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Research Article

Anti-Hyperglycemic Effect of Salvadora Persica Leaf Extracts in Alloxanized Rats

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Abstract

In this study thirty-five male albino rats weighing 170-190 -g (two months age). Were used to evaluating the Anti-hyperglycemic effect of Salvadora persica leaf extract in hyperglycemic rats induced by alloxan in addition to its effects on kidney functions, lipids profile, and hepatic functions. These rats were fed on the standard diet for two weeks to adjust before the experiment began; Rats were separated into five groups. Each group contains seven rats. The healthy control rats (Group1) were fed on the standard diet. The (group 2), (group 3), (group 3) and (group 5) were injected with one dose of alloxan monohydrate at (150 mg per kg of body weight). The hyperglycemic control rats (group 2) were fed on standard diet. The hyperglycemic rats for group 3, group 4 and group 5 were treated with leaf extract of Salvadora persica orally at 50,100 and 150 mg / kg of body weight per day for six weeks respectively. From the results of present work indicate that, the hyperglycemic rats untreated with Salvadora persica leaf extracts (group 2) showed increased in serum glucose levels, glycosylated hemoglobin (HbA1c), cholesterol, triglycerides, total lipids, (LDL-c) low density lipoprotein, (VLDL-c) very low density lipoprotein, renal function, Serum, (AST) aspartate aminotransferase activity and (ALT) alanine aminotransferase and decreased in insulin and (HDL-c) high density lipoprotein relative to healthy control rats (group 1). Treating the hyperglycemic rats in group 3, group 4 and group 5 with leaf extract of Salvadora persica were improved the histological and biochemical changes nearly to the healthy rats (group 1).

Keywords: *Salvadora persica leaf extracts, Anti-hyperglycemic effect, Lipid profile, hepatic functions, kidney functions.*

Introduction

Diabetic illness is a major disturbance of carbohydrate metabolism, which in general encompasses absolute or relative deficiency of insulin and / or insulin resistance and eventually leads to elevation of sugars level in the blood. There has been an increase in the utilization of natural products with antidiabetic activity. Undesirable side effects of chemical drugs, consumption or availability easier and the fact that they are not appropriate for use during pregnancy were some of the factors that lead to a strong desire to use hypoglycemic agents of vegetarian sources (Yadev et al., 2008; Jeloder et al., 2007) [1,2].

Diabetic illness is a chronic metabolic disorder in glucose tolerance and an elevated hazard of cardiovascular disease (Schnell and Standle 2006) [3]. Hyperglycemia can be handled initially with oral agents and insulin therapy, which sometimes required achieving targeted glycemic levels. However, these chemical drugs produce some serious side effects and relatively expensive for developing countries (Edoga et al., 2013) [4].

Salvadora persica L. (toothbrush tree) is a perennial tree belongs to the family salvadoraceae from which, meswak, a stick chewing gum changed into prepared from its pitting and the roots to the teeth cleaning in the Arab nations. Meswak is vastly used in Islamic countries due to the reality that it is part of the religious practice of Islam and its use in maintaining dental hygiene and, ultimately, potential and on safe security as a dental cure (Ahmad and Rajagopal 2014) [5]. The leaf of Salvadora persica was eaten, used in the sauce and taken as a salad in tropical and eastern Africa as vegetables and used as anti-cough, anti-asthma and in the remedy of rheumatism, its fragrant flower are used as a stimulant and purgative two (Chaurasia et al., 2013) [6]. The leaf of Salvadora persica is bitter in taste, corrective, non-toxic, astringent for intestinal, liver tonic, diuretic, analgesic, anesthetic, beneficial in ozone and other nose problems, piles, scabies, leukemia, alleviate inflammation, and strengthens teeth. Leaf and flowers also used for toothache, gum problems, skin diseases, kidney stones, constipation anthelmintic, and leaf juice was used in scurvy. (Akhtar et al., 2011) [7]. Bioactive components and minerals had been observed in the leaf of Salvadora persica which includes flavonoids, calcium, saponins, tannins,

glycosides, alkaloids, fluoride, pyrrolidine, phosphorous and ascorbic acid (Halawany 2012) [8]. The aim of this research was to evaluate the anti-hyperglycemic effect of Salvadorsa persica plant extract in alloxan-induced hyperglycemic rats.

Material and Methods

Material

Plant materials

Leafs of *Salvadora persica* tree were collected from Jeddah, Saudi Arabia.

Preparation of extracts

The leaf of Salvadora persica were cleaned, washed and then dried at 40^0 C in an electric oven for 12 hours and milling to pass through a 60 mesh

Leaf of Salvadora persica powder (100g) were macerated in 1000 ml of 70% aqueous ethanol and kept in dark for 48 h at room temperature. The extract was filter and ethanol was vaporized under the reduced pressure at 50^0 C. The remaining water extract was dried under reduced pressure by using freeze- drying.

The dried ethanolic extracts were dissolved in deionized water to a concentration of 300 mg/ml before administration in hyperglycemic rats.

Experiment design

Thirty- five male albino rats weighing 170-190 g (two months age) were obtained from King Abdul-Aziz University. These rats were fed on the basal diet for two weeks for adaptation prior to commencement of the experiment, housed in well- aerated cages under hygienic conditions and water. The 35 rats were separated as follows: 7 rats for the first group (group 1) the healthy control group fed basal diet. The other 28 rats were intraperitoneally injected with a single dose of alloxan monohydrate (150 mg/kg between dissolved in distilled water) after fasting for 12 h to induce hyperglycemia (Dash et, al., 2001) [9]. After 5 days of injection, rats with blood glucose higher than 200 mg/dl in the fasting state were considered as being hyperglycemic and were divided into 4 groups; the was the hyperglycemic control rats (group 2) were fed on basal diet. The group 3, group 4 and group 5 were fed on basal diet and treated with leaf extract of Salvadora persica orally at 50,100 and 150 mg /kg of body weight per day, for six weeks respectively.

Blood sampling

At the end of the experimental period, all rats were fasted overnight then sacrificed. Blood samples were immediately collected from the retro-orbital plexus with capillary tubes under mild ether anesthesia, into clean dried centrifuge tubes. The tubes were then centrifuged at 3000 rpm for 15 minutes. Clear serum samples were carefully separated using Pasteur pipettes, and frozen at - 20°C until biochemical analysis (Margoni et al., 2011) [10].

Animals were sacrificed by cervical dislocation, and then the abdomen was dissected and the target organs (the liver, the two kidneys and the pancreas) were rapidly excised. A piece of liver (100 mg) was rinsed in saline and then saved in ice-cold for enzymes estimation in liver tissue homogenate. The rest of the liver, one kidney and the pancreas were rinsed in saline for a few seconds, and then kept in 10% formalin for histopathological investigations.

Analytical methods

Serum glucose was estimated by enzymatic GOD / POD kits according to the method defined by (Trinder, 1969) [11]. Insulin was estimated by using the method explained with (Clark and Hales 1994) [12].

Glycated hemoglobin (HbA1c) was decided in whole blood according to the method explained with (Variant 1997) [13]. Serum cholesterol was determination by using the method (Allain et al., 1974) [14].

Serum triglycerides (TG) were estimated by Enzymatic colorimetric GPO-PAP kit according to the method explained by (Trinder 1969) [15].

High-Density Lipoprotein Cholesterol (HDL-c) was estimated colorimetrically according to the method defined by using (Lopes-Virella et al., 1977) [16].

Low-Density Lipoprotein Cholesterol (LDL-c) and Very Low - Density Lipoprotein Cholesterol (VLDL-c), were estimated calorimetrically by the method explained with (Fridewald et al., 1972) [17].

Serum Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) activities were estimated enzymatically based on color reaction formation according to the method the method defined by using (Bergmeyer et al., 1978) [18]. Serum urea was spectrophotometrically estimated of the technique defined by (Fawcett and Scott 1960) [19]. Uric acid was spectrophotometrically determined by the method explained by (Fossati et al., 1980) [20].

Serum creatinine was estimated by the method explained with (Tietz 1976) [21]. Statistical analysis was conducted using the Social Sciences Statistical Package (SPSS) for Windows, version 22 (SPSS Inc., Chicago, Illinois, USA). The data obtained was presented as means Standard Error (SE). Statistical analysis of the difference between mean values of different groups was performed using one trend (ANOVA) test was used for determining the significances among different groups explained by (Armitage and Berry, 1987) [22]. All differences were considered significant if $P < 0.05$.

Results and Discussion

Effect of Salvadora persica leaf extract on Body weight in hyperglycemic rats is presented in Fig (1). Results of present work indicate that, the body weight in healthy control rats (group1) were increased by 722% 1012% and 16.61% after the two weeks, four weeks and six weeks respectively of experimental period when compared to

body weight at initial periods of experimental. In contrast to this, body weight of hyperglycemic control rats (group 2) were decreased by 5.57% , 9.38%, and 13.47% respectively after the two weeks, four weeks and six weeks of experimental period compared with their initial body weight (Zero day). Results also indicated that, the hyperglycemic rats treated with leaf extract of Salvadora persica at different concentrations (50, 100 and 150 mg/kg of body weight/day) showed the increased in the body weight. Hyperglycemic rats treated with leaf extract of Salvadora persica at 50 mg/kg of body weight/ day) (group 3) was increased in body weight by 4.15% after six weeks. Hyperglycemic rats treated with leaf extract of Salvadora persica at 100 mg/kg of body weight/day) (group 4) was increased in body weight by 8.48% in body weight was observed after 6 weeks of treatment. Hyperglycemic rats treated with leaf extract of Salvadora persica at 150 mg/kg of body weight/day (group 5) were increased in body weight by 5 7.22%, 10.12% and 16.65 in body weight respectively after two weeks, four weeks and six weeks.

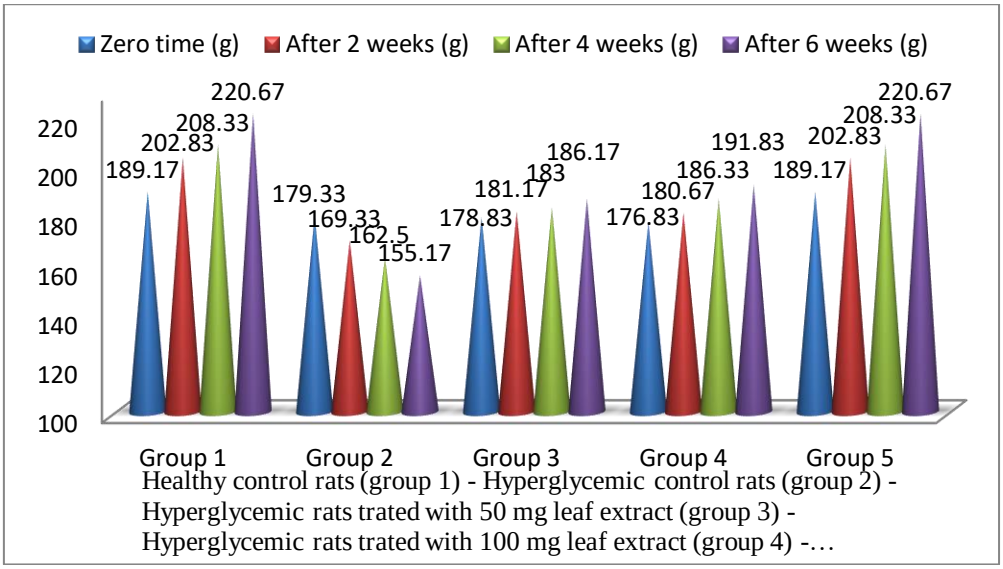

Figure 1: Effect of Salvadora persica leaf extract on Body weight in hyperglycemic.

Treatments	Glucose mg/dl				
	Zero time	After 2 weeks	After 4 weeks	After 6 weeks	Decease %
healthy Control rats (Group 1)	119.00^{b} ±5.29	116.50^{e} ±5.20	115.25^{e} ± 4.03	114.00^{e} ± 4.32	- 4.20
hyperglycemic Control rats – (Group 3)	369.50^{a} ±19.16	349.25^{a} ±14.86	329.25^{a} ±11.81	306.50^{a} ±10.28	- 15.91
hyperglycemic rats treated with 50 mg leaf extract (Group 3)	366.50^{a} ±15.35	326.75^{b} ±13.72	265.00^{b} ±10.61	214.75^{b} ±9.60	- 41.41
hyperglycemic rats treated with 100 mg leaf extract (Group 4)	363.25^{a} ±16.40	331.25^{c} ±12.07	245.00^{c} ±8.06	180.00^{c} ±7.30	- 50.45
hyperglycemic rats treated with 150 mg leaf extract (Group 5)	364.75^{a} ±15.88	322.00^{d} ±13.49	230.25^{d} ±9.14	149.75^{d} ±8.54	- 58.94

The values of each column which have different characters are significantly different (P<0.05).

Table 1: Effect of leaf extract from *Salvadora persica* on serum glucose levels in hyperglycemic rats.

Effect of different ratio of leaf extracts from Salvadora persica on the serum glucose levels in hyperglycemic rats is illustrated in Table (1). The hyperglycemic control rats (group 2) had a significant (p<0.05) increase in serum glucose level compared with healthy control rats (group 1) by 210.50 %. Results, also indicated that, the hyperglycemic rats treated with Salvadora persica leaf extract at 50, 100 and 150 mg/kg of body weight were significantly (P<0.05) decreased in serum glucose level by 29.93, 41.27 and 51.14 % for (group 3), (group 4) and (group 5) respectively compared with hyperglycemic control rats (group 2) after six weeks from experimental study. These results are agreement with (Gay et al., 2000) [23]. They reported that, reduced of glucose levels in hyperglycemic rats due to the

presence of compounds in the leafs extract that have an insulin-like effect on the surrounding tissues either by encouraging metabolism to absorb glucose or by absorbing glucose into the muscle and fatty tissue by stimulating the regeneration process and reactivating the remaining beta cells. These results are similar with that reported by (Tuorkey et al., 2015) [24]. Induced hyperglycemia by alloxan has been described as a useful experimental model for studying the activities of hypoglycemic agents because it selectively destroys of the pancreatic cells in rats.

Effects of Salvadora persica leaf extract on insulin in hyperglycemic rats are shown in Fig (2). Results of biochemical analyses revealed that the hyperglycemic control rats (group 2) had a significant (p<0.05) decreased by 49.67 % for insulin compared with healthy control rats (group 1).

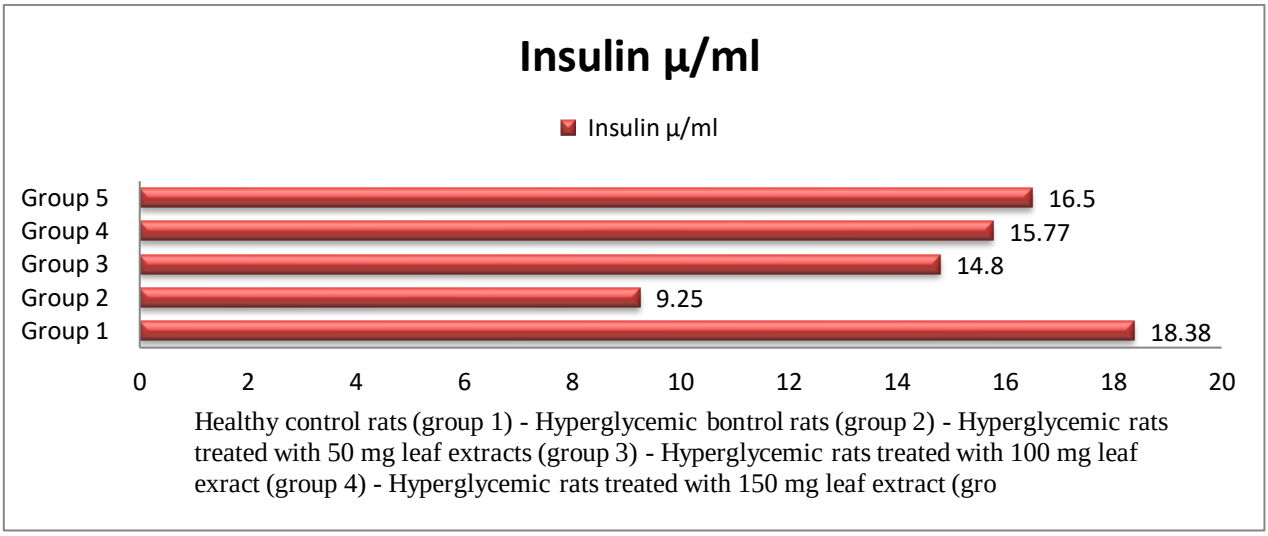

Figure 2: Effects of leaf extract from Salvadora persica on insulin in hyperglycemic rats.

Results of present work indicate that, the Hyperglycemic rats treated with Salvadora persica leaves extract at 50, 100 and 150 mg/kg of body weight were significantly (P<0.05) increased in serum insulin by 60.0, 70.49 and 78.38 % for (group 3), (group 4) and (group 5) respectively compared with hyperglycemic control rats (group 2). These results are agreement with (Gupta and Misra, 2006) [25] they reported that, the extract contains of Bioactive components, which induce their ant-hyperglycemic effect by produce increased insulin production and inhibition of glucose by intestinal absorption or facilitating metabolism in insulin.

Effects of leaf extract from Salvadora persica on glycosylated hemoglobin (HbA1c) in Hyperglycemic rats is shown in table (3). Results of present work indicate that, the Hyperglycemic control rats (group 2) had a significant (p<0.05) Increased by 68.51 % of the glycosylated hemoglobin (HbA1c) relative to healthy control rats (Group 1). Hyperglycemic rats treated with leaf extract of Salvadora persica at 50, 100 and 150 mg/kg of body weight were significantly decreased by 12.87, 24.51 and 30.08 % in glycosylated hemoglobin (HbA1c) for (group 3), (group 4) and (group 5) respectively compared with Hyperglycemic control rats (group 2).

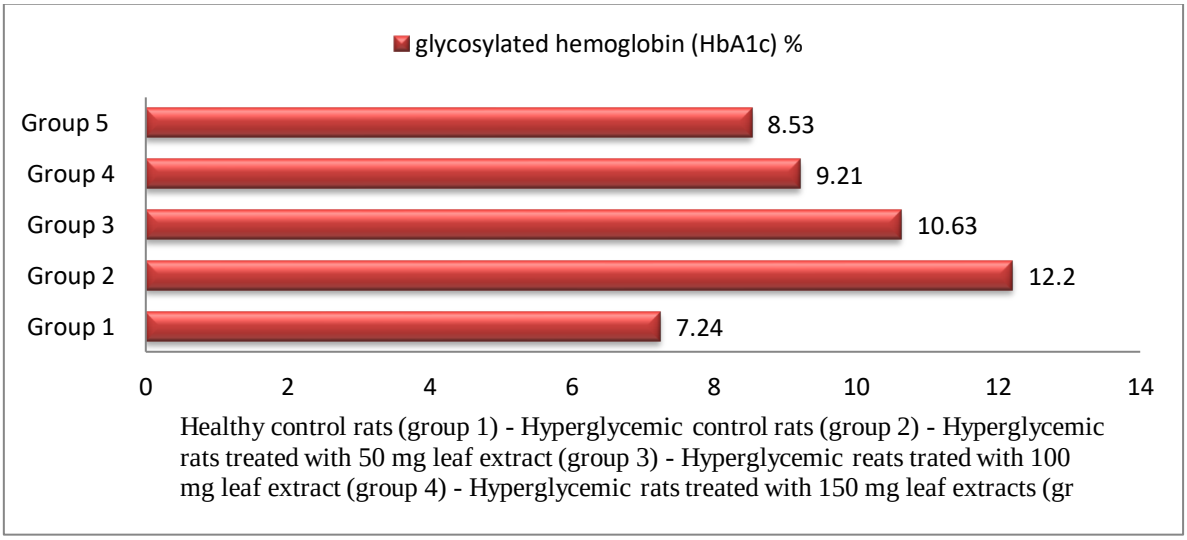

Figure 3: Effects of leaf extract from Salvadora persica on glycosylated hemoglobin (HbA1c) in Hyperglycemic rats.

Effects of leaf extracts from Salvadora persica on Total cholesterol, Triglycerides and total lipids in hyperglycemic rats are presented in Fig (4). Results of present work indicate that, the hyperglycemic control rats (group 2) had a significantly (p<0.05) increased in total cholesterol by 13.83 %, triglycerides by 7.94 % and total lipids 13.24 % compared with healthy control rats (group 1). Hyperglycemic rats treated with leaf extracts of Salvadora persica at 50, 100 and 150 mg/kg of body weight were significantly (p<0.05) decreased in serum total cholesterol by 0.69, 11.11 and 11.81 % for (group 3), (group 4) and (group 5) respectively compared with hyperglycemic control rats (group 2). While, hyperglycemic rats treated with leaf extracts of Salvadora persica at 50, 100 and 150 mg/kg of body weight were significantly (p<0.05) reduced of Triglycerides levels by 1.04, 3.24 and 6.73 % for (group 3), (group 4) and (group 5) respectively when compared to hyperglycemic control rats (group 2). On the other side, hyperglycemic rats treated with leaf extracts of Salvadora persica at 50, 100 and 150 mg/kg of body weight were significantly (p<0.05) reduced in total lipids levels by 10.17, 15.86 and 18.43 % for (group 3), (group 4) and (group 5) respectively compared with hyperglycemic control rats (group 2).

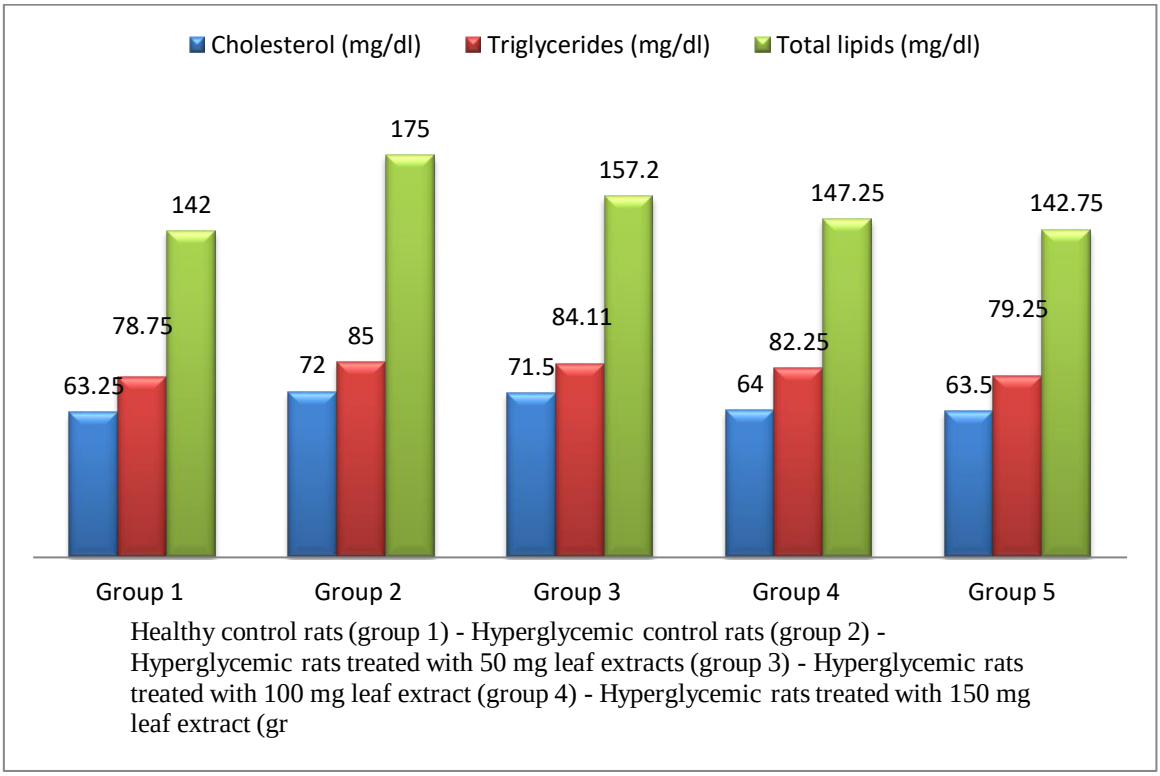

Figure 4: Effects of leaf extracts from Salvadora persica on Total cholesterol, Triglycerides and total lipids in hyperglycemic rats.

Effect of leaf extract from Salvadora persica on high-density lipoprotein cholesterol HDLc, low- density lipoprotein cholesterol LDLc and very low-density lipoprotein cholesterol VLDLc in hyperglycemic rats are shown in table (6). Results of present work indicate that, the hyperglycemic control rats (group 2) had a significantly (p< 0.05) increased in LDLc and VLDLc compared with the healthy control rats (group 1) by 101.20 and 10.16% respectively. While, the hyperglycemic control rats (group 2) had a significantly (p< 0.05) decreased in HDLc compared with the healthy control rats (group 1) by 18.57%. Results also indicate that, the Hyperglycemic rats treated with leaf extract of Salvadora persica at 50, 100 and 150 mg/kg of body weight were significantly (P<0.05) increase in high density lipoprotein cholesterol HDLc by 2.63, 7.02 and 15.79 % respectively. on the other side, the hyperglycemic rats treated with leaf extract of Salvadora persica at 50, 100 and 150 mg/kg of body weight were significantly (P<0.05) decreased of LDLc and VLDLc by 9.54, 33.00 and 51.75% for LDLc, while the decreasing rate in VLDL by 2.88, 4.03 and 8.65% respectively compared with hyperglycemic control rats (group 2).

Treatments	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
healthy Control rats (Group 1)	$35.00^{a} \pm 1.83$	$12.50^{e} \pm 5.85$	$15.75^{c} \pm 0.34$
hyperglycemic Control rats-(Group 3)	$28.50^{d} \pm 5.45$	$25.15^{a} \pm 7.75$	$17.35^{a} \pm 0.66$
hyperglycemic rats treated with 50 mg leaf extract (Group 3)	$29.25^{cd} \pm 1.71$	$22.75^{d} \pm 2.41$	$16.85^{b} \pm 1.50$
hyperglycemic rats treated with 100 mg leaf extract (Group 4)	$30.50^{c} \pm 3.08$	$16.85^{c} \pm 3.29$	$16.65^{bc} \pm 1.51$
hyperglycemic rats treated with 150 mg leaf extract (Group 5)	$33.00^{b} \pm 2.71$	$14.65^{d} \pm 3.53$	$15.85^{c} \pm 1.43$

The values of each column which have different characters are significantly different (P<0.05).

Table 2: Effect of leaf extract from *Salvadora persica* on lipoprotein fraction in hyperglycemic rats.

Treatments	Aspartate aminotransferase (AST) (IU/L)	Alanine aminotransferase (ALT) (IU/L)
healthy Control rats (Group 1)	$29.33^{d} \pm 9.18$	$11.00^{d} \pm 2.61$
hyperglycemic Control rats – (Group 3)	$73.67^{a} \pm 8.94$	$26.50^{a} \pm 3.54$
hyperglycemic rats treated with 50 mg leaf extract (Group 3)	$44.00^{b} \pm 4.23$	$15.00^{b} \pm 2.65$
hyperglycemic rats treated with 100 mg leaf extract (Group 4)	$40.00^{c} \pm 7.72$	$12.00^{c} \pm 1.53$
hyperglycemic rats treated with 150 mg leaf extract (Group 5)	$28.67^{d} \pm 6.80$	$10.23^{d} \pm 1.61$

The values of each column which have different characters are significantly different (P<0.05).

Table 3: Effect of leaf extracts from *Salvadora persica* on serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) of hyperglycemic rats.

Effect of leaf extract from Salvadora persica on Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) in hyperglycemic rats are presented in Table (4). Results of present work indicate that, the Hyperglycemic control rats (Group 2) had a significantly (p<0.05) increased in levels of alanine aminotransferase (ALT), and Aspartate aminotransferase (AST) enzymes comparing with healthy control (group 1) by 151.18% and 140.91 % respectively. On the other side, hyperglycemic rats treated with leaf extracts of Salvadora persica at 50, 100 and 150 mg/kg of body weight were significantly decreased in alanine aminotransferase by 40.27, 54.72 and 61.39 % for (group 3), (group 4) and (group 5) respectively compared with hyperglycemic rats (group 2). While, the decreases in aspartate aminotransferase (AST) of hyperglycemic rats were 43.40, 62.26 and 69.81 % respectively for (group 3), (group 4) and (group 5) respectively compared with hyperglycemic rats (group 2). These results are similar with (Ghada and Soliman 2013) [26] they reported that, this decline in AST and ALT may be due to antioxidant activity such as phenolic and flavonoid compounds in the leaf extract.

Treatments	Uric acid (mg/dl)	Creatinine (mg/dl)	Urea (mg/dl)	Blood urea nitrogen(mg/dl)
healthy Control rats (Group 1)	$1.50^{e} \pm 0.40$	$0.50^{c} \pm 0.04$	$43.00^{e} \pm 3.85$	$20.02^{e} \pm 1.60$
hyperglycemic Control rats – (Group 3)	$3.93^{a} \pm 0.87$	$0.70^{a} \pm 0.02$	$80.50^{a} \pm 7.68$	$38.50^{a} \pm 3.26$
hyperglycemic rats treated with 50 mg leaf extract (Group 3)	$3.80^{b} \pm 1.82$	0.64 ± 0.25	$63.00^{b} \pm 4.45$	$30.46^{b} \pm 2.64$
hyperglycemic rats treated with 100 mg leaf extract (Group 4)	$2.83^{c} \pm 0.93$	0.60 ± 0.08	$58.67^{c} \pm 3.21$	$27.41^{c} \pm 1.50$
hyperglycemic rats treated with 150 mg leaf extract (Group 5)	$2.15^{d} \pm 0.30$	0.54 ± 0.07	$55.00^{d} \pm 2.21$	$25.70^{d} \pm 2.37$

The values of each column which have different characters are significantly different (P<0.05).

Table 4: Effect of leaf extracts from Salvadora persica on Uric acid, Creatinine, Urea and Blood urea nitrogen in hyperglycemic rats.

Effect of leaf extracts from Salvadora persica on Uric acid, Creatinine, Urea and Blood urea nitrogen in hyperglycemic rats are shown in Table (4). The hyperglycemic control rats (group 2) had a significantly ($p<0.05$) increased in renal function compared with healthy control rats (group 1) by 162.0, 40.0, 87.21 and 91.41 for Uric acid, Creatinine, Urea and Blood urea nitrogen respectively. hyperglycemic rats treated with leaf extracts of Salvadora persica at 50 mg/kg of body weight were significantly ($P<0.05$) decreased by 3.31,8.57, 21.74 and 21.88% for Uric acid, Creatinine, Urea and Blood urea nitrogen respectively compared with hyperglycemic control rats (group 2). On the other side hyperglycemic rats treated with leaf extracts of Salvadora persica at 150 mg/kg body weight (group5) were significantly ($P<0.05$) decreased by 45.29, 22.86, 31.68 and 33.25% for Uric acid, Creatinine, Urea and Blood urea nitrogen respectively compared with hyperglycemic control rats (group 2). These results are confirmed with (Gad-Elkareem et al 2019) [27] they reported that, the extract may contain some phytochemical compounds such as flavonoids and polyphenols known for their antioxidant activities and their reduced of serum creatinine and urea levels.

Histopathological examination

Histopathological examination of liver

Liver of rats from healthy control rats (group 1) revealed the normal histological structure of hepatic Lobule photo 1. Meanwhile, liver of hyperglycemic control rats (group 2) revealed cytoplasmic vacuolation of hepatocytes, dilatation of hepatic sinusoids (photo 2) and mononuclear cells infiltration in the portal triad photo 3. However, liver from hyperglycemic rats treated with leaf extracts of *Salvadora persica* at 50 mg (group3), hyperglycemic rats treated with leaf extracts of *Salvadora persica at* 100 mg (group 4) and hyperglycemic rats treated with leaf extracts of *Salvadora persica* at150 mg (group 5) showed the normal histological structure of hepatic Lobule (photo 4 and photo 5).

Histopathological examination of Pancreas

Pancreas of healthy control rats (group 1) showed no histopathological changes (photo6). In contrary, pancreas of hyperglycemic control rats (group 2) revealed vacuolations of acinar epithelium (photo 7). However, pancreas of hyperglycemic rats treated with 50 mg *Salvadora persica* leaf extracts (group 3), hyperglycemic rats treated with 100 mg leaf extracts of *Salvadora persica* (group 4), and hyperglycemic rats treated with 150 mg leaf extracts *Salvadora persica* (group 5) revealed no histopathological changes photo 8, 9 and 10 respectively.

Histopathological examination of Kidneys

Kidneys of healthy control rats (group 1) showed the healthy control rats (group 1) showed the normal histological structure of renal parenchyma (photo 11), while the renal of hyperglycemic control rats (group 2) revealed congestion of renal blood vessels, vacuolation of endothelial Lining glomerular tuft and vacuolation of epithelial lining renal tubules (photo 12). However, kidneys of hyperglycemic rats treated with leaf extracts of *Salvadora persica* at 50 mg (group 3) revealed presence of focal regenerating renal tubules (photo 13). On the other sides, hyperglycemic rats treated with 100 mg leaf extracts *Salvadora persica* (group 4) and hyperglycemic rats treated with 100 mg leaf extracts of *Salvadora persica* (group 5) revealed no histopathological changes (photo 14 and photo 15) respectively.

Conclusion

The present study revealed that the leaf extract from Salvador persica were reducing hyperglycemia in male rats with hyperglycemic caused by alloxan, and almost all biochemical factors and affected kidney, liver and pancreatic tissues were restored to the healthy control rate (group 1).

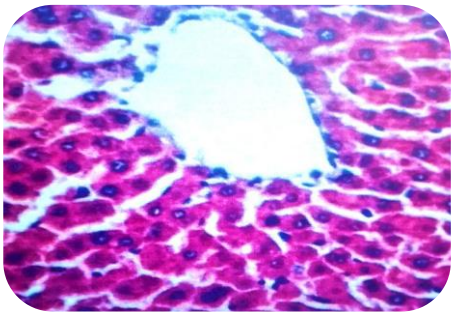

Photo 1. Liver of healthy control rats (group 1), showing the normal histological structure of hepatic lobule.

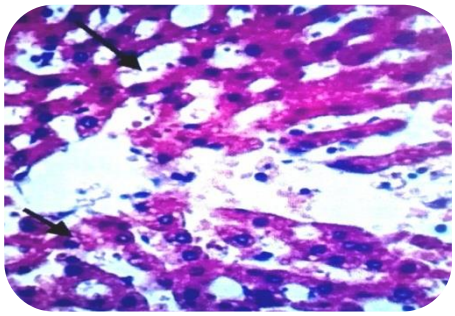

Photo 2. Liver of hyperglycemic contol rats (group 2) showing the cytoplasmic vacuolation of hepatocytes and dilatation of hepatic sinusoids.

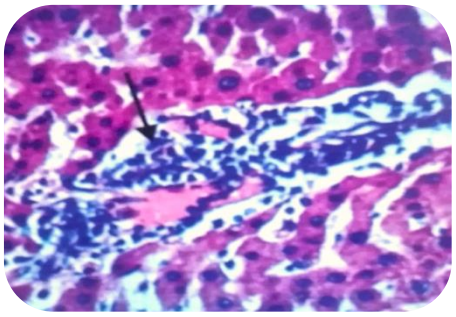

Photo 3. Liver of hyperglycemic control rats (group 2) showing the mononuclear cells infiltration in the portal triad.

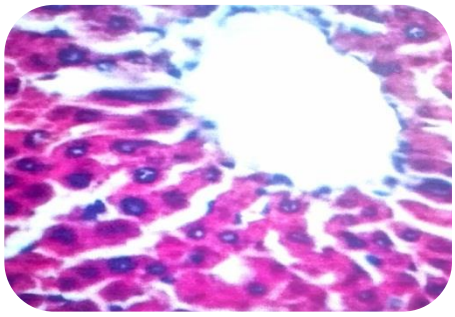

Photo 4. Liver of hyperglycemic rats (group 3) treated with 50 mg leaf extract of *Salvadora persica*, showing the normal histological structure of hepatic lobule

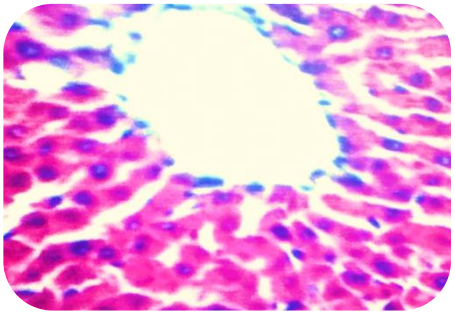

Photo 5. Liver of hyperglycemic rats (group 4 and group 5) treated with 100 mg 150 mg leaf extract of *Salvadora persica* respectively, showing the showing the normal histological structure of hepatic lobule.

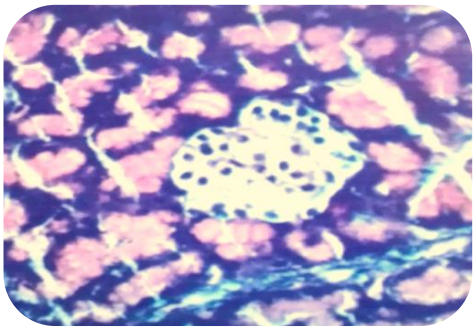

Photo 6. Pancreases of healthy control rats (group 1), showing no histopathological changes.

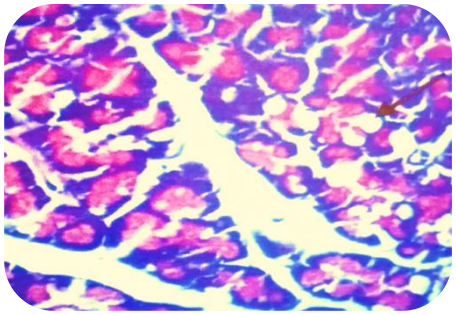

Photo 7. Pancreases of hyperglycemic conrol rats (group 2), showing vacuolation of acinar epithelium.

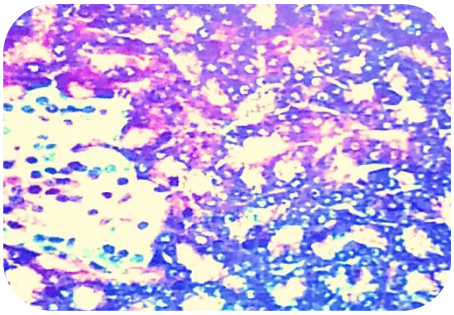

Photo 8. Pancreases of hyperglycemic rats (group 3) treated with 50 mg leaf extract of *Salvadora persica*), showing no histopathological changes

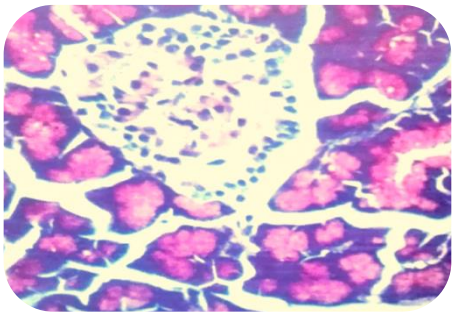

Photo 9. Pancreases of hyperglycemic rats (group 4) treated with 100 mg leaf extract of *Salvadora persica*, showing no histopathological changes

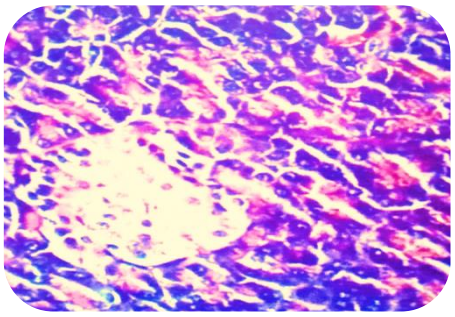

Photo 10. Pancreases of hyperglycemic rats (group 5) treated with 150 mg leaf extract of *Salvadora persica*, showing no histopathological changes.

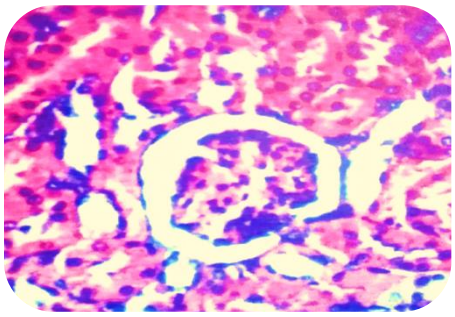

Photo 11. Kidney of healthy control rats (group 1), showing the normal histological structure of renal parenchyma.

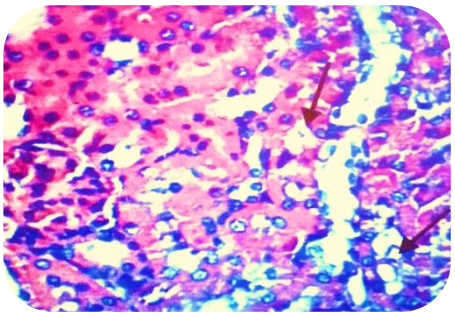

Photo 12. Kidney of hyperglycemic control rats (group 2), showing the vacuolation of epithelial renal tubules.

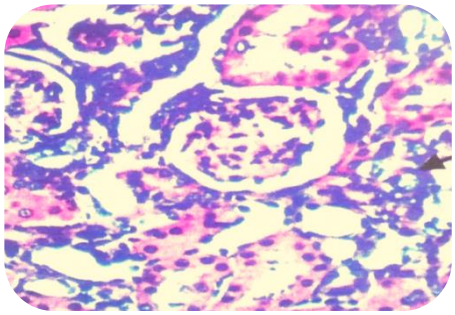

Photo 13. Kidney of hyperglycemic rats (group 3) treated with 50 mg leaf extract of *Salvadora persica*, showing focal regenerating renal tubules.

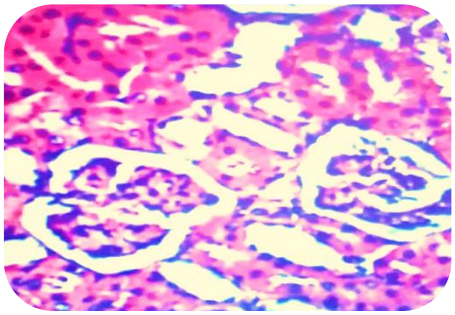

Photo 14. Kidney of hyperglycemic rats (group 4) treated with 100 mg leaf extract of *Salvadora persica*, showing no histopathological changes.

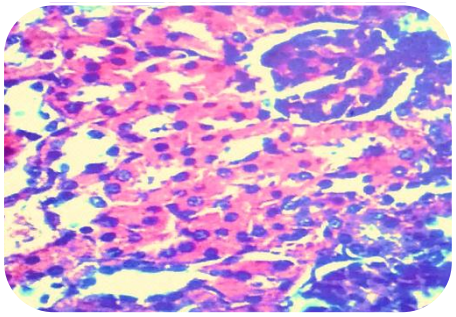

Photo 15. Kidney of hyperglycemic rats (group 5) treated with 150 mg leaf extract of *Salvadora persica*, showing no histopathological changes

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