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Antioxidative and Antidiabetic Effect of Goldenberries Juice and Pomace on Experimental Rats Induced with Streptozotocin *In Vitro*

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ABSTRACT

This study aimed to observe antidiabetic and antioxidant activities of *Physalis peruviana* L. (Solanaceae) fruit juice and pomace in streptozotocin (STZ)-induced diabetic rats. *Physalis peruviana* L is well- known as a goldenberry or harankash in Egypt, is used to administer diabetes and its problems. Diabetes was induced using STZ (65 mg/kg, b.w). Three days after STZ induction, diabetic rats daily received 5.0 mL/kg/ body weight of *P. Peruviana* crude fruit juice and *P. Peruviana* fruit pomace at 10% level mixed with the diet for 35 days. Metformin (0.5 mg/kg, orally) as a reference. The serum urea and creatinine were measured. In addition to CAT, SOD enzymes, and thiobarbituric acid reactive substances (TBARS) were evaluated in pancreas tissue. *P. peruviana* fruit juice and pomace significantly ($P < 0.05$) normalized levels of glucose in blood compared to STZ control group. Serum biochemical parameters including lipid profile and antioxidant status were significantly ($P < 0.05$) restored toward normal levels in *P. peruviana* fruit juice and pomace -treated rats as compared to STZ control animals. The protective effect was further confirmed by histological improvements in pancreatic cells of the treated diabetic rats. Encouraging nature medication of hyperglycemia and diabetic complications by *Physalis peruviana* L. fruit juice and pomace.

Keywords: Functional Food, Goldenberry, Antidiabetic, Pomace, Hypoglycemic, Antioxidant.

***Abbreviations**: STZ,* streptozotocin; CAT, Catalase; SOD, superoxide dismutase; TBARS, thiobarbituric acid reactive substances; TG, triglyceride; TC, total cholesterol; LDL-c, low- density lipoprotein cholesterol; VLDL-c, very low lipoprotein cholesterol.

INTRODUCTION

Diabetes mellitus (DM) is one of metabolic diseases characterized by high blood glucose concentration (hyperglycemia) and disorder in carbohydrate, fat, and protein metabolism that outcomes from faults in both insulin emission actions (Anon., 2012). Diabetes mellitus leads to many other disorders including hyperlipidemia, hypertension, atherosclerosis and microcirculatory disorders (Luo *et al*., 2004). The International Diabetes Federation (IDF) estimates that 382 million people around the world suffered from diabetes in 2013 and this number is possible to surge more than 592 million by 2035. An estimated 7.5 million people with diabetes live in Egypt, and by 2035 this number is expected to increase to 13.1 million (IDF, 2013). Despite different diabetic medications have been manufactured, many hypoglycemic agents are related with side effects, secondary failure rates, cardiovascular disorders and coma (May *et al*., 2002). Thus, the search for antidiabetic agents with slight side effects which are moderately cheap is still a challenge to the medical market (Sun *et al*., 2008). Traditional medicines have been widely used as an alternative medicine for promising management of diabetes (Mahalingam and Krishnan ., 2008).

Healthy food is a main factor for regulatory hyperglycemia; avoiding its problems and improving life quality (Schiller and Bernadel., 2004). Berries, which are a sample of functional foods with healthy benefits (Zhao., 2007). Goldenberry showed various medicinal properties, including antidiabetic, antispasmodic, antiseptic (Luis *et al*., 2020). Goldenberry (*Physalis peruviana* L. Solanaceae) is a shrubby herb native to South America. It has been grown in a wide different places around world. *Physalis peruviana* is widely grown in Egypt and known locally as Harankash. Currently, different products, processed from the fruit of golden berry such as jams, chocolate-covered candies, and raisins (Ramadan and Moersel., 2007), (Ramadan and Moersel., 2009). The juice of goldenberry fruits is gorgeous in vitamins A, B, and C as well as essential minerals, so it might be a unique origin of efficient foods (Ramadan., 2012). The fruit pomace (seeds and skins) is rich in polyunsaturated fatty acids, antioxidants, phytosterols, and crude fiber. Medically, *Physalis peruviana* and its extracts have been used as a cancer traditional medication (Yen *et al*., 2010), eye inflammation (Pardo *et al.* 2008), ear edema (Franco *et al*., 2007), hepatitis and hepatotoxicity (Arun and Asha. 2007; Chang *et al*., 2008). Recent studies have reported that *Physalis* is very much respected worldwide for its blood glucose-lowering effects (El-Mehiry *et al*., 2012; Abo and Lawal., 2013). Moreover, suggested that the *Physalis peruviana* fruit extract exhibits hypoglycemic activity and improves the antioxidant status of the streptozotocin-diabetic rats (Mora *et al*., 2010). The consumption of *P. peruviana* pomace has hypocholesterolemia and hypolipidemic activities. However, not many studies have considered the antidiabetic and antioxidant activity of goldenberry juice and pomace as a functional food in animal models. Therefore, the present study attempts to investigate the antihyperglycemic, antihyperlipidemic and antioxidant potential activities of the *Physalis peruviana* fruit juice and pomace in STZ-induced diabetic rats.

MATERIALS AND METHODS

1. Plant Material

Ripe *Physalis peruviana* fruits were obtained from special farms around Minia University at Minia Governorate,

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Egypt. The plant was identified by Dr. A. Galal Faculty of Science, Botany Department, Minia University, Egypt.

2. Chemicals and reagents

Streptozotocin (STZ) and metformin (Sigma Chemical Co, USA). Streptozotocin 0.1 M freshly prepared sodium citrate buffer (pH 4.4), while metformin was dissolved in sterile distilled water. Kits for blood glucose, urea, creatinine, TG, TC, HDL-c, CAT, SOD, and TBARS were purchased from Bio diagnostic, Egypt.

3. Preparation of *Physalis peruviana* fruit juice and pomace.

Whole fresh fruits of *P. peruviana* were cleaned and blended in Moulinex Ovatio 3 blender for 10 min. The fruit juice was obtained by filtration through cheese cloth to remove residues (fruit pomace). Pomace was freeze-dried to reach 15% moisture level. Then grinded and kept at 4°C until application.

4. Measurement of Total Polyphenols, Flavonoids, and Vitamin C

Total Phenolics Content.

The total polyphenolic contents (TPC) in *P. peruviana* fruit juice and pomace were measured using Folin-Ciocalteau method (Ainsworth and Gillespie., 2007). Calibration curve was built using a standard of tannic acid and the values were expressed as mg tannic acid equivalents (TAE)/ 100 mL fruit juice or 100 g fruit pomace.

Total Flavonoids Content.

Total flavonoids (TFC) in *P. peruviana* fruit juice and pomace was measured (Moreno *et al*., 2000). Quercetin was used as standard to build the calibration curve. TFC values were expressed as mg quercetin equivalents (QE)/ 100 mL fruit juice or 100 g fruit pomace.

Determination of Vitamin C.

Ascorbic acid (Vitamin C) in *P. peruviana* fruit juice and pomace was determined by titration method of oxy-reduction (AOAC., 2000).

5. Experimental animals.

Thirty Male Sprague-Dawley rats 190-220 g were housed in the biological laboratory of the Agricultural Chemistry Department, Minia University, Egypt. Animals were housed in plastic cages and maintained on standard conditions of water, diet, light cycle, and temperature. Rats were adapted for one week on diet before the experimental treatment. All experimental rats were approved by the university ethical committee.

6. Experimental protocol.

Type II diabetes was induced using a single I.P injection of streptozotocin (STZ) 65 mg/kg b.w. Three days after STZ treatment, fasting blood glucose level of each rat was measured. Rats with fasting blood glucose levels >300 mg/dl were considered diabetic and included in the current study. Streptozotocin dose has also been used before to induce type II of diabetes in rats (Mendez and Ramos.,1994). Animals were divided into 5 groups. The non-diabetic control (NC) rats were treated with saline instead of STZ group (A). The STZ-induced diabetic rats were randomly divided into 4 groups of 6 rats each as follows:

B) Group B (DBC): Diabetic control group.
C) Group C (DM): The D+Metformin group received metformin (500 mg/kg/body weight/day) by oral administration as a reference drug.
D) Group D: The D+PpFJ group orally administrated 5.0 mL/kg/body weight/day of *P. Peruviana* fruit juice.
E) Group E: The D+PpFP group received *P. peruviana* fruit pomace at 10% level mixed with the diet.

Food intake was checked daily and body weight was determined weekly. Determination of blood glucose levels during experimental period (5 weeks) was done every week in blood samples collected from tail veins of the rats after the animals had been fasted for 12 h by using a single touch Glucometer (Roche group, UK).

7. Blood sampling.

After treatment for 35 days, the rats abstained for 12 hrs. Blood was received from the eye orbital plexus and left to clot, then centrifuged for 15 min at 3000 rpm (Trinder., 1969), the serum was stored at -20°C until used. The animals were sacrificed by cervical dislocation, pancreas tissues were stained by hematoxylin and eosin (H&E) stain. Pancreas tissues were placed in iced normal saline, and homogenized in cold phosphate buffer, then centrifuged for 10 min/3000 rpm/4°C, and the supernatant was used for oxidant/antioxidant parameters estimation.

8. Biochemical Evaluation.

Blood glucose level was measured in serum immediately. The determination of serum urea and creatinine was performed (Fawcett and Scott., 1960; Larsen., 1972). TG, TC, and HDL-c were calorimetrically determined in rat serum (Fossati and Prencipe. 1982; Richmond. 1973; Lopes-Virella *et al*., 1977). LDL-c and VLDL-c were calculated (mg/dl) as shown (Friedewald *et al*., 1972);

$$\textbf{VLDL-c = TG/5}$$

$$\textbf{LDL-c = TC – (HDL-c + VLDL-c)}$$

The activity of CAT and SOD activities, as well as TBARS, were evaluated in pancreas tissue. The protein content, CAT activity, and SOD activity was measured (Aebi., 1974; Beuchamp and Fridovich., 1971). TBARS are the markers of lipid peroxidation and their concentration were measured (Uchiyama and Mihara., 1978) using malondialdehyde (MDA) as standard.

9. Histopathological study.

Pancreas samples were taken and set in 10% salty solution/24 hrs, then washed with distilled water for 12 hours, the tissue samples were treated with absolute ethyl alcohol, then xylene and embedded in paraffin at 56°C in an oven for 24 hours. The paraffin blocks were sectioned at 3 microns thickness by sludge microtome then collected on glass slides, deparaffinized and stained with H&E stain (Ramadan, 2011).

10. Statistical analysis.

GraphPad Prism software (version 6) was used and results was expressed as mean ±SD using ANOVA followed by Tuckey's test. Data were considered statistically significant at P value < 0.05.

RESULTS AND DISCUSSION

1. Phytochemical Screening of *Physalis peruviana* fruit juice and pomace.

Table 1 shows bioactive compounds namely the total polyphenolic, flavonoids and vitamin C contents of *P. peruviana* L. fruit juice and pomace. The total polyphenolic content was 87.6 and 63.5 mg tannic acid (TAE) of polyphenols/100 mL fruit juice and 100 g pomace, respectively. Flavonoids content in *peruviana* L. fruit juice and pomace was 78.1 and 65.9 mg quercetin (QE) of flavonoids/ 100 mL fruit juice and 100 g pomace, respectively. Meanwhile, vitamin C content was 35.8 and 34.3 mg/100 mL fruit juice and 100 g pomace, respectively.

2. Biological assay.

Effect of treatment with *P. peruviana* fruit juice, pomace, and metformin on body weight, blood glucose levels, kidney function, lipid profile, and antioxidants enzyme were determined and showed as follows.

Table 1. Total polyphenolic, flavonoids and vitamin C contents of *Physalis peruviana* fruit juice and pomace*

	Total polyphenols	Flavonoids	Vitamin C
P. peruviana juice	87. 62±1.32	78.11±1.54	35.82 ± 0.65
P. peruviana pomace	63.49±0.83	65.91±1.11	34.31± 0.49

***The values are Mean ± SD of two independent experiments each performed in duplicate**

Total polyphenols are expressed as mg tannic acid equivalent of polyphenols /100 mL juice or 100 g pomace. Flavonoids are expressed as mg quercetin equivalents of flavonoids/ 100 mL juice or 100 g pomace

Vitamin c is expressed as mg ascorbic acid /100 mL juice or 100 g pomace

5. Changes in body weight.

Diabetes induction using STZ has been considered as a helpful model for experimenting the activity of antidiabetic agents. Effect of treatment with *P. peruviana* fruit juice, pomace, and metformin on body weight of diabetic rats was recorded in Table 2. Results indicated that no significant change in body weight (g) among all groups (p<0.05). During the experimental period, the mean ± SD values of body weight (g) of STZ diabetic control rats were significantly reduced.

Table 2. Body weight (gm) of normal and diabetic rats treated with *Physalis peruviana* fruit juice, pomace and metformin*

	Body weight (gm) per week					
Rat Groups	**Initial**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Week 5**
NC	205.5±7.17	252.8±11.85	281.5±14.98	304.3±14.32	317.2±18.68	339.0±17.49
DBC	205.0±8.48	$191.3^{a}\pm9.56$	$181.5^{a}\pm8.38$	$171.8^{a}\pm8.93$	$168.0^{a}\pm7.99$	$165.2^{a}\pm7.66$
D+Metformin	209.8±7.94	$206.0^{a,b}\pm5.54$	$210.0^{a,b}\pm6.56$	$215.0^{a,b}\pm9.35$	$215.5^{a,b}\pm8.79$	$219.2^{a,b}\pm9.98$
D+ PpFJ	208.8±6.86	$202.8^{a}\pm9.92$	$207.3^{a,b}\pm9.54$	$210.3^{a,b}\pm8.85$	$210.8^{a,b}\pm9.18$	$214.2^{a,b}\pm9.82$
D+ PpFP	203.5±9.81	$197.5^{a}\pm6.87$	$202.0^{a,b}\pm8.46$	$204.7^{a,b}\pm9.72$	$203.5^{a,b}\pm9.83$	$207.0^{a,b}\pm8.16$

****The values are Mean ± SD of 6 rats in each group ^{a} Significantly different from control at p < 0.05 ^{b} Significantly different from diabetic at p < 0.05***

3. Changes in blood glucose levels.

Effects of *P. peruviana* fruit juice, pomace and metformin on blood glucose levels in STZ-induced diabetic rats were shown in Table 3. Blood glucose levels increased significantly (more than 3 folds) in the diabetic group in compared with normal group. Although no difference between the diabetic control and group treated with *P. peruviana* fruit juice, pomace as well as metformin groups before treatment was observed, these groups showed a significant decrease in blood glucose levels after the 1st week of treatment, compared with the untreated diabetic one. Blood glucose levels were significantly decreased with increasing duration of the treatment. The metformin group had more significant reduction in blood glucose levels, compared with *P. peruviana* fruit juice and pomace groups at the 2nd, 3rd and 4th weeks of sample administration. At the end of the experiment, the reduction in blood glucose concentration was continued and reached to 62.6%, 57.6%, and 54.8% for metformin, *P. peruviana* fruit juice, and pomace respectively.

Table 3. Blood glucose levels (mg⁄dL) of normal and diabetic rats treated with *Physalis peruviana* fruit juice, pomace and metformin*

	Blood glucose level mg/dL					
Rat Groups	**Initial**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Week 5**
NC	84.5±3.53	86.3±3.86	87.5±4.88	85.0±2.32	85.5±3.68	81.5±4.49
DBC	$441.5^{a}\pm19.48$	$438.8^{a}\pm18.65$	$437.5^{a}\pm22.38$	$435.0^{a}\pm24.93$	$430.5^{a}\pm13.19$	$427.5^{a}\pm19.36$
D+Metformin	$449.3^{a}\pm12.94$	$396.0^{a,b}\pm12.84$	$352.7^{a,b}\pm10.76$	$301.0^{a,b}\pm11.35$	$245.5^{a,b}\pm7.79$	$168.0^{a,b}\pm7.58$
D+ PpFJ	$447.5^{a}\pm11.96$	$401.5^{a,b}\pm15.92$	$362.3^{a,b}\pm11.54$	$319.3^{a,b}\pm14.85$	$263.3^{a,b}\pm9.18$	$198.8^{a,b}\pm9.22$
D+ PpFP	$442.5^{a}\pm15.99$	$402.7^{a,b}\pm17.87$	$359.0^{a,b}\pm13.46$	$318.5^{a,b}\pm13.72$	$258.5^{a,b}\pm7.83$	$200.0^{a,b}\pm8.66$

****The values are Mean ± SD of 6 rats in each group. ^{a} Significantly different from control at p < 0.05 ^{b} Significantly different from diabetic at p < 0.05***

4. Changes in kidney functions.

STZ injection leads to a significant increase in the level of serum creatinine and urea compared to control group. After treatment of STZ-diabetic rats with *P. peruviana* fruit juice and pomace, the levels of serum creatinine and urea were significantly (p<0.05) decreased by 33, 34 and 20, 28%, respectively as mentioned in (Fig.1 A, B). Similarly, metformin treatment significantly lowered serum creatinine and urea by 32 and 23% respectively.

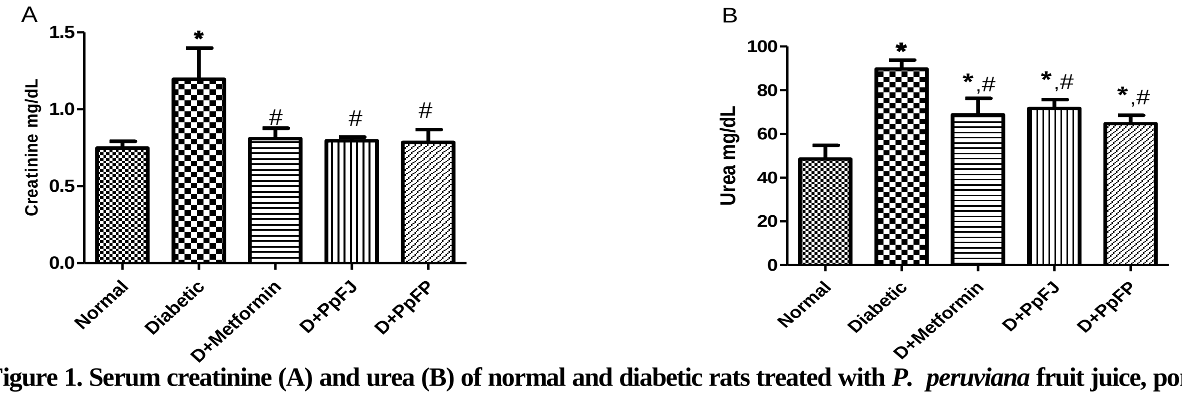

Figure 1. Serum creatinine (A) and urea (B) of normal and diabetic rats treated with *P. peruviana* fruit juice, pomace and metformin. Data represent means ± SD of 6 rats in each group. **P* <0.05 significantly different compared with control group; #*P* < 0.05 significantly different compared with diabetic group as analyzed by Tuckey's test.

6. Changes in lipid profile.

Data in Table 4 indicates that STZ-induced rats showed a significant increases in serum TG, TC, LDL-c and VLDL-c (p< 0.05), while the mean value of HDL-c was significantly decreased. The administration of diabetic rats with *P. peruviana* fruit juice significantly reduced the elevated TG, TC, LDL-c, and VLDL-c levels by 39, 27, 29 and 39%, respectively. Also, diabetic rats treated with the *P. peruviana* fruit pomace (as functional food) showed a significant reduction in TG, TC, LDL-c, and VLDL-c levels by 40, 20, 19 and 40% respectively. Following with metformin administration, TG, TC, LDL-c and VLDL-c levels were significantly declined in diabetic rats group by 33, 20, 28 and 33% respectively when compared with untreated STZ-diabetic group. In contrast, serum HDL-c presented a significant increase after 5 weeks of metformin oral administration compared with diabetic rats. Meanwhile, serum HDL-c level in diabetic rats treated with *P. peruviana* fruit juice and pomace revealed a nonsignificant increase.

Table 4. Lipid profile (mg/dL) in normal and STZ-induced diabetic rats treated with *Physalis peruviana* fruit juice, pomace and metformin*

	Lipid profile mg/dL				
Rat Groups	**TG**	**TC**	**HDL-c**	**LDL-c**	**VLDL-c**
NC	107. 65±3.45	82.11±3.54	28.56 ± 1.55	32.02 ±1.93	21.53±1.18
DBC	208.36^{a}±9.13	129.84^{a}±4.63	16.16^{a} ± 0.89	69.18^{a} ±2.18	41.97^{a}±1.19
D+Metformin	139.39^{b}±5.04	103.35^{b}±4.75	25.58^{b} ± 1.24	49.92^{b}±1.88	27.88^{b}±1.09
D+ PpFJ	127.75^{b}±4.43	94.36^{b}±3.89	22.11 ± 1.12	48.64^{b}±1.93	25.51^{b}±0.98
D+ PpFP	125.57^{b}±3.55	104.41^{b} ±5.61	23.4^{b} ± 1.18	55.74^{b}±2.03	25.11^{b}±0.83

**The values are Mean ± SD of 6 rats in each group. [a] Significantly different from control at p < 0.05 [b] Significantly different from diabetic at p < 0.05*

7. Changes in TBARS level and activities of antioxidant enzymes.

Table 5 shows the levels of thiobarbituric acid reactive substances (TBARS) and the activities of SOD and CAT enzymes as indicators for protein oxidative damage in tissues of normal and diabetic animals. However, TBARS concentrations were considerably increased in the pancreas of diabetic groups. Treatment with *P. peruviana* fruit juice and pomace for the diabetic rats presented a suggestive decrease in TBARS levels in the pancreas tissue by 32.9 and 31.6%, respectively. Activities of these enzymes were significantly ($p<0.05$) decreased in the diabetic group. STZ-diabetic rats group treated with *P. peruviana* fruit juice and pomace showed a significant increase in the activities of SOD by 44.1 and 46.4 % and of CAT by 79.7 and 87.5%, respectively in the pancreas tissue. Similarly, metformin treatment to diabetic rats resulted in enhancement the levels of TBARS, SOD and CAT activities in the pancreas tissue of those diabetic rats. Data analysis showed the improvement effect of the *P. peruviana* fruit juice and pomace which appeared to be more potent than metformin.

8. Changes in histopathology of pancreas.

Pancreas sections of normal control rat group showed no histopathological changes in islets of Langerhans cells (Fig. 2A). In contrast, hypertrophy, hyperplasia, and necrosis of β-cells of islets of Langerhans associated with the pinkness of their nuclei were found in diabetic control rats as shown in Fig. 2B. However, slight hypertrophy of islets of Langerhans was found in pancreas sections of administrated rats with *P. peruviana* fruit juice as shown in Fig. 2D. Pancreas sections of treated rats with *P. peruviana* fruit pomace revealed congestion of pancreatic blood vessels (Fig 2E). Meanwhile, a section in rat's beta-cells of the pancreas of metformin treated diabetic group showed moderate islet reduction and moderate mononuclear inflammatory cellular infiltrates (Fig 2C).

Table 5. thiobarbituric acid reactive substances level and activities of antioxidant enzymes in normal and STZ-induced diabetic rats treated with *Physalis peruviana* fruit juice, pomace and metformin*

Rats Group	**TBARS (nmol MDA/g tissue)**	**SOD (U/mg protein)**	**CAT (µM of H2O2/min/mg protein)**
NC	6. 62±0.37	115.01±5.74	91.89 ± 5.55
DBC	13.59^{a}±1.03	54.49^{a}±2.13	34.01^{a} ± 1.89
D+Metformin	$9.87^{a,b}$ ±0.84	$75.19^{a,b}$ ±4.05	$54.91^{a,b}$± 2.18
D+ PpFJ	$9.12^{a,b}$ ±0.43	$78.51^{a,b}$ ±3.39	$61.12^{a,b}$± 3.12
D+ PpFP	$9.29^{a,b}$ ±0.55	$79.76^{a,b}$ ±2.68	$63.77^{a,b}$± 3.24

**The values are Mean ± SD of 6 rats in each group.*
[a] Significantly different from control at p < 0.05
[b] Significantly different from diabetic at p < 0.05
SOD; Superoxide dismutase.
CAT; Catalase.

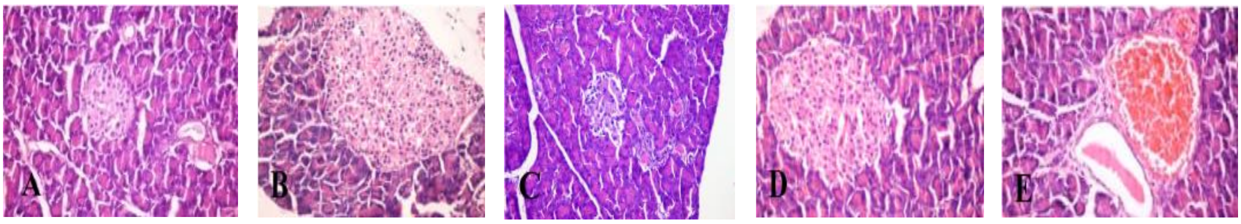

Figure 2. A photomicrograph of the pancreas of rats in normal control group (A), untreated diabetic control group (B), diabetic rats treated with metformin (C), diabetic rats treated with *P. peruviana* fruit juice (D) diabetic rats treated with *P. peruviana* fruit pomace (E). Hematoxylin/eosin staining; magnification 400x.

Discussion

According to the present results, the benefits associated with the fruit juice and pomace of *P. peruviana*, as functional foods are mainly due to their nutritional composition. They have good nutritional value and contain characteristics biologically active components such as polyphenols and flavonoids that provide health advantages and reduce risk for certain diseases (Ramadan., 2012). Administration of *P. peruviana* fruit juice and pomace ,as well as metformin, caused significant increases in body weight (g) in all treated STZ diabetic groups when compared with the untreated diabetic control group. STZ-induced diabetes is illustrated by an obvious loss in body weight and some hyperglycemic problems (Zhao *et al*., 2011). The decrease in body weight perceived in diabetic rats might be the result of protein consuming due to the unavailability of carbohydrates for utilization as an energy source (Chen and Ianuzzo., 1982). *P. peruviana* fruit juice and pomace showed significant recovery in body weight gain after 5 weeks of treatment, compared to diabetic control. This is implying that these plant materials may possess some protective effect in controlling muscle wasting, probably by reversal of gluconeogenesis, improvement in insulin secretion and/ or glycemic control.

The principal reason of STZ-induced beta-cell death is DNA alkylation by its methyl nitrosourea moiety, resulting in DNA fragmentation. Moreover, STZ may also be involved in other deleterious changes (Lenzen., 2008). The significant reduction in glucose level in this study after the administration of *P. peruviana* fruit juice and pomace was following another study (Rodríguez and Rodríguez., 2007) who indicated that eating 25 g of *P. peruviana* fruits significantly reduced blood glucose levels after 90 min postprandial in young adults. In the same trend, the oral administration of polysaccharide isolated from *Physalis alkekengi* L. fruit considerably reduced levels of blood glucose in diabetic mice (Tong *et al*., 2008). Different mechanisms are involved in suppressing blood glucose levels by *P. peruviana* fruit and pomace supplementation: modulation of glucose transport; glucose disposal and increasing the pancreatic secretion of insulin (Kasali *et al*., 2013). Also, some components (that are found in the functional foods *P. peruviana* fruit and pomace) such as with anolides, physlains, phytosterols, citric acid, and vitamin C are known to be responsible for hypoglycemic activity.

The chronic hyperglycemia of diabetes is strongly related to injury, dysfunction, and failure of kidneys (Uladimir., 2003). Renal disorders in rats is correlated with tissue damage following ischemic insult (Jarald *et al*., 2008). Also, the increased oxidative stress and the reduced antioxidant ability in diabetes led to glomerular sclerosis, gradual loss of physiological function, and changes in the structure of the kidney (Shah *et al*., 2007). STZ-diabetic rats treated with *P. peruviana* fruit juice and pomace, showed their ability to restore the normal functional status of their damaged kidney. Our results run parallel with the results that showed STZ-diabetic rats had a suggestive rise in the levels of creatinine and urea. Also, the present study showed that oral administration of *P. peruviana* extract and powder normalized the renal functions of STZ-diabetic rats. The mechanism by which the *P. peruviana* fruit juice and pomace improved kidney functions may be related to their antioxidant activity. Our results showed the antioxidant constituents of *P. peruviana* fruit juice and pomace such as vitamin E, phenolic components, ascorbic acid, and flavonoids Table 1.

Diabetes increase LDL-c, triacylglycerol and bad cholesterol levels. These rise the danger of heart sicknesses and stroke- this condition is called diabetic dyslipidemia which is characterized by elevated serum levels of TG and LDL-c (Florkowski., 2002) and TC (Farombi and Ige., 2007). Moreover, type 2 diabetes, diabetic dyslipidemia, and insulin resistance factors raise risk of heart attack and stroke (Ronald and Krauss., 2004). Our results matched with other studies (Oladele *et al*., 2013) reported that oral administration of diabetic rats with *Physalis angulata* root extract showed a significant decrease in TC, TG, and LDL-c with an increase in HDL-c compared with untreated diabetic rats. the obtained results indicated that rats fed *Physalis peruviana* fruit pomace showed lower levels of TC, TG, and LDL-c as well as higher levels of HDL-c in comparison with animals fed high cholesterol diet. In this study, STZ-diabetic rats treated with *P. peruviana* fruit juice and pomace decrease the levels of serum cholesterol, TG, LDL-c, but the HDL-c level was increased. This is possibly due to the beneficial phytosterols in *P. peruviana* fruit and pomace which decrease the LDL-c levels in total plasma. This action of *P. peruviana* fruit juice and pomace support their lipid-lowering activity in diabetic conditions and therefore it helps to prevent diabetic associated complications.

The significant increase of the pancreatic TBARS level in diabetic rats was agreed with another data (Oladele *et al*., 2013) reported that increasing in the level of lipid peroxidation with a decrease in the activities of SOD and CAT enzymes. This may be due to increased oxidative stress (Severcan *et al*., 2005**).** The increased level of TBARS is a marker of lipid peroxidation, which leads to an increase in free radical activity in type 2 diabetes (Kalaivanam *et al*., 2006). On the other hand, diabetic rats receiving *P. peruviana* fruit juice and pomace showed a meaningful reduction in lipid peroxides with a significant rise in antioxidant activities. These results showed the administration of the *P. peruviana* fruit extract showed an increase in SOD and CAT activities as well as a reduction in lipid peroxidation and protein oxidation in STZ-diabetic rats. The beneficial effects of *P. peruviana* fruit juice and pomace in improving oxidative stress parameters in diabetic rats could be related to its high levels of polyphenols and flavonoids, which improved the procedure of renewal by annihilation of free radicals (Coskun *et al*., 2005).

Histopathological examination, indicated that insulin depletion in STZ-diabetic rats may led to changes of tissue structure (Das *et al*., 1996). Pancreatic injuries induced by STZ were significantly reduced by the treatment with *P. peruviana* fruit juice and pomace. The results could be attributed to polyphenols of *P. peruviana* fruit and pomace, which prevent the pancreatic β-cells injury and motivate the renewal of these cells in diabetic rats. polyphenols, like quercetin and epicatechin protects the construction of pancreatic β-cells and domains the excretion of insulin (Zold *et al*., 2009).

CONCLUSION

In conclusion, the daily oral administration for at least one time of *Physalis peruviana* L. fruit juice and pomace as functional foods not only exhibit pronounced antihyperglycemic and antihyperlipidemic activities, but also decrease the lipid peroxidation process as well as enhance the antioxidant defense system in the pancreas of the STZ-diabetic rats. These results suggest *Physalis peruviana* L. fruit juice and pomace a good natural source of anti-diabetic phytochemicals and its complications through its possible impact of anti-free radicals in the β-cells of the pancreas.

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التأثير المضاد للأكسدة ومرض السكري لعصير وتفل نبات الحرنكش علي الفئران المصابة بالسكري والمعاملة بالستربتوزوتوسين (STZ) معمليا

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تهدف هذه الدراسة إلى ملاحظة نشاط مضاد الاكسدة ومضاد السكري لعصير ثمار وتفل لنبات (*Physalis peruviana* L.) الذي يتبع العائلة النباتية Solanaceae والمعروف أيضًا باسم Goldenberry أو الحرنكش Harrankash في مصر و ذلك للفئران المصابة بداء السكري عن طريق المعاملة بمركب ستريبتوزوتوسين (STZ) streptozotocin . في هذه الدراسة تم أصابه الفئران بداء السكري باستخدام ٦٥ مجم STZ / كجم من وزن الجسم) و بعد أربعة أيام من تناول الفئران لمركب STZ ، أعطيت الفئران المصابة بداء السكري (٠,٥مل / كجم / وزن الجسم) من عصير وتفل فاكهة الحرنكش بنسبة ١٠ ٪ مضافا يوميًا للنظام الغذائي لمدة ٣٥ يومًيا. و أستخدم الميتفورمين بمعدل (٠,٥ مجم / كجم) عن طريق الفم كمجموعة ضابطة. تم قياس اليوريا والكرياتينين في الدم كما تم تقييم إنزيمات السوبرأكسيد ديسميوتاز SOD و الكتاليز CAT والمواد التفاعلية لحمض الثيوباربيتوريك (TBARS) في أنسجة البنكرياس. و أظهرت النتائج المتحصل عليها ان عصير وتفل ثمار الحرنكش أدت الي تحسين مستويات الجلوكوز في الدم معنويا (P <٠,٠٥) وجعلها في مستوياتها الطبيعية مقارنة بالمجموعة القياسية STZ. كما أدت الي تعديل القياسات البيوكيميائية في سيرم الدم بما في ذلك محتوى الدهون والحالة المضادة للأكسدة وجعلها في المستويات الطبيعية (P <٠,٠٥) في الفئران المعاملة بعصير و تفل ثمار الحرنكش مقارنة بفئران المجموعة الضابطة STZ. تم تأكيد التأثير الوقائي لعصير وتفل ثمار الحرنكش من خلال التحسينات الهستولوجية المثبتة في خلايا البنكرياس للفئران المصابة بداء السكري والمعاملة بعصير و تفل ثمار الحرنكش . من هذه النتائج توصي هذه الدراسة تشجيع علاج سكر الدم ومضاعفات مرض السكري عن طريق عصير ثمار وتفل نبات *Physalis peruviana* او الحرنكش..