

Portulaca oleracea extract increases lecithin:cholesterol acyltransferase and paraoxonase 1 activities and enhances reverse cholesterol transport in streptozotocin-induced diabetic rat

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ABSTRACT

Background: Plant extracts are generally assumed to be more acceptable and less hazardous than synthetic compounds and could be alternative antidiabetic treatments. *Portula caoleracea* has been used as one of the traditional edible and medicinal plant in Algeria to treat diabetes. The aim of the present study was to determine the effects of lyophilized aqueous extract of *Portulaca oleracea* on high-density lipoproteins composition, paraoxonase (PON1) and lecithin:cholesterol acyltransferase (LCAT) activities in streptozotocin-induced diabetic rat. **Methods:** Diabetes was induced intraperitoneally by a single injection of streptozotocin (STZ) (60mg/kg bw). Twelve diabetic rats, weighing 263 ± 5 g, were divided into two groups fed a casein diet supplemented or not with *Portulaca oleracea* extract (1g/kg bw), for 4 weeks. **Results:** At d28, in *Portulaca oleracea* treated vs untreated diabetic group, glycemia, serum total cholesterol (TC), triacylglycerols (TG) and phospholipids (PL) concentrations were decreased significantly ($p < 0.05$). The hypolipidemic effect induced by *Portulaca oleracea* extract was due to the reduction of total cholesterol (TC) in LDL-HDL₁ (-51%) and C-HDL₃ (-21%). *Portulaca oleracea* treatment improved PON1 and LCAT activities by 48%. HDL₃-UC (acyl group acceptor) and -PL (enzyme substrate) were diminished respectively by 47% and 82%, whereas HDL₂-CE concentrations (product of LCAT reaction) were increased by 44%. Moreover, HDL-C levels were found to be positively correlated with PON1 activity ($r = 0.96$, $p < 0.05$). Serum, LDL-HDL₁, HDL₂ and HDL₃ TBARS levels were respectively, 2.9-, 2.6-, 2.4- and 2.8-fold lower in *Portulaca oleracea* treated than untreated diabetic groups. **Conclusion:** These findings reflect the potential antihyperglycemic and hypolipidemic of *Portulaca oleracea* extract, in STZ-induced diabetic rat. Moreover, *Portulaca oleracea* extract restores PON1 and ameliorates the reverse cholesterol transport (RCT) by enhancing LCAT activity, therefore could prevent many diabetic complications by reducing dyslipidemia and oxidative damage.

Keywords: Rats, Streptozotocin, *Portulaca oleracea*, Cholesterol, PON1, LCAT, apo A-I, lipoprotein peroxidation

BACKGROUND

Diabetes mellitus (DM) is increasingly common metabolic disorder and one of the five leading causes of death in the world. Such disorders lead to various profound secondary complications like as, atherosclerosis, myocardial infarction, retinopathy and nephropathy.^[1] DM is associ-

ated with an elevated level of oxidative stress, increased susceptibility to coronary heart disease, and reductions in Lecithin-cholesterol acyltransferase (LCAT)^[2] and paraoxonase activities.^[3] Lecithin-cholesterol acyltransferase (LCAT, EC 2.3.1.43) is one of the major modulators of plasma high-density lipoprotein cholesterol (HDL-C) and plays a central role in the reverse cholesterol transport (RCT) process.^[4] LCAT was first described as a plasma enzyme responsible for the formation of cholesteryl esters in plasma. Human paraoxonase (EC.3.1.8.1, aryldialkylphosphatase) is a calcium-dependent esterase closely associated with high density lipoprotein (HDL)-containing apolipoprotein A-I (apo A-I),^[5] which has been shown to confer antioxidant properties to HDL. Patients with DM, have characteristic abnormalities of plasma lipids and lipoprotein concentrations that almost certainly play a

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significant role in the increased risk for coronary heart disease.^[6] This dyslipidemia is characterized by higher plasma triglyceride levels, both in the fasting and the post-prandial state, reduced levels of high-density lipoprotein cholesterol (HDL-C), and abnormal low-density lipoprotein (LDL) particles.^[7] Indeed, plasma lipoprotein metabolism is influenced by several factors, such as hyperglycemia, one of the main features of diabetes, results in non-enzymatic glycation of plasma proteins, including apo A-I, the most abundant apolipoprotein in HDL. Glycation affects the structure of apoA-I and its ability to activate LCAT, the key enzyme in the reverse cholesterol transport.^[8] Moreover, LCAT is glycosylated and oxidized as a result of chronic hyperglycemia, the mechanism of paraoxonase reduction in oxidative stress status is not clearly known. However, it is suspected that ROS overproduction leads to increased deactivation of paraoxonase.^[9] Several studies also reported that LCAT activity was lower in both type 1 and type 2 diabetic patients than in control subjects.^[10] Another study reported significantly higher malondialdehyde concentration and lower paraoxonase activity in patients with type 2 diabetes, illustrating a negative correlation between paraoxonase activity and lipid peroxidation.^[11] Traditional medicines derived mainly from plants have played and still plays major role in the management of DM.^[12] *Portulaca oleracea* L (from *Portulacaceae* family) locally named “Redjila” is widely used in Algerian popular medicine, shows some benefits in the treatment of diabetes, cardiovascular diseases and enhancing immunity.^[13] Tender stems and leaves are usually eaten raw, alone or with other greens. They are also cooked or pickled for consumption. The traditional use of *Portulaca oleracea* in the treatment of diabetes have not yet been studied in great detail. Decoction and infusion are the methods mostly used for preparation of the traditional medicine. Recent research demonstrated that this plant is a good source of compounds with a positive impact in human health. Those compounds include omega-3 fatty acids, phenolics, coumarins and alkaloids. The aqueous extracts of *Portulaca oleracea* show no cytotoxicity or genotoxicity, and have been certified safe for daily consumption as a vegetable.^[14] Thus, the present study was designed to assess the effects of the lyophilized aqueous extract of *Portulaca oleracea* on lipid profile, lipoprotein peroxidation, LCAT and paraoxonase activities, in the streptozotocin-induced diabetic rat.

MATERIAL AND METHODS

Plant material

Portulaca oleracea was collected in Southern of Algeria (Touggourt), between March and April 2012, identified

taxonomically and authenticated by the Botanical Research Institute of Oran University (voucher specimen number *Po1965*). The plant material was stored at room temperature in a dry place before use. Fresh aerial parts (leaves) of the plant were dried at ambient temperature (24°C) for 7 days and ground to a powder. The *Portulaca oleracea* extract was prepared as follows: 50 g of the powdered aerial parts was refluxed at 60-70°C in 500 ml distilled water for 30 minutes and the decoction was filtered with cotton wool. The filtrate was concentrated at 65°C by a rotavapor (BuchiLabortechnik AG, Postfach, Switzerland) under a reduced pressure and frozen at -70°C before lyophilization (Christ, alpha 1-2 LD). The crude yield of the lyophilized extract was approximately 25% (wt/wt). It was stored at ambient temperature until further use.

Preliminary phytochemical screening

Preliminary phytochemical screening was carried out by using standard procedure described by Harborne.^[15]

Animals and experimental design

Male Wistar rats (Iffa Credo, l'Arbresle, Lyon, France), weighing 263±5g were housed under standard environmental conditions (23±1°C, 55±5% humidity and a 12 h light/dark cycle) and maintained with free access to water and a standard diet *ad libitum*. The General Guidelines on the Use of Living Animals in Scientific Investigations^[16] were followed, and Institutional Animal Ethical Committee (CPCSEA Reg. No. 12/314/2012) approval for experimental protocol was obtained.

Induction of diabetes in rats

Diabetes was induced by intraperitoneal injection of streptozotocin (STZ) (Sigma, St Louis, Mo, USA) at a dose of 60 mg/kg bw STZ was dissolved in 0.05 mol/L cold sodium citrate buffer, pH 4.5 immediately before use. After 48 h, hyperglycemia was confirmed using a Glucometer (Accu-Chek® active, Germany). Only animals with fasting blood glucose levels greater than 16 mmol/L were considered diabetic and then included in this study. Diabetic rats (n=12) were randomly divided into two groups. The untreated group received a casein diet and the treated group received the same diet supplemented and mixed with the *Portulaca oleracea* extract (0.1%), for 4 weeks. The ingredient composition of the diets is shown in Table 1.

Blood samples

After the 4 weeks of the experiment, the rats were fasted overnight and anesthetized with chloral hydrate 10% (3 ml/kg bw) and euthanized with an overdose. Blood was

Table 1. Ingredient composition of the diets fed to rats (g/kg diet)¹

Ingredients	D	DPo
Casein ²	200	200
Corn starch ³	590	573.4
Sunflower oil ⁴	50	50
Sucrose ⁵	50	50
Cellulose ²	50	50
Vitamin mix ⁶	20	20
Mineral mix ⁷	40	40
<i>Portulaca oleracea</i> extract ⁸	0	1

¹Diets were isoenergetic (16.28 MJ/kg) and given in powdered form.

²PROLABO (Paris, France).

³ONAB (Sidi Bel Abbès, Algeria).

⁴CEVITAL (Béjaïa, Algeria).

⁵ENASUCRE (Sfisef, Algeria).

⁶UAR 200 (Villemoisson, 91360). Vitamin mixture provided the following amounts (mg/kg diet): vitamin A, 39 600 UI; vitamin D₃, 5000 UI; vitamin B₁, 40; vitamin B₂, 30; vitamin B₃, 140; vitamin B₅, 20; vitamin B₆, 300; vitamin B₁₂, 0.1; vitamin C, 1600; vitamin E, 340; vitamin K, 3.80; vitamin PP, 200; choline, 2720; folic acid, 10; paraaminobenzoic acid, 180; biotin, 0.6; and cellulose, qsp, 20 g.

⁷UAR 205B (Villemoisson, 1360, Epinay/S/Orge, France). Mineral mixture provided the following amounts (mg/kg diet): CaHPO₄, 17 200; KCl, 4000; NaCl, 4000; MgO, 420; MgSO₄, 2000; Fe₂O₃, 120; FeSO₄, 7H₂O, 200; MnSO₄, H₂SO₄, H₂O, 98; CuSO₄, 5H₂O, 20; ZnSO₄, 80; CuSO₄, 80; CuSO₄, 7H₂O; and KI, 0.32.

⁸Prepared in our laboratory as previously described.

obtained from the abdominal aorta of rats and collected into dried tubes and centrifuged at 1000g for 20 minutes at 4°C. Serum samples were stored at -70°C until use.

Lipoprotein separation

Serum LDL-HDL₁ were isolated by precipitation using MgCl₂ and phosphotungstate (Sigma Chemical Company, France) by the method of Burstein *et al.*¹⁷ HDL₂ and HDL₃ were separated by precipitation according to the method of Burstein *et al.*¹⁸ using MgCl₂ and dextran sulfate (Sigma Chemical Company, France).

Biochemical analysis

Blood glucose levels were determined as described above. Glycosylated haemoglobin (HbA_{1c}) was estimated by ion exchange chromatography method (KitBiocon, Germany). Serum urea and creatinine were analyzed by enzymatic methods (KitsBiocon, Germany) and apo A-I concentrations were determined by immuno-turbidimetric method (kit Orion Diagnostica, Spain). Total cholesterol (TC) Triacylglycerol (TG) and phospholipids (PL) of serum and each fraction were determined with enzymatic method kit (Kits Spinreact, Girona Spain). In HDL₂ and HDL₃ fractions, unesterified cholesterol (UC) contents were determined using enzymatic method (Kit Wako, Germany). Esterified cholesterol (EC) concentrations were obtained by calculating the difference between TC and UC values.

Cholesteryl esters (CE) levels were estimated as 1.67 times the esterified cholesterol content. Protein concentrations were measured according to the method of Lowry *et al.*,¹⁹ using bovine serum albumin (Sigma Chemical Company, St Louis, MO, USA) as a standard.

Lipid peroxidation assay

Thiobarbituric acid-reactive substances (TBARS) were determined in serum and lipoproteins fraction according to the method of Quantanilha *et al.*²⁰ One milliliter of diluted serum or each fraction was added to 2 ml of thiobarbituric acid (TBA) (final concentration, 0.017 mmol/l), plus butylated hydroxytoluene (concentration, 3.36 μmol/l) and incubated for 15 min at 100°C. After cooling and centrifugation, the absorbance of supernatant was measured at 535 nm.

Lecithin:cholesterol acyltransferase (LCAT) activity assay

Serum LCAT activity was assayed by the conversion of unesterified [³H] cholesterol to esterified [³H] cholesterol, according to the method of Glomset and Wright,²¹ modified by Knipping.²² Cholesterol and egg phosphatidylcholines (PC) were used for the preparation of liposomes. Specifically, 2 mg cholesterol and 16 mg egg PC in chloroform-methanol (2:1, vol/vol) were evaporated to dryness under nitrogen stream. After adding 1.0 ml of (10 mmol/l Tris-HCl, 150 mmol/l NaCl and 1.0 mmol/l EDTA, pH 7.4), the solution was sonicated for 30 minutes at 100 W and 25°C. LCAT activity was determined using liposomes as substrate. The cholesterol esterifying activity was expressed as nanomoles of esterified cholesterol/h/ml of Serum.

Paraoxonase (PON1) activity assay

Serum PON1 activity was estimated spectrophotometrically by the method of Schiavone *et al.*²³ Briefly, the assay mixture consisted of 500 μl of 2.2 mmol/l paraoxone substrate in 0.1 mol/l tris-HCl buffer, pH 8, containing 2 mmol/L CaCl₂ and 50 μl of fresh serum. The absorbance was monitored at 405 nm, at 25°C. The PON1 activity was expressed in international units (IU). One IU was defined as 1 μmol of p-nitrophenol which was formed/min/L.

Statistical analysis

All data are presented as means ± SEM of 6 rats per group. Statistical analysis was carried out by the Student "t" test. The calculations were performed using STATISTICA (Version 10, StatSoft, Tulsa, Okla). Value of *P* < 0.05 was

considered to be statistically significant. Linear regression analysis was used to determine correlation coefficient between PON1 activity and HDL-C levels.

RESULTS

Phytochemical screening

Preliminary phytochemical screening of *Portulaca oleracea* aqueous extract revealed the presence of tannins, flavonoids, phenolics, carbohydrates, steroids, saponins, amino acids and proteins (Table 2).

Glycemia, glycosylated hemoglobin, serum urea, and creatinine concentrations

In the diabetic rats, daily administration of *Portulaca oleracea* extract induced a significant decrease of glycemia and glycosylated haemoglobin levels (Table 3). However, serum urea and creatinine concentrations were reduced by 27% and 31%, respectively.

Serum lipids concentrations and atherogenicity ratios

Portulaca oleracea treatment lowered significantly serum TC (-38%) and LDL-HDL₁-C (-51%), whereas HDL-C concentrations were increased by 26% (Table 4). Serum TG and PL levels were enhanced respectively by 53% and 62% in *Portulaca oleracea*-treated compared to untreated diabetic group. TC/HDL-C and LDL-HDL₁-C/HDL-C ratios were respectively, 2.2- and 2.7-fold lower in *Portulaca oleracea* treated than untreated diabetic group.

Serum HDL₂ and HDL₃ amounts and compositions

The amounts of lipoproteins which represents the sum of apolipoproteins (apos), UC, CE, TG and PL contents reduced by -29% in HDL₂, in *Portulaca oleracea* treated *vs*

untreated diabetic group (Figure 1). The contents of apos and UC were similar in the both groups, whereas CE concentrations were 1.5-fold higher. Inversely, TG and PL levels were 1.4-, 1.3-fold lower, in *Portulaca oleracea*-treated *vs* untreated diabetic group.

Portulaca oleracea treatment reduced significantly HDL₃ amount (-61%) (Figure 2). However, UC and PL concentrations were respectively decreased by 48% and 83% in *Portulaca oleracea* treated compared with untreated diabetic rats. In addition, apos, CE and TG contents were similar in the both groups.

Serum and lipoproteins lipid peroxidation

Lipid peroxidation was significantly decreased in *Portulaca oleracea* group. Serum, LDL-HDL₁, HDL₂ and HDL₃ TBARS contents were respectively, 2.9-, 2.6-, 2.4- and 2.8-fold lower in *Po* treated than untreated diabetic groups (Table 5).

Serum apo A-I concentrations, LCAT and PON1 activities

Serum apo A-I concentrations tended to be higher but not significantly (Table 6). However, in *Portulaca oleracea*-treated *vs* untreated diabetic group, a higher LCAT and PON1 activities were noted (+48%).

DISCUSSION

Evaluation of plant products to treat *diabetes mellitus* is of growing interest as they contain many bioactive substances with therapeutic potential. As mentioned above, various phytotherapeutic products (phenolics, coumarins and alkaloids) are already used; and convey satisfactory results. In essence, *Portulaca oleracea* was widely used in traditional medicine for their various pharmacological

Table 2. Preliminary phytochemical components screening of *Portulaca oleracea* extract

Phytochemical Compounds	Presence
Tannins	+++
Flavonoids	++
Phenolics	++
Carbohydrates	+
Steroids	+
Saponins	+
Proteins and amino acids	+

All tests were performed six times. +++ = appreciable amount (positive within 5 mins.); ++ = moderate amount (positive after 5 mins); + = trace amount (positive after 10 mins).

Table 3. Glycemia, glycosylated hemoglobin, urea, and creatinine concentrations

	D	DPo
Glycemia (mmol/L)	27.09 ± 2.29	9.54 ± 2.18***
HbA1c (%)	10.11 ± 0.38	5.94 ± 0.58**
Urea (mmol/L)	8.16 ± 1.10	5.96 ± 0.45*
Creatinine (µmol/L)	61.03 ± 8.06	42.09 ± 8.41*

Values are mean ± SEM of 6 rats per group. Statistical analysis was performed using the student't' test.

***p*<0.01, diabetic rats treated with *Portulaca oleracea* extract (DPo) *vs* untreated diabetic rats (D)

****p*<0.001, diabetic rats treated with *Portulaca oleracea* extract (DPo) *vs* untreated diabetic rats (D)

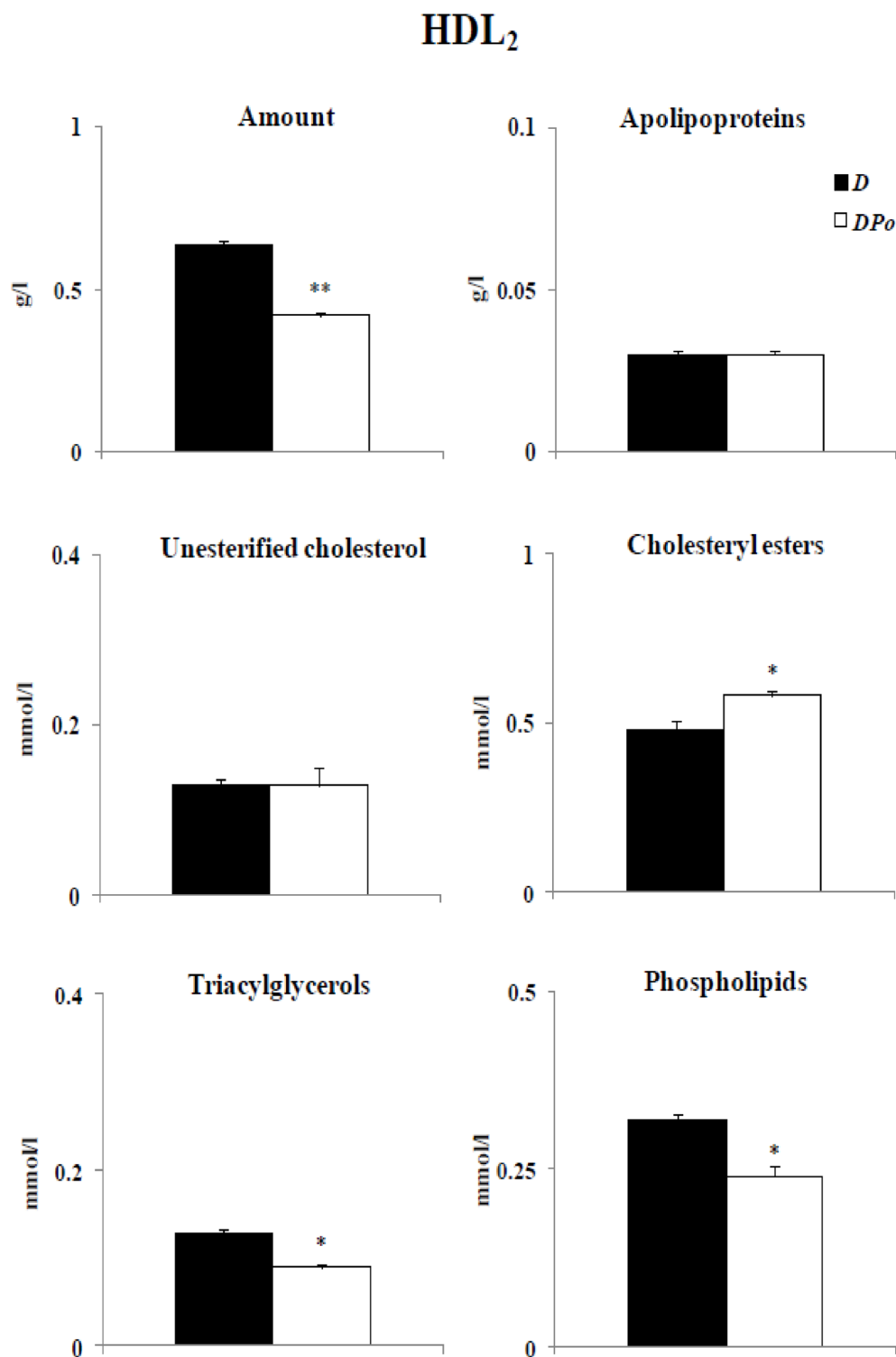


Figure 1. Serum HDL₂ amounts and compositions.

Values are mean ± SEM of 6 rats per group. Statistical analysis was performed using the student's t test.

*p<0.05, diabetic rats treated with the *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D).

**p<0.01, diabetic rats treated with the *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D).

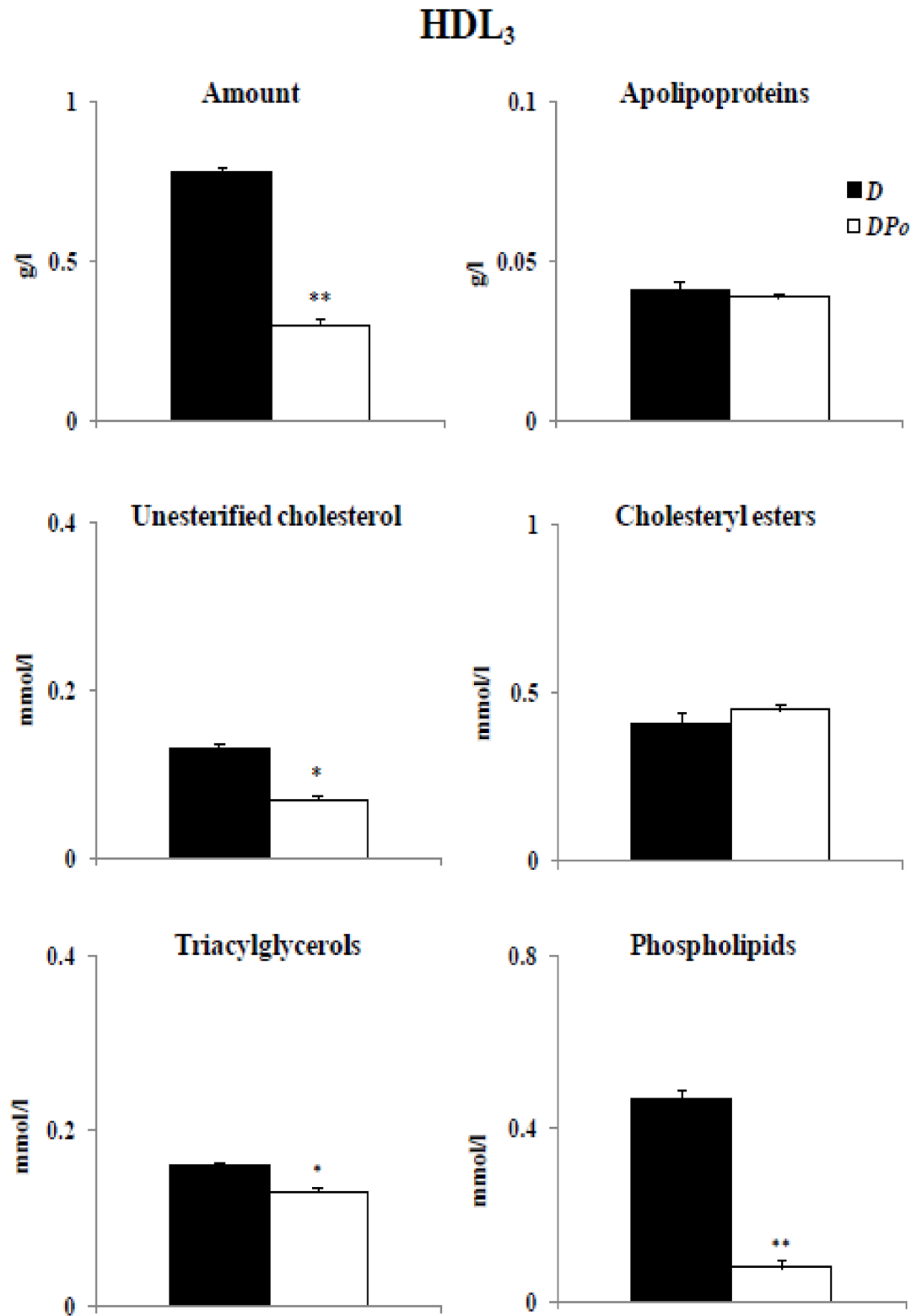


Figure 2. Serum HDL₃ amounts and compositions.

Values are mean ± SEM of 6 rats per group. Statistical analysis was performed using the student's t test.

*p<0.05, diabetic rats treated with the *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D).

**p<0.01, diabetic rats treated with the *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D).

Table 4. Serum lipids concentrations (mmol/L) and atherogenicity ratios

	D	DPo
Serum-TC	2.00 ± 0.21	1.24 ± 0.19*
LDL-HDL ₁ -C	0.73 ± 0.04	0.35 ± 0.09*
HDL-C	0.43 ± 0.01	0.58 ± 0.06*
TC/HDL-C	4.74 ± 0.09	2.19 ± 0.56*
LDL-HDL ₁ -C/HDL-C	1.71 ± 0.14	0.62 ± 0.22*
Serum-TG	0.96 ± 0.02	0.45 ± 0.06***
Serum-PL	1.31 ± 0.07	0.49 ± 0.09***

Values are mean ± SEM of 6 rats per group. Statistical analysis was performed using the student 't' test.

* $p < 0.05$, diabetic rats treated with *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D)

*** $p < 0.001$, diabetic rats treated with *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D)

Table 6. Apolipoprotein (apo A-I), lecithin:cholesterol acyltransferase (LCAT) and paraoxonase (PON1) activities

	D	DPo
apo A (g/L)	1.19 ± 0.80	2.14 ± 0.32
LCAT(nmol/mL/h)	11.60 ± 3.17	21.90 ± 03.16***
PON1 (IU)	4.30 ± 0.62	8.44 ± 0.97**

Values are mean ± SEM of 6 rats per group. Statistical analysis was performed using the student 't' test. Values were considered to be different at $p < 0.05$ and $p < 0.01$.

** $p < 0.01$, diabetic rats treated with *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D)

*** $p < 0.001$, diabetic rats treated with *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D)

effects. In this paper, we had experimentally investigated the anti-diabetic effect of *Portulaca oleracea* lyophilised aqueous extracts, with special focus on their impact on High-density lipoprotein composition and paraoxonase, LCAT activities.

Previous studies have shown that polysaccharides, flavonoids, steroids and alkaloids present in the medicinal plants can justify the properties of some herbs in decreasing the blood sugar.^[24] At day 28, our results showed that the treatment with *Portulaca oleracea* extract decreased significantly glycemia value. This hypoglycemic effect could be directly related to the polyphenolic compounds of the extract [Table 2]. Glycosylated haemoglobin is one of those glycosides compounds in particular that reflects average blood glucose in patients 2 or 3 months before blood collection.^[25] The results obtained from the measurement of HbA_{1c} show a clear deference between untreated diabetic (10%) and *Portulaca oleracea*-diabetic groups (6%). This result was concomitant with the hypoglycemic effect induced by *Portulaca oleracea* extract. It is well known that diabetes leads to alterations of renal function essentially due to an accumulation of advanced glycated end products (AGE).^[26] Diabetic nephropathy in uncontrolled

Table 5. TBARS levels in serum and lipoproteins fraction (nmol/mL)

	D	DPo
Serum	12.91 ± 01.43	4.51 ± 1.59**
LDL-HDL ₁	3.25 ± 00.11	1.26 ± 0.46**
HDL ₂	1.31 ± 00.39	0.54 ± 0.10*
HDL ₃	1.74 ± 00.23	0.63 ± 0.11**

Values are mean ± SEM of 6 rats per group. Statistical analysis was performed using the student 't' test.

* $p < 0.05$, diabetic rats treated with *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D)

** $p < 0.01$, diabetic rats treated with *Portulaca oleracea* extract (DPo) vs untreated diabetic rats (D)

diabetes is a serious micro-vascular complication which results in increased blood urea and creatinine concentrations.^[27] Interestingly, the higher levels of urea and creatinine in diabetic rats are diminished significantly after the administration of *Portulaca oleracea*, which could be a result of improved renal function due to the reduced plasma glucose concentration and subsequent glycosylation of renal basement membranes.

Diabetes mellitus is related to a hyperlipidemia and leads to serious anomalies in lipids composition and concentration.^[28] These anomalies can induce cardiovascular diseases.^[29] The high level of total cholesterol in the blood could be seen as a major risk factor generating coronary heart disease.^[30] It is known that the increase in serum lipids in STZ-induced diabetic rats played an important role in such pathology.^[31] In our study, *Portulaca oleracea* aqueous extract supplementation prevented hyperlipidemia by reducing the levels of cholesterol in LDL-HDL₁ and increasing serum HDL₂-C. It could be suggested that these effects were explained by presence of flavonoids in *Portulaca oleracea* extract. Since these compounds have effectiveness in reducing blood lipid, as an anti-oxidative, in assimilating cholesterol, inhibiting thrombosis and dilating the coronary artery^[32]. In some other studies, supplementation with omega-3 fatty acids resulted in significant increase in the HDL cholesterol.^[33] *Portulaca oleracea* is a rich source of Omega 3 fatty acids and it has been reported that Omega 3 fatty acids reduce LDL-C.^[34] Moreover, TC/HDL-C ratio or LDL-C/HDL-C which are a marker of dyslipidemia was reduced in *Portulaca oleracea*-diabetic group than untreated diabetic group. These decreased ratios are predictors of coronary risk.^[35] High density lipoprotein (HDL) is one of the most important independent protective factors for the arteriosclerosis which underlies coronary heart disease. Flavonoids may also decrease cholesterol absorption by increasing the excretion of bile acids.^[36] Increased HDL-C level can also facilitate the transport of cholesterol from tissues to liver.^[37] The possible mechanism of this activity may result from

the enhancement of lecithin:cholesteryl acyltransferase (LCAT).^[38] In *Portulaca oleracea* treated compared with untreated diabetic group, LCAT activity was increased and the concentrations of plasma apo A-I tended to be higher but not significantly. Recent research findings from animal and human studies have revealed a potential beneficial role of LCAT in reducing atherosclerosis.^[39] In the present study, *Portulaca oleracea* treatment decreased significantly HDL₃-PL (the enzyme substrate) and HDL₃-UC (acyl group acceptor) concentrations and increased HDL₂-CE levels (product of enzymatic reaction). These findings showed that *Portulaca oleracea* extract enhanced LCAT activity ensuring HDL₃-HDL₂ conversion and the subsequent hepatic uptake.

The previous report of Sinha *et al.*^[40] suggests that, the hypolipidemic activity may be attributed to inhibition of oxidative stress. In addition, our result showed that TBARS levels in serum, LDL-HDL₁, HDL₂ and HDL₃ were decreased significantly in *Portulaca oleracea*-treated diabetic rats compared to untreated diabetic rats. These results indicated that *Portulaca oleracea* extract might protect the plasma the cytotoxic action and oxidative stress of streptozotocin. In fact, we know that a low HDL concentration is usually accompanied by a reduction in PON1 activity or concentration in diabetic patients.^[41] In this data, higher paraoxonase activity and lower TBARS concentration in *Portulaca oleracea*-treated diabetic rats, illustrating a positive correlation between paraoxonase activity and serum HDL-C levels ($r = +0.96, p < 0.01$). Several studies have indicated that PON1 can prevent lipid peroxide accumulation on LDL.^[42] Recently studies demonstrated that PON1 is an important antioxidant enzyme and is responsible for antioxidant effects of HDL-C^[43] and its activity can be modified by factors such as diet and lifestyle.^[44] Therefore, the increased PON1 activity is shown in our study and could be due to polyphenols contained in *Portulaca oleracea*. Polyphenols have antioxidant activity and also, modulates gene expression of PON1 leading to increased PON1 activity.^[45]

CONCLUSIONS

These findings reflect clearly the potential antihyperglycemic and hypolipidemic of *Portulaca oleracea* aqueous lyophilized extract in streptozotocin-induced diabetic rat. Moreover, *Portulaca oleracea* extract prevents lipoprotein oxidation by enhancing PON1 activity, and ameliorates the reverse cholesterol transport by enhancing LCAT activity, thereby providing protection against diabetic dyslipidemia.

ABBREVIATIONS

Apo A-I: Apolipoprotein A-I; CE: cholesteryl esters; DM: *Diabetes mellitus*; HbA_{1c}: Glycosylated haemoglobin; HDL-C: High density lipoprotein-cholesterol; LCAT: Lecithin:cholesterol acyltransferase; LDL-C: Low density lipoprotein-cholesterol; PON1: Paraoxonase 1; PL: Phospholipids; *Po*: *Portulaca oleracea*; STZ: Streptozotocin; TBARS: Thiobarbituric acid-reactive substances; TC: Total cholesterol; TG: Triglycerides; UC: Unesterified cholesterol.

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COMPETING INTERESTS

All authors of this research have no conflict of interest related with employment, consultancies, stock ownership, grants or other funding.

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