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Antihyperglycemic, antihyperlipidemic and antioxidant activities of polysaccharides from *Catathelasma ventricosum* in streptozotocin-induced diabetic mice

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ABSTRACT

It is the first time to extract polysaccharides (CVPs) from *Catathelasma ventricosum*. The antihyperglycemic and antioxidant activity of CVPs in streptozotocin-induced diabetic mice were examined. Compared with untreated diabetic mice, the administration of CVPs for 30 days caused a significant decrease in the concentrations of blood glucose, total cholesterol (TC), triglycerides (TGs), low-density lipoprotein-cholesterol (LDL-C) and maleic dialdehyde (MDA), and a significant increase in the concentrations of high density lipoprotein-cholesterol (HDL-C) and the activities of antioxidant enzymes. Specially, when normal mice were treated with CVPs, all detection indexes and pathologic morphologies of liver, kidney and pancreas are similar to untreated normal mice, which indicated CVPs are safe for normal mice. In addition, the average molecular weight of CVPs was estimated to be from 3.7×10^3 to 1.7×10^7 Da and they were mainly composed of glucose (93.5%) with the conformation of α-D-Glucopyranose.

1. Introduction

Diabetes mellitus is considered as a major health risk in the world. The number of adults with diabetes mellitus in the world will increase to 300 million by the year 2025. The major part of this numerical increase will occur in Asia, mainly China and India (Chan et al., 2001; King et al., 1998). Diabetes mellitus is a group of diseases characterized by chronic hyperglycemia due to deficiency of insulin action. The deficiency of insulin action, a common basis of diabetes, leads to characteristic abnormalities in the metabolism of carbohydrate, lipid, protein and so on (Kuzuya et al., 2002). Although different hypoglycemic drugs have been synthesized for the treatment of diabetes mellitus, many synthetic drugs have a number of serious side effects (May et al., 2002). Management of hyperglycemia with minimal side effects in clinical experience and relatively low costs is still a challenge to the medical system (Sun et al., 2008). Comparatively low side-effects and low cost, phytochemicals from natural resources open new avenues for the treatment of various diseases including diabetes (Li et al., 2011a).

Catathelasma ventricosum is a resource of traditional Chinese herbal medicine. Even now, the parturient woman in many rural communities will drink *C. ventricosum* soup to boost immunity. *Compendium of Materia Medica*, an ancient Chinese medical book, has some records about *C. ventricosum*. It is grown massively in southwestern China and it also can be found in northern North America. It is recognized as a source of various bioactive compounds possessing medicinal properties such as anticancer, antihyperglycemic and antioxidant activity (Liu et al., 2012; Ohtsuka et al., 1973).

In our previous study, the aqueous extract of *C. ventricosum* showed high antihyperglycemic and antioxidant potential (Liu et al., 2012). As we know, polysaccharide is one of the most important active compounds in the aqueous extract. However, there is not any report about the polysaccharide from *C. ventricosum* hitherto, let alone its bioactivity. Therefore, the aim of the present work was to evaluate its antihyperglycemic, antihyperlipidemic and antioxidant effects in streptozotocin (STZ)-induced mice.

2. Materials and methods

2.1. Chemicals

Glibenclamide, Streptozocin (STZ), T-series dextran, uronic acid standards and monosaccharide standards were from Sigma–Aldrich Co. LLC. (USA). SXT Blood Glucose Monitoring System and Test Strip were from Sinocare Co., Ltd. (China). Reagent

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kits for the determination of total cholesterol (TC), triglyceride (TG), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), catalase (CAT), maleic dialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), vitamin C, vitamin E, insulin and glycogen were from the Jianchen Bioengineering Institute (China). All other chemicals and solvents were of the highest commercial grade and obtained from Sinopharm Chemical Reagent Co., Ltd. (China).

2.2. Materials and preparation of the extract

The samples of *C. ventricosum* were collected under *Pinus massoniana* and *Picea asperata* in Sichuan mountainous area (Southwest China). All samples were freeze-dried and powdered (40 meshes). *C. ventricosum* powder (200 g) was defatted and decolorized with 95% ethanol. After centrifugation (5000 rpm, 10 min), supernatant was discarded. The residue was extracted thrice with 4 L distilled water (85 °C, each time for 3 h). The extracts were combined and concentrated in a rotary evaporator. After removing protein (according to the Sevag method (Vilkas and Radjabi-Nassab, 1986)), the extract was dialysed in a DEAE cellulose bag against distilled water for 2 days to remove low molecular weight materials. Subsequently, 3-fold volumes of ethanol (48 h, 4 °C) were added to the extract, and the precipitates were collected by centrifugation (5000 rpm, 10 min). Polysaccharides (CVPs) powder was obtained by lyophilizing the precipitates (32.77 g).

2.3. Analysis of polysaccharides

The content of CVPs was determined by the phenol–sulphuric acid method (Dubois et al., 1956) the protein in the CVPs was quantified according to Bradford's method (Bradford, 1976); the Fourier transform infrared (FT-IR) spectra and ultraviolet (UV) spectra of samples were recorded; the relative molecular weight, monosaccharide composition and uronic acids composition were determined by high performance gel permeation chromatography (HPGPC), GC (Li et al., 2011b) and high performance anion-exchange chromatography (HPAEC) respectively (Wang et al., 2010).

2.4. Animals and experimental design

Male ICR mice (18 ± 2 g) were purchased from Shanghai SLAC Slac laboratory animal Company. The mice were housed in a segregated air-conditioned room at 25 °C with a lighting schedule of 12 h light and 12 h dark. Mice were provided with a basal diet (purchased from Shanghai SLAC Slac laboratory animal Company) and free access to drinking water. The approval of this experiment was obtained from the Institutional Animal Ethics Committee of Jiangnan University (Wuxi, China). All experimental animals were overseen and approved by the Animal Care and Use Committee of our Institute before and during experiments.

Mice were adapted to diet for 1 week before the start of the experiments. The mice were fasted for 12 h prior to the induction of diabetes. STZ freshly prepared in buffer solution (0.1 mol/L sodium citrate and 0.1 mol/L citric acid, pH 4.2–4.5), was immediately injected intraperitoneally with a single dose of 150 mg/kg. After 72 h, the mice displaying polydipsia and polyuria were chosen for measuring fasting glucose levels by blood glucose test strips. Hyperglycemic mice with blood glucose levels greater than 16.8 mmol/L were considered diabetic and were selected for experiments (Fujita et al., 2005).

Mice were randomly allocated into the following groups (six mice in each group): Group I: normal mice as control; Group II: STZ-induced diabetic mice; Group III: normal mice received CVPs at the high dose (2 g/kg/day) by oral administration; Group IV: STZ-induced diabetic mice receiving glibenclamide (20 mg/kg/day) by oral administration as positive control; Group V: STZ-induced diabetic mice receiving CVPs at the low dose (0.5 g/kg/day) by oral administration; Group VI: STZ-induced diabetic mice receiving CVPs at the high dose (2 g/kg/day) by oral administration.

After 30 days of treatment, the animals were fasted overnight. The body weight and blood glucose levels were measured. Blood was collected from the eyes and immediately centrifuged for 5 min at 5000 rpm at 4 °C to obtain serum (stored at −70 °C), then the animals were sacrificed by cervical dislocation, pancreas and parts of liver and kidney tissues were excised from the animals for the pathological histology by hematoxylin and eosin (HE) stain. Other parts of the liver and kidney were removed promptly and stored at −70 °C.

2.5. Biochemical analysis

Blood samples were obtained from the tail vein of the overnight fasted mice and their glucose levels were tested by blood glucose test strips.

The serum concentration of insulin, TC, TG, HDL-C and LDL-C were determined using commercial available kits and and according to their manuals.

Livers and kidneys were homogenized with 5 mmol/L Tris–HCl containing 2 mmol/L EDTA, pH 7.4. Homogenates were centrifuged (3000 rpm 10 min, 4 °C) and the supernatant was immediately used for the assays of hepatic glycogen (just in livers), CAT, MDA, SOD, GSH-Px, vitamin C and vitamin E level according to the instructions of their corresponding kits respectively.

2.6. Statistical analysis

All assays were carried out in triplicate. The results were expressed as mean ± SD and analyzed through one-way analysis of variance (ANOVA) followed by Tukey's test. This test was carried out by use of the SPSS (v. 16.0 program). A value of $p < 0.05$ was considered significant.

3. Results and discussion

3.1. Analysis of polysaccharides

In order to explore the relationship between structural features and antihyperglycemic and antioxidant activity of CVPs, some

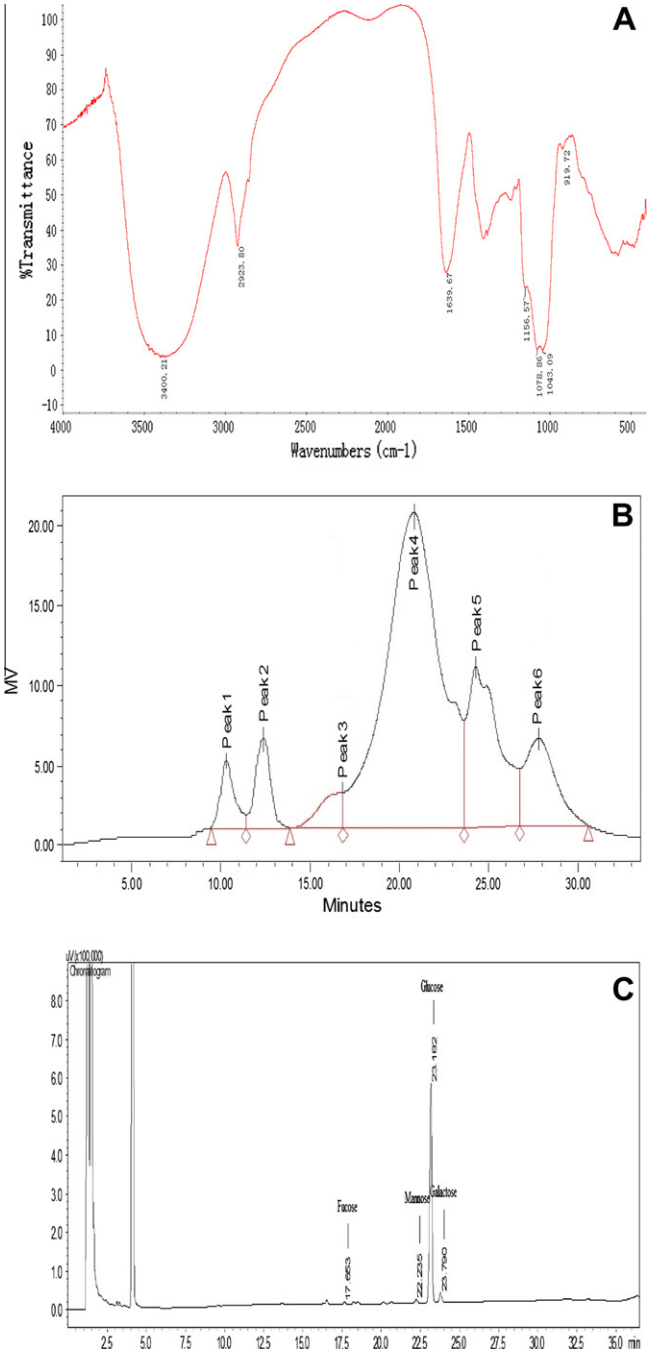

Fig. 1. Analysis of polysaccharides (FT-IR spectra (A), average molecular weight (B) and monosaccharide composition (C) of CVPs).

Table 1
Effect of CVPs on body weight and blood glucose level in STZ-induced diabetic mice.

Group	Body weight (g)		Blood glucose (mmol/L)	
	Pre-experiment	Post-experiment	Pre-experiment	Post-experiment
I, control	31.27 ± 2.34[b]	36.66 ± 1.63[b]	5.97 ± 0.62[b]	5.89 ± 0.36[b]
II, diabetic mice	25.29 ± 3.58[a]	28.41 ± 2.63[a]	27.39 ± 3.07[a]	28.42 ± 2.12[a]
III, normal mice + CVPs[c]	30.97 ± 2.01[b]	37.03 ± 4.19[b]	6.18 ± 0.44[b]	6.59 ± 1.01[b]
IV, positive control	25.32 ± 2.35[a]	31.94 ± 3.02[a]	27.14 ± 1.82[a]	10.93 ± 2.64[a,b]
V, diabetic mice + CVPs[d]	25.63 ± 2.13[a]	30.11 ± 3.54[a]	27.89 ± 2.22[a]	14.38 ± 1.94[a,b]
VI, diabetic mice + CVPs[c]	25.94 ± 1.77[a]	31.06 ± 2.24[a]	27.66 ± 1.14[a]	14.82 ± 0.96[a,b]

Values are expressed as mean ± SD for six mice in each group. One-way ANOVA repeated measures with Duncan's multiple rang test was used to calculate statistical significance.
[a] Indicates statistical significance of $p < 0.05$ compared to the I group.
[b] $p < 0.05$ compared to the II group.
[c] Administration of CVPs with high dose.
[d] Administration of CVPs with low dose.

Table 2
Effect of CVPs on MDA level, activities of antioxidant enzymes and concentrations of non-enzymic antioxidants in liver and kidney of STZ-induced diabetic mice.

Group	I, control	II, diabetic mice	III, normal mice + CVPs[c]	IV, positive control	V, diabetic mice + CVPs[d]	VI, diabetic mice + CVPs[c]
Liver						
GSH-Px (U/mg protein)	689.63 ± 39.74[b]	414.92 ± 42.25[a]	709.28 ± 45.82[b]	491.22 ± 32.55[a]	665.42 ± 43.04[b]	659.15 ± 36.84[b]
SOD (U/mg protein)	342.92 ± 21.40[b]	286.49 ± 18.48[a]	386.44 ± 23.19[b]	306.62 ± 20.06[a]	326.72 ± 23.39[b]	344.71 ± 19.83[b]
CAT (U/mg protein)	109.92 ± 9.24[b]	49.34 ± 10.48[a]	114.82 ± 8.73[b]	63.82 ± 13.73[a]	82.31 ± 12.77[b]	81.23 ± 12.29[b]
MDA (nmol/mg protein)	2.74 ± 0.64[b]	6.82 ± 0.96[a]	2.83 ± 0.73[b]	5.24 ± 1.04[a]	3.69 ± 0.93[b]	3.77 ± 1.23[b]
Vitamin C (μg/mg protein)	5.29 ± 1.08[b]	1.93 ± 0.28[a]	5.12 ± 1.46[b]	2.84 ± 0.73[a]	2.96 ± 0.74[a]	2.78 ± 1.18[a]
Vitamin E (μg/g tissue)	27.29 ± 2.84[b]	13.93 ± 2.07[a]	33.83 ± 4.34[b]	14.80 ± 1.84[a]	17.90 ± 3.99[a]	18.03 ± 2.74[a]
Kidney						
GSH-Px (U/mg protein)	494.13 ± 23.85[b]	318.30 ± 19.72[a]	593.32 ± 24.88[a,b]	362.82 ± 17.73[a]	507.73 ± 22.19[b]	524.72 ± 34.81[b]
SOD (U/mg protein)	194.73 ± 12.83[b]	105.72 ± 9.63[a]	397.73 ± 19.55[a,b]	122.84 ± 10.03[a]	249.38 ± 13.27[b]	293.77 ± 10.74[b]
CAT (U/mg protein)	63.92 ± 6.42[b]	37.63 ± 3.84[a]	67.32 ± 6.28[b]	39.82 ± 3.92[a]	49.72 ± 5.11[a,b]	49.02 ± 8.20[a,b]
MDA (nmol/mg protein)	2.18 ± 0.18[b]	6.08 ± 0.33[a]	2.24 ± 0.21[b]	4.92 ± 0.72[a]	2.11 ± 0.14[b]	2.33 ± 0.28[b]
Vitamin C (μg/mg protein)	3.37 ± 1.38[b]	1.69 ± 0.05[a]	3.60 ± 0.72[b]	1.33 ± 0.45[a]	2.04 ± 0.19[a]	1.84 ± 0.32[a]
Vitamin E (μg/g tissue)	37.38 ± 6.72[b]	12.28 ± 5.82[a]	39.73 ± 11.09[b]	17.54 ± 4.82[a]	36.72 ± 7.29[b]	41.73 ± 14.37[b]

Values are expressed as mean ± SD for six mice in each group. One-way ANOVA repeated measures with Duncan's multiple rang test was used to calculate statistical significance.
[a] Indicates statistical significance of $p < 0.05$ compared to the I group.
[b] $p < 0.05$ compared to the II group.
[c] Administration of CVPs with high dose.
[d] Administration of CVPs with low dose.

Table 3
Effect of CVPs on concentrations of serum TC, TG, HDL-C and LDL-C in STZ-induced diabetic mice.

Group	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
I, control	1.85 ± 0.21[b]	1.12 ± 0.15[b]	0.96 ± 0.03[b]	0.73 ± 0.11[b]
II, diabetic mice	3.52 ± 0.38[a]	2.31 ± 0.24[a]	0.38 ± 0.14[a]	1.23 ± 0.25[a]
III, normal mice + CVPs[c]	1.58 ± 0.24[b]	0.97 ± 0.03[b]	1.05 ± 0.03[b]	0.72 ± 0.12[b]
IV, positive control	2.32 ± 0.37[a,b]	1.35 ± 0.33[a,b]	0.77 ± 0.12[b]	0.84 ± 0.05[b]
V, diabetic mice + CVPs[d]	2.13 ± 0.14[b]	1.57 ± 0.20[a,b]	0.86 ± 0.06[b]	0.93 ± 0.06[a,b]
VI, diabetic mice + CVPs[c]	1.97 ± 0.06[b]	1.42 ± 0.11[a,b]	0.92 ± 0.04[b]	0.96 ± 0.10[a,b]

Values are expressed as mean ± SD for six mice in each group. One-way ANOVA repeated measures with Duncan's multiple rang test was used to calculate statistical significance.
[a] Indicates statistical significance of $p < 0.05$ compared to the I group.
[b] $p < 0.05$ compared to the II group.
[c] Administration of CVPs with high dose.
[d] Administration of CVPs with low dose.

analyses of polysaccharides were performed. And the results are as follows:

The content of the polysaccharide in CVPs was more than 99%, CVPs had a negative response to the Bradford test and no absorption at 280 or 260 nm in the UV spectrum, indicating the absence of proteins and nucleic acids.

Fig. 1 showed the FT-IR spectra of CVPs, the band of absorption between 3600 cm^{-1} and 3200 cm^{-1} was due to O–H stretching. The band of absorption between 1200 cm^{-1} and 1000 cm^{-1} was due to C–O stretching. The absorption at 3400.21 cm^{-1}, 2923.80 cm^{-1} and 1639.67 cm^{-1} were assigned to the –OH stretching, C–H stretching and hydration respectively. The characteristic absorption at 919.72 cm^{-1} was ascribed to α-D-Glucopyranose. Yu et al. (2009) and Ye et al. (2011) reported their polysaccharides (with hypoglycemic activity) possessed the similar glucose conformation with us.

CVPs were eluted as six main peaks with HPGPC, and their average molecular weight were estimated to be 1.7×10^7, 1.0×10^6,

Table 4
Effect of CVPs on hepatic glycogen content and insulin level in STZ-induced diabetic mice.

Group	I, control	II, diabetic mice	III, normal mice + CVPs[c]	IV, positive control	V, diabetic mice + CVPs[d]	VI, diabetic mice + CVPs[c]
Glycogen content (mg/g)	3.82 ± 0.24[b]	2.06 ± 0.05[a]	3.79 ± 0.17[b]	3.55 ± 0.33[b]	2.82 ± 0.07[a,b]	2.80 ± 0.13[a,b]
Insulin level (μIU/ml)	18.72 ± 2.73[b]	6.82 ± 1.25[a]	18.44 ± 3.02[b]	17.59 ± 2.15[b]	12.44 ± 1.04[a,b]	13.17 ± 0.96[a,b]

Values are expressed as mean ± SD for six mice in each group. One-way ANOVA repeated measures with Duncan's multiple rang test was used to calculate statistical significance.
[a] Indicates statistical significance of $p < 0.05$ compared to the I group.
[b] $p < 0.05$ compared to the II group.
[c] Administration of CVPs with high dose.
[d] Administration of CVPs with low dose.

7.2×10^5, 1.4×10^4, 5.4×10^3 and 3.7×10^3 Da respectively in reference to dextran T-series standard. After hydrolyzation and acetylation, the sample was detected by GC analysis. The result showed that CVPs were mainly composed of glucose (93.5%), simultaneously fucose (0.7%), mannose (1.4%) and galactose (4.3%) were also detected. The result of HPAEC indicated CVPs did not contain uronic acid. Though, many different molecular weight, component and conformation of polysaccharides were reported recently (Tong et al., 2008; Ye et al., 2011; Zou et al., 2010), the relationship between structural features of polysaccharides and their bioactivity is still not clear.

3.2. Effect of CVPs on body weight and blood glucose level in STZ-induced diabetic mice

STZ- induced diabetes has been considered as a useful experimental model for studying the activity of hypoglycemic agents. STZ-induced diabetes is characterized by a severe loss in body weight and some diabetic complications (Junod et al., 1969; Li et al., 2006; Sarkhail et al., 2007; Zhao et al., 2011).

Table 1 shows the body weight and blood glucose level of different experimental groups. The diabetic mice exhibited a significant increase in fasting blood glucose level and a significant loss of body weight as compared to normal mice (I group). The administration of CVPs or glibenclamide for 30 days caused a significant decrease ($p < 0.05$) in blood glucose levels (<16.8 mmol/L) in diabetic mice when compared with untreated diabetic mice (II group). Simultaneously, the body weight of diabetic mice was also observed after administration of CVPs or glibenclamide, but there was no significant increase ($p > 0.05$) when compared with II group. The decrease in body weight observed in diabetic mice might be the result of protein wasting due to unavailability of carbohydrate for utilization as an energy source (Chen and Ianuzzo, 1982). Yu et al. (2009) and Cui et al. (2012) reported the similar results, however Zhang et al. (2012) and Huang et al. (2012) indicated the body weights of treated groups administrated with polysaccharides were significantly increased as compared to diabetic mice.

3.3. Effect of CVPs on MDA level, activities of antioxidant enzymes and concentration of non-enzymic antioxidants in liver and kidney of STZ-induced diabetic mice

Diabetes mellitus is associated with generation of reactive oxygen species leading to oxidative damage particularly in liver and kidney (Kakkar et al., 1998; Mohamed et al., 1999). And Can et al. (2004) indicated the liver damage caused by diabetes is probably due to lipid peroxidation subsequent to free radical production. Many researches demonstrated the presence of antioxidant enzymes such as SOD, CAT, and GSH-Px and non-enzymic antioxidants such as vitamins E and C in diabetes mellitus can scavenge free radicals and increase the response of antioxidant defense systems to oxidative stress in the body (Aksoy et al., 2005; Yu et al., 2009). And MDA level is associated with the diminution of the activities of SOD, GSH-Px and CAT and the levels of vitamin C

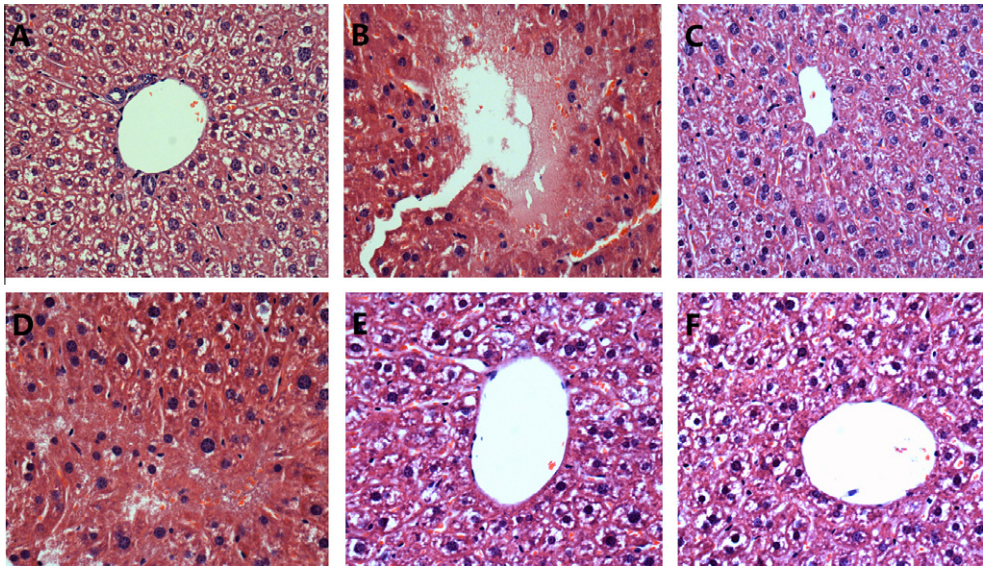

Fig. 2. Effects of CVPs treatment on liver damage in STZ-induced diabetic mice. A: I group (normal mice); B: II group (untreated diabetic mice); C: III group (administration of CVPs with high dose for 30 days in normal mice); D: IV group (administration of glibenclamide for 30 days in diabetic mice); E: V group (administration of CVPs with low dose for 30 days in diabetic mice); F: VI group (administration of CVPs with high dose for 30 days in diabetic mice). Hematoxylin/eosin staining; magnification 400×.

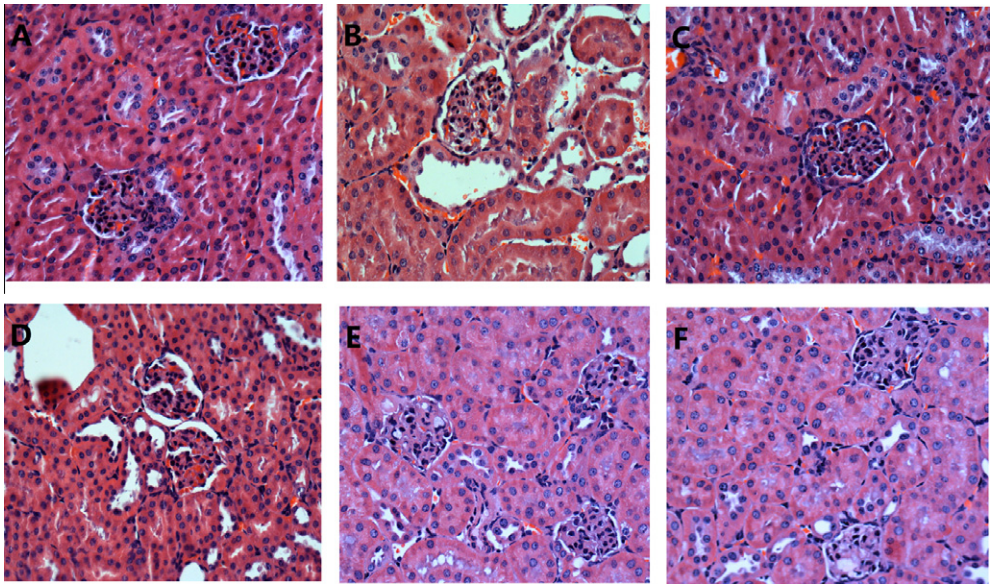

Fig. 3. Effects of CVPs treatment on kidney damage in STZ-induced diabetic mice. A: I group (normal mice); B: II group (untreated diabetic mice); C: III group (administration of CVPs with high dose for 30 days in normal mice); D: IV group (administration of glibenclamide for 30 days in diabetic mice); E: V group (administration of CVPs with low dose for 30 days in diabetic mice); F: VI group (administration of CVPs with high dose for 30 days in diabetic mice). Hematoxylin/eosin staining; magnification 400×.

and vitamin E in liver and kidney of diabetic mice in comparison with normal mice (Yu et al., 2009).

As shown in Table 2, MDA level in liver and kidney was significantly increased ($p < 0.05$) in diabetic mice whereas activities of antioxidant enzymes and concentrations of non-enzymic antioxidants in liver and kidney were significantly decreased ($p < 0.05$) in diabetic mice when compared to I group. After the administration of CVPs for 30 days, MDA level was significantly decreased ($p < 0.05$) and GSH-Px, SOD, CAT activity were significantly increased in liver and kidney of treated mice but no dose-related effect as compared to II group. Simultaneously, vitamin C and vitamin E as non-enzymic antioxidants were also determined after administration of CVPs for 30 days, except vitamin E was significantly increased in kidney, there were no significant increase ($p > 0.05$) in liver and kidney of treated mice when compared with II group. The results indicated CVPs can reduce reactive oxygen free radicals and improve the activities of antioxidant enzymes. Zhao et al. (2011) indicated the antioxidant activity of *Opuntia dillenii* polysaccharides might have played the primary role in the treatment of diabetes. And Huang et al. (2012) also suggested that polysaccharides appear to be more effective to boost antioxidant status, there by protects liver cells against hyperglycemia-induced oxidative damage.

3.4. Effect of CVPs on concentrations of serum TC, TG, HDL-C and LDL-C in STZ-induced diabetic mice

Diabetes mellitus is one of the most common human metabolic diseases, and derangements in lipid metabolism in diabetes which are often important determinants of the course and status of the

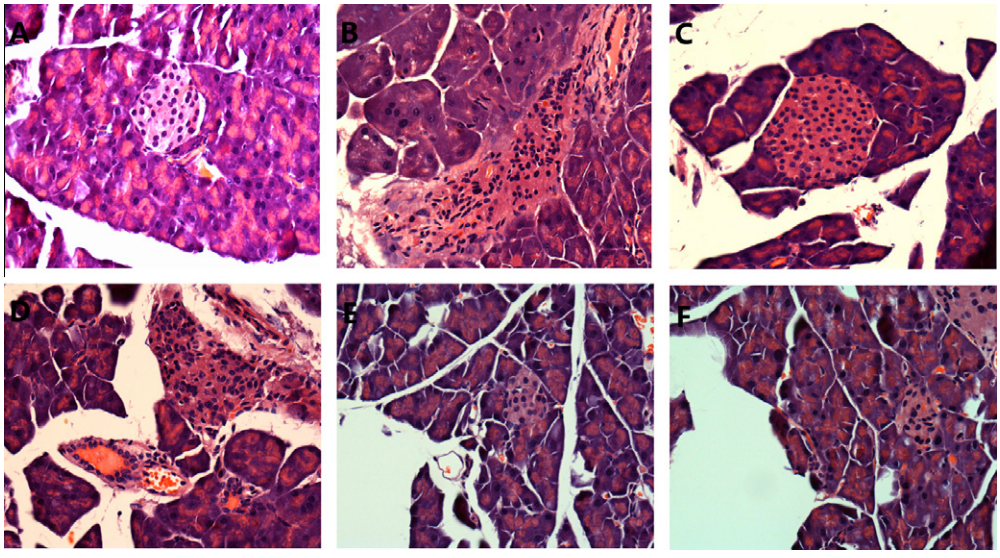

Fig. 4. Effects of CVPs treatment on pancreas damage in STZ-induced diabetic mice. A: I group (normal mice); B: II group (untreated diabetic mice); C: III group (administration of CVPs with high dose for 30 days in normal mice); D: IV group (administration of glibenclamide for 30 days in diabetic mice); E: V group (administration of CVPs with low dose for 30 days in diabetic mice); F: VI group (administration of CVPs with high dose for 30 days in diabetic mice). Hematoxylin/eosin staining; magnification 400×.

diseases, are characterized as increase in TC, TG, LDL-C but fall in HDL-C (Fumelli et al., 1996; Yu et al., 2009).

The levels of lipids and lipoprotein in serum of normal and experimental animals in each group are shown in Table 3. The TC, TG and LDL-C level of untreated diabetic mice were significantly increased ($p < 0.05$), while HDL-C level was decreased as compared to I group ($p < 0.05$). When diabetic mice were treated for 30 days, the CVPs (low and high dose) and glibenclamide significantly decreased ($p < 0.05$) the levels of TG, TC and LDL-C and simultaneously increased the HDL-C level compared to II group ($p < 0.05$). The results indicate CVPs showed marked therapeutic effect on decreasing concentrations of serum TG, TC and LDL-C and increasing concentration of serum HDL-C in diabetic mice but no dose-related effect. Many similar results were reports (Cui et al., 2012; Yu et al., 2009; Zhao et al., 2011).

3.5. Effect of CVPs on hepatic glycogen and insulin level in STZ-induced diabetic mice

After STZ injection to the fasting mice, the lipid peroxidation product MDA content of pancreas increased, which result in the damage of pancreas β cells, and led to the reduction of serum insulin contents and production of glucose via glycogenolysis (Roden and Bernroider, 2003; Zhang et al., 2003).

As shown in Table 4, the levels of hepatic glycogen and insulin were significantly decreased ($p < 0.05$) in untreated diabetic mice compared to I group. When diabetic mice were treated for 30 days, the CVPs (low and high dose) and glibenclamide significantly increased the levels of hepatic glycogen and insulin compared to II group ($p < 0.05$). Pari and Latha (2005) indicated glibenclamide increases insulin levels in diabetes by closure of K^+-ATP channels, membrane depolarization and stimulation of Ca^{2+} influx, an initial key step in insulin secretion. CVPs may act with the same mechanism of glibenclamide. But levels of hepatic glycogen and insulin in diabetic mice treated with CVPs were remarkable lower than I group. The results indicate the effect of CVPs on increasing the secretion of insulin and promoting glycogen syntheses is not significant. Zhao et al. (2011) got the similar result as us, the insulin level in the mice with STZ-induced diabetes were not significantly affected by *O. dillenii* polysaccharides. While Li et al. (2006) reported polysaccharides from *Cordyceps sinensis* produced a significant increase of insulin level in diabetic animals by administration of the polysaccharides. And Li et al. (2006) indicated *C. sinensis* polysaccharides with hypoglycemic properties increased circulating insulin level in diabetic animals, which suggests *C. sinensis* polysaccharides may stimulate pancreatic release of insulin and/or reduce insulin metabolism. We propose that CVPs exerts its antihyperglycemic effect by protecting the liver, kidney and pancreas tissues from peroxidation damage and improving the sensitivity and response of target cells in diabetic mice to insulin. Sarkhail et al. (2007) indicated there is other possible mechanism, polysaccharides might be mediated through liver and affecting gluconeogenesis, glycogenesis or glycogenolysis.

3.6. Changes in histopathology of liver, kidney and pancreas

STZ-induced diabetic mice showed the degeneration in almost all tissues (especial in liver, kidney and pancreas tissues), such as hepatic cords, focal necrosis, congestion in central vein and infiltration of lymphocytes (leading to inflammation). Most of these pathologic morphologies were seen in the liver, kidney and pancreas tissues of II and IV group (Figs. 2–4). Das et al. (1996) indicated insulin depletion may result in degenerative structural changes of tissue. According to the microscopic examinations, the severe hepatic, renal and pancreatic lesions induced by STZ were considerably reduced by the administration of CVPs at low and high doses (V and VI group, there was no dose-related effect). In addition, the morphological appearance of these three tissues in III group was similar to that of I group. The results indicated liver, kidney and pancreas tissues of STZ-induced diabetic mice can be protected and repaired by intervention with CVPs. And Huang et al. (2012) indicated protection of pancreatic β-cells by polysaccharide may attribute to its antidiabetic activity. But it seems glibenclamide do not have protective effect on these tissues.

4. Conclusion

The present investigation showed that the CVPs possess potent antioxidant activity, which may be directly or indirectly responsible for its hypoglycemic and hypolipidemic properties. And CVPs have much protective effect on liver, kidney and pancreas tissues. Furthermore based on the results of biochemical analysis and histopathology, CVPs are safe for normal mice. Therefore, the SPS should be considered as a candidate for future studies on diabetes.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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