S., Tritschler H., Ziegler H., NawrothP. P. (1999): The role of oxidative stress and NF(β) activation in late diabetic complications. Biofactors10,175-179

PanicoA.M., CardileV., Garufi F., Puglia C., Bonina F., Ronsisvalle G. (2005): Protective effects of *Capparisspinosa* on chondrocytes. Life Sci. 77, 2479-2488

Park E. H., KahngJ. H., PaekE. A. (1998): Studies on the pharmacological actions of cactus: identification of is anti-inflammatory effect. Arch. Pharm. Res. 21, 30-34

Qiao W., Zhao C., Qin N., Zhai H. Y., Duan H. Q. (2011): Identification of trans-tiliroside as active principle with anti-hyperglycemic, anti-hyperlipidemic and antioxidant effects from *Potentillachinesis*. J. Ethnopharmacol. 135,515-521

SadurC. N., Yost T. J., Eckel R. H. (1984): Insulin responsiveness of adipose tissuelipoprotein lipase is delayed but preserved in obesity. J. Clin. Endocr.Metab.59,1176-82

SaumyaS. M., BashaP. M. (2011): Antioxidant effect of *Lagerstroemia speciosaPers*(Banaba) leaf extract in streptozotocin-induced diabetic mice. Indian J. Exp. Biol. 49,125-131

Shim H. C., Hwang H. J., Kang K. J., Lee B. H. (2006): An antioxidative and antiinflammatory agent for potential treatment of osteoarthritis from *Ecklonia cava*. Arch. Pharm. Res. 29,165-171

SivajyothiV., DeyA.,Jayakar B., Rajkapoor B. (2006): Antihyperglycemic, antihyperlipidemic and antioxidant effect of *Phyllanthusrheedii* on streptozotocin induced diabetic rats. Iran. J. Pharm. Res. 7,53-59

Steinberger J., Moorehead C., Katch V., Rocchini A. P. (1995): Relationship between insulin resistance and abnormal lipid profile in obese adolescents. J. Pediatr. 126, 690-5

Suzuka I., Daidoji H., Matsuoka M., Kadowaki K., Takasaki Y., NakaneP.K., Moriuchi T. (1989): Gene for proliferating-cell nuclear antigen (DNA polymerase δ auxiliary protein) is present in both mammalian and higher plant genomes. Proc. Natl. AcadSci. USA. 86, 3189-3193

Suzuki M., Kajuu T. (1983): Suppression of hepatic lipogenesis by pectin and galacturonic acid orally-fed at the separate timing from digestion-absorption of nutrient in rats. J. Nutr. Sci. Vitaminol. 29,553-562

Tesoriere L., Fazzari M., Allegra M., LivreaM. A. (2005): Biothiols, taurine, and lipid-soluble antioxidants in the edible pulp of Sicilian cactus pear (*Opuntiaficus-indica*) fruits and changes of bioactive juice components upon industrial processing. J. Agr. Food Chem. 53,7851-7855

Trejo-González A., Gabriel-Ortiz G., Puebla-PérezA. M., Huízar-Contreras M.D., Munguía-MazariegosM.R., Mejía-Arreguín S., Calva E. (1996): A purified extract from prickly pear cactus (*Opuntiafuliginosa*) controls experimentally induced diabetes in rats. J. Ethnopharmacol. 55, 27-33

Yang N., Zhao M., Zhu B., Yang B., Chen C., Cui C., Jiang Y. (2008): Anti-diabetic effects of polysaccharides from *Opuntiamonacantha* cladode in normal and streptozotocin induced diabetic rats.Innov.Food Sci. Emerg.9,570-574

Yaryura-Tobias J. A., Pinto A., Neziroglu F. (2001): Anorexia nervosa, diabetes mellitus, brain atrophy, and fatty liver. Inter. J. Etiol. Disorders **30,** 350-353.