

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 (Group 1) 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

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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 anti diabetic 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 [1,2]. Diabetic illness is a chronic metabolic disorder in glucose tolerance and an elevated hazard of cardiovascular disease [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 [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 [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 [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 [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 [8]. The aim of this research was to evaluate the anti-hyperglycemic effect of *Salvadora persica* plant extract in alloxan-induced hyperglycemic rats.

Material and Methods

Material

Plant materials: *Salvadora persica*

Preparation of extracts: The leaf of *Salvadora persica* were cleaned, washed and then dried at 40°C in an electric oven for 12 hours and milling to pass through a 60 mesh.

Leaf of *Salvadora persica* powder (100 g) 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° 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 [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 [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 earlier [11]. Insulin was estimated by using the method explained earlier [12].

Glycated hemoglobin (HbA1c) was decided in whole blood according to the method explained earlier [13]. Serum cholesterol was determination by using the method [14]. Serum triglycerides (TG) were estimated by Enzymatic colorimetric GPO-PAP kit according to the method explained earlier [15].

High-Density Lipoprotein Cholesterol (HDL-c) was estimated colorimetrically according to the method defined by using a study [16].

Low-Density Lipoprotein Cholesterol (LDL-c) and Very Low-Density Lipoprotein Cholesterol (VLDL-c), were estimated calorimetrically by the method explained with a study [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 a study [18].

Serum urea was spectrophotometrically estimated of the technique defined by a study [19]. Uric acid was spectrophotometrically determined by the method explained by a study [20]. Serum creatinine was estimated by the method explained with a study [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 a study [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 Figure 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.

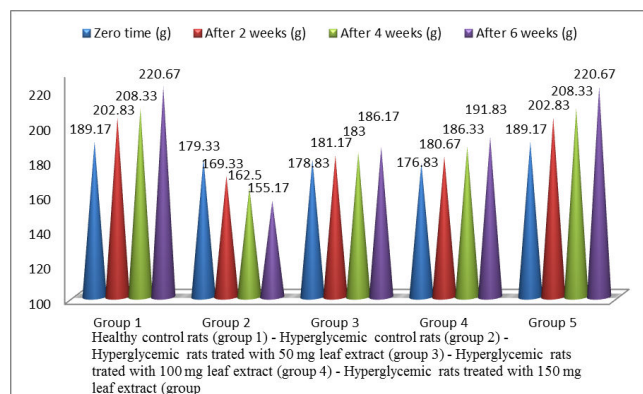


Figure 1: Effect of *Salvadora persica* leaf extract on Body weight in hyperglycemic.

Table 1: Effect of leaf extract from *Salvadora persica* on serum glucose levels in hyperglycemic rats. The values of each column which have different characters are significantly different ($p < 0.05$).

Treatments	Glucose mg/dl				Decease%
	Zero time	After 2 weeks	After 4 weeks	After 6 weeks	
Healthy Control rats (Group 1)	119.00b ± 5.29	116.50e ± 5.20	115.25e ± 4.03	114.00e ± 4.32	-4.2
Hyperglycemic Control rats – (Group 3)	369.50a ± 19.16	349.25a ± 14.86	329.25a ± 11.81	306.50a ± 10.28	-15.91
Hyperglycemic rats treated with 50 mg leaf extract (Group 3)	366.50a ± 15.35	326.75b ± 13.72	265.00b ± 10.61	214.75b ± 9.60	-41.41
hyperglycemic rats treated with 100 mg leaf extract (Group 4)	363.25a ± 16.40	331.25c ± 12.07	245.00c ± 8.06	180.00c ± 7.30	-50.45
hyperglycemic rats treated with 150 mg leaf extract (Group 5)	364.75a ± 15.88	322.00d ± 13.49	230.25d ± 9.14	149.75d ± 8.54	-58.94

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 a study [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 a study [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 Figure 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).

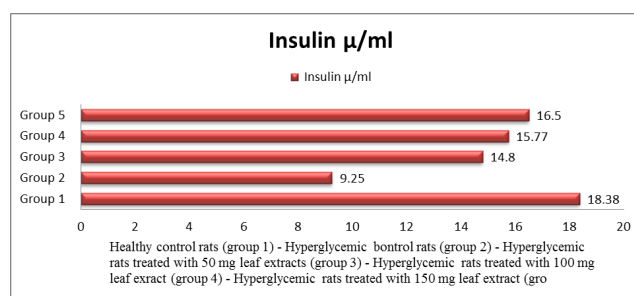


Figure 2: Effects of leaf extract from *Salvadora persica* on insulin in hyperglycemic rats

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 a study [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 [25].

Effects of leaf extract from *Salvadora persica* on glycosylated hemoglobin (HbA1c) in Hyperglycemic rats is shown in Figure 3. Results of present work indicate that, the Hyperglycemic control rats (group 2) had a significant ($p < 0.05$) Increase 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).

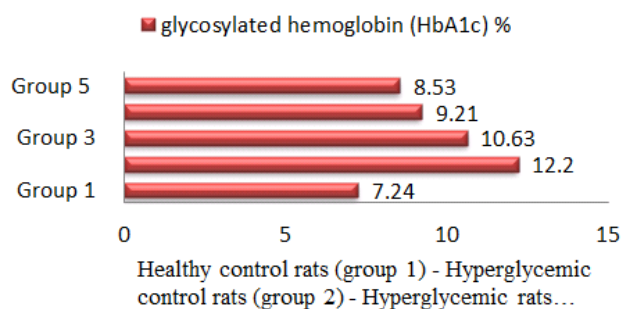


Figure 3: Effects of leaf extract from *Salvadora persica* on glycosylated hemoglobin (HbA1c) in Hyperglycemic rats

Effects of leaf extracts from *Salvadora persica* on Total cholesterol, Triglycerides and total lipids in hyperglycemic rats are presented in Figure 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).

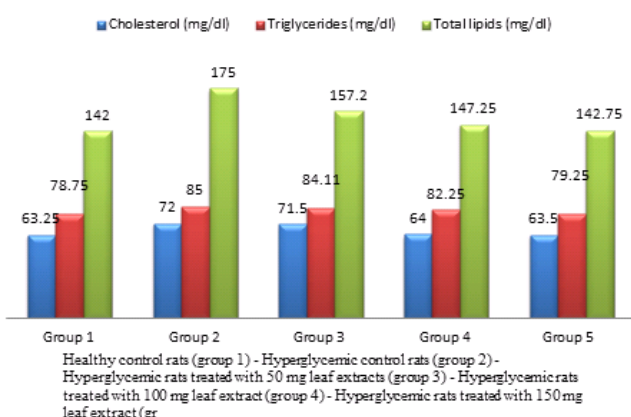


Figure 4: Effects of leaf extracts from *Salvadora persica* on Total cholesterol, Triglycerides and total lipids in hyperglycemic rats.

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 2. Results of

present work indicate that, 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 ($p < 0.05$) on the other side, hyperglycemic rats treated with leaf extract of *Salvadora persica* at 50, 100 and 150 mg/kg of body weight were significantly ($p < 0.05$) 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).

Table 2: Effect of leaf extract from *Salvadora persica* on lipoprotein fraction in hyperglycemic rats. The values of each column which have different characters are significantly different ($p < 0.05$).

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

Table 3: Effect of leaf extracts from *Salvadora persica* on serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) of hyperglycemic rats. The values of each column which have different characters are significantly different ($p < 0.05$).

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

Effect of leaf extract from *Salvadora persica* on Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) in hyperglycemic rats are presented in Table 3. 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 a study [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 [26].

Table 4: Effect of leaf extracts from *Salvadora persica* on Uric acid, Creatinine, Urea and Blood urea nitrogen in hyperglycemic rats. The values of each column which have different characters are significantly different ($p < 0.05$).

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

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 (group 5) 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 a study [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 (Figure 5). Meanwhile, liver of hyperglycemic control rats (group 2) revealed cytoplasmic vacuolation of hepatocytes, dilatation of hepatic sinusoids (Figure 6) and mononuclear cells infiltration in the portal triad (Figure 7).

However, liver from hyperglycemic rats treated with leaf extracts of *Salvadora persica* at 50 mg (group 3), hyperglycemic rats treated with leaf extracts of *Salvadora persica* at 100 mg (group 4) and hyperglycemic rats treated with leaf extracts of *Salvadora persica* at 150 mg (group 5) showed the normal histological structure of hepatic Lobule (Figures 8 and 9).

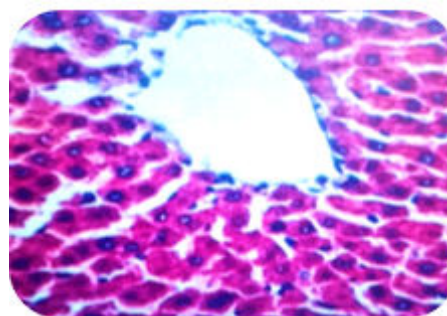


Figure 5: Liver of healthy control rats (group 1), showing the normal histological structure of hepatic lobule.

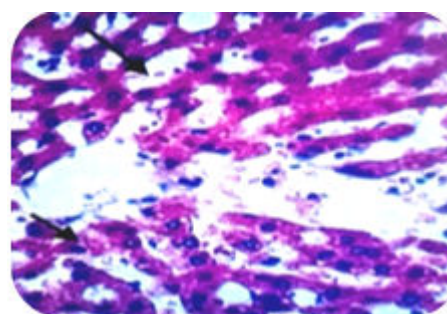


Figure 6: Liver of hyperglycemic control rats (group 2) showing the cytoplasmic vacuolation of hepatocytes and dilatation of hepatic sinusoids.

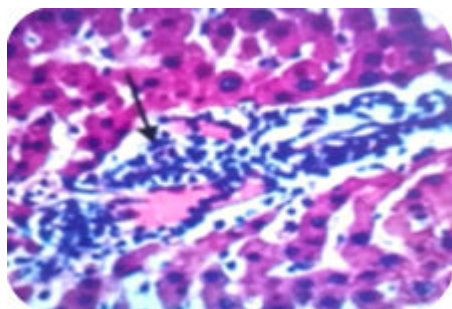


Figure 7: Liver of hyperglycemic control rats (group 2) showing the mononuclear cells infiltration in the portal triad.

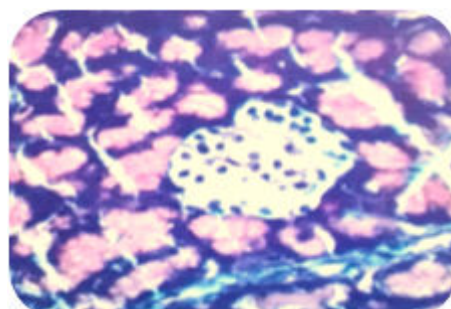


Figure 10: Pancreases of healthy control rats (group 1), showing no histopathological changes.

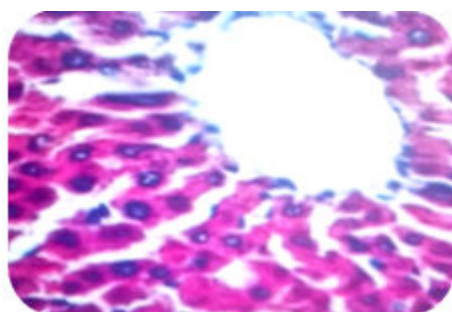


Figure 8: Liver of hyperglycemic rats (group 3) treated with 50 mg leaf extract of *Salvadora persica*, showing the normal histological structure of hepatic lobule

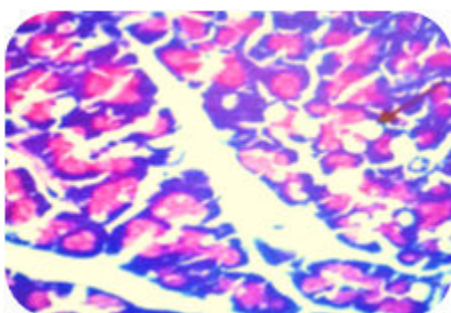


Figure 11: Pancreases of hyperglycemic control rats (group 2), showing vacuolation of acinar epithelium.

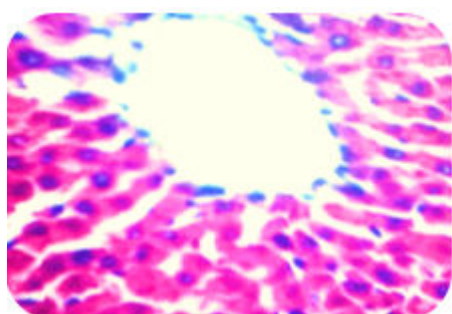


Figure 9: Liver of hyperglycemic rats (group 4 and group 5) treated with 100 mg 150 mg leaf extract of *Salvadora persica* respectively, showing the showing the normal histological structure of hepatic lobule.

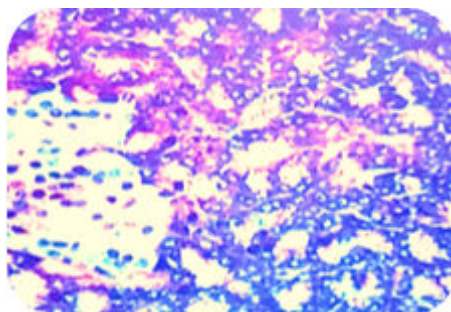


Figure 12: Pancreases of hyperglycemic rats (group 3) treated with 50 mg leaf extract of *Salvadora persica*, showing no histopathological changes

Histopathological examination of Pancreas

Pancreas of healthy control rats (group 1) showed no histopathological changes (Figure 10). In contrary, pancreas of hyperglycemic control rats (group 2) revealed vacuolations of acinar epithelium (Figure 11). 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(Figures 12, 13 and 14 respectively).

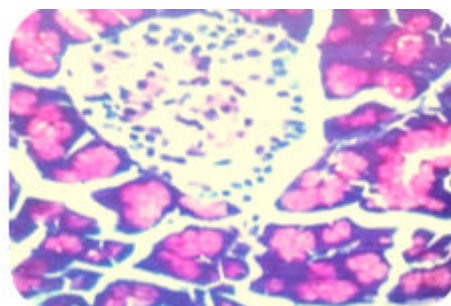


Figure 13: Pancreases of hyperglycemic rats (group 4) treated with 100 mg leaf extract of *Salvadora persica*, showing no histopathological changes

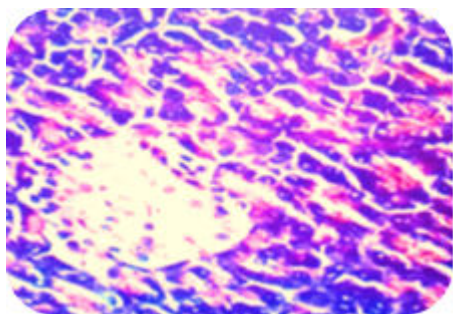


Figure 14: Pancreases of hyperglycemic rats (group 5) treated with 150 mg leaf extract of *Salvadora persica*, showing no histopathological changes.

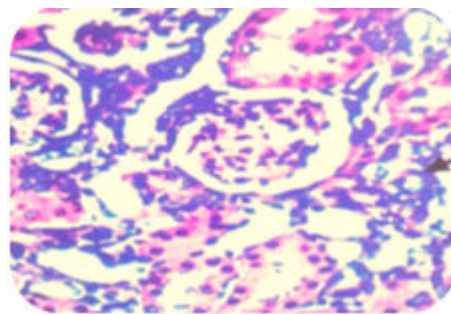


Figure 17: Kidney of hyperglycemic rats (group 3) treated with 50 mg leaf extract of *Salvadora persica*, showing focal regenerating renal tubules.

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 (Figure 15), 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 (Figure 16). However kidneys of hyperglycemic rats treated with leaf extracts of *Salvadora persica* at 50 mg (group 3) revealed presence of focal regenerating renal tubules (Figure 17). 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 (Figures 18 and 19) respectively.

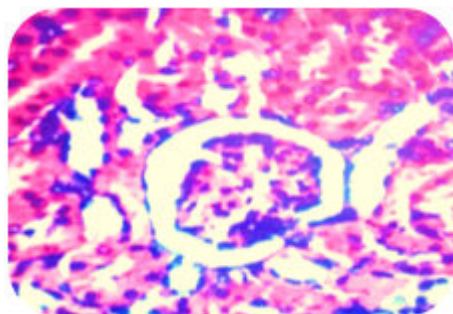


Figure 15: Kidney of healthy control rats (group 1), showing the normal histological structure of renal parenchyma.

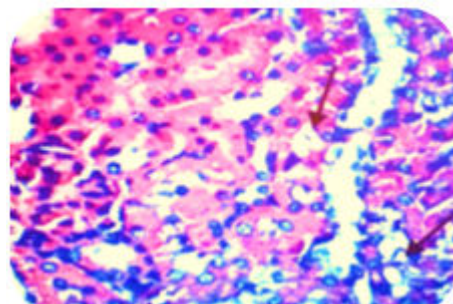


Figure 16: Kidney of hyperglycemic control rats (group 2), showing the vacuolation of epithelial renal tubules.

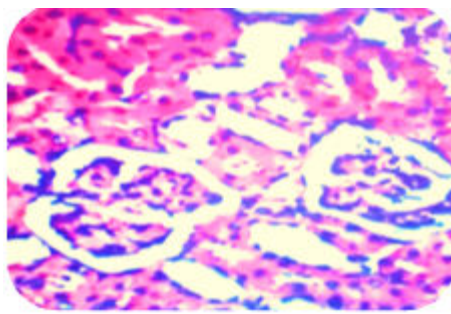


Figure 18: Kidney of hyperglycemic rats (group 4) treated with 100 mg leaf extract of *Salvadora persica*, showing no histopathological changes.

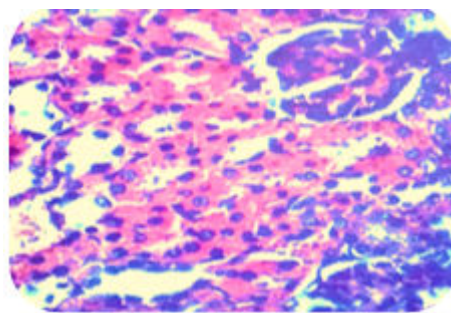


Figure 19: Kidney of hyperglycemic rats (group 5) treated with 150 mg leaf extract of *Salvadora persica*, showing no histopathological changes

Conclusion

The present study revealed that the leaf extract from *Salvadora 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).

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