EFFECT OF ALCOHOLIC *ANASTATICA HIEROCHUNTICA* EXTRACT ON SOME BIOCHEMICAL AND HISTOLOGICAL PARAMETERS IN ALLOXAN INDUCED DIABETIC RATS

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Abstract

The methanolic extract of *Anastatica hierochuntica* was investigated for its antidiabetic effect in male Albino rats. Blood glucose levels, lipids profile were significantly reduced in all treated group of alloxan diabetic rats in comparison to their pre-treatment values, in addition to, intake of orally dose of 100 mg/kg b.w of methanolic extract daily for four consecutive weeks to diabetic rats significantly decreased the activity levels of all those biomarker liver damage enzymes (S.GOT, S. GPT and S.ALP), and restored it to normal values. Levels of SOD activity were significantly decreased in diabetic rats compared with the healthy group, but these levels increased significantly to a value similar to the healthy rat when treated with a daily single dose of *Anastatica hierochuntica* extract (100mg/kg b.w) for four weeks. The same pattern was seen with another antioxidant enzyme GPx, its levels significantly decreased in diabetic and increased when the animals fed on the extract daily for four weeks. Histopathological observations in both pancreas and liver rat's tissues revealed that methanolic *Anastatica hierochuntica* extract was non-toxic and regenerated the toxic effects of alloxan. In conclusion the decreased blood glucose accompanied with decreased lipid profile and changes in the activities of the antioxidant enzymes SOD and GPx, in addition to biomarker liver damage enzymes showed the antidiabetic, hypolipidmic and a potent antioxidant agent.

تأثيرالمستخلص الكحولي لنبات كف مريم على بعض المتغيرات البايوكيميائية والسايتولوجية في الجرذان المصابة بالسكري المستحدث بالالوكسان

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الخلاصة

تم دراسة تاثير المستخلص الكحولي لنبات كف مريم على جرذان اصحاء واخرى مصابة بالسكر المحدث عن طريق حقنها بمادة الالوكسان، اظهرت النتائج ان تناول 100 ملغم / كيلوغرام من وزن الجرذ من المستخلص الكحولي للنبات له تاثير معنوي على خفض مستويات سكر الكلوكوز والكولستيرول والدهون الثلاثية عند الجرذان المصابة بالسكر المستحدث بالالوكسان بعد مرور اربعة اسابيع ، مقارنة بالمجموعة غير المعالجة ،كذلك تبين ان للمستخلص تاثير وقائي لانزيمات الكبد اذ انخفضت مستويات فعالية هذه الانزيمات الى مستويات مقاربة لمجموعة السيطرة كذلك لوحظ امتلاك المستخلص لفعالية مضادة للاكسدة من خلال تاثيره على مستويات انزيمات السوبر دايميوتيز SOD وانزيم الكلوتاثايون بيروكسديز GPx ، اذ لوحظ انخفاض مستويات هذه الانزيمات عند الجرذان المصابة بالسكري مقارنة

بمجموعة الجرذان الطبيعية ،لكن عند تناول تناول 100 ملغم / كيلوغرام من وزن الجرذ من المستخلص الكحولي للنبات لمدة اربعة اسابيع له تاثير معنوي على رفع مستويات تلك الانزيمات الى مستويات مقاربة للجرذان الاصحاء. بينت الدراسات النسيجية للبنكرياس والكبد ان للمستخلص الكحولي للنبات تاثيرات على خلايا بيتا لبنكرياس الجرذان المصابه بالسكر بعد تناولها لجرعة المستخلص لمدة اربعة اسابيع، اذ ادى الى تحسن الصوره الهستولوجية لانسجة البنكرياس و تحفيز ظهور خلايا بيتا وتزايد اعدادها مقارنة بالجرذان المصابة بالسكر وغير المعالجة بمستخلص النبات،كذلك لوحظ امكانية المستخلص النباتي على حماية الكبد من التاثيرات السمية للالوكسان.

Introduction

Diabetes mellitus is one of the common metabolic disorder with micro and macrovascular complications that results in significant morbidity and mortality. It is considered as one of the five leading causes of death in the world (1,2). In modern medicine no satisfactory effective therapy is still available to cure diabetes mellitus (3). There is increasing demand by patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents (4–6). There are numerous traditional medicinal plants reported to have hypoglycemic properties such as *Allium sativum* (Garlic), *Azadirachta indica* (Neem), *Vinca rosea* (Nayantara), *Trigonella foenum* (Fenugreek), *Momordica charantia* (Bitter ground), *Ocimum santum* (Tulsi). Many of these are less effective in lowering glucose levels in severe diabetes (7). *Anastatica hierochuntica* was widely used as medicinal plant either by itself or in combination with other herbs. The whole plants of *Anastatica hierochuntica* is commonly called "Kaff maryam" or "Rose of Jericho", which is a winter annual plant of the Sahara-Arabian deserts, was prescribed in Egyptian folk medicine and used as a charm for child birth (8).

The methanolic extract from the whole plants of *Anastatica hierochuntica* was found to show potent hepatoprotective effect on D-galactosamine-induced cytotoxicity in primary cultured mouse hepatocytes (9), antioxidant activities (10). *Anastatica hierochuntica* does not lower blood glucose levels in normal subjects (11). The objective of the present work was to make an analysis of the antidiabetic properties of the anstatica hierochuntica extract by evaluating the comparative antihyperglycemic, hypolipidmic and antioxi-dant activities of this extract in normal, and alloxan induced diabetic rats.

Material and Methods

Plant material: Samples of *Anastatica hierochuntica* plant were purchased from Iraqi local market in Baghdad. The plant material was authenticated by a taxonomist professor Ali Al-Mosowi at the Department of Botany College of science, University of Baghdad, Iraq. The samples were washed with clean tap water to remove dirt on the leaves. The dried plant material was manually powdered and the powder kept in polyethylene bags until used.

Alcoholic Extraction: The powdered whole plant (100 g) kept in a thimble was extracted with 200 ml 70% methanol in a soxhlet extractor. The extract was evaporated to dryness under vacuum and dried in vacuum desiccator.

Animals: Male Swiss albino rats (Rattus norvegicus UJ-1) weighing 175 ± 25 g were used in this study .The experimental rat were provided by the department of Biological Sciences, University of Jordan. Rats were fed with pellet diet (Hammoudeh Company for Diary Products, Amman) and tap water was delivered ad libtitum. The animals were kept in polypropylene cages (three in each cage) at an ambient temperature of 25 ± 20C and 55-65% relative humidity 12 ± 1 hr light and dark schedule was maintained in the animal house till the animals were acclimatized to the laboratory conditions. The experiments were designed and conducted in accordance with the institutional guidelines. Animals described as fasting were deprived of food and water for 16 hours ad libitum.

Introduction of expermintal diabetes: Male Swiss albino rats were fasted overnight (12-14 hours) and their weights and fasting blood glucose levels were recorded. Rats were then made diabetic by a single intraperitoneal injection of alloxan monohydrate (150 mg/kg body weight). Alloxan was first weighed

individually for each animal according to its weight & then solublized with 0.5 ml distilled water just prior to injection (12).
Food and water were presented to the animals 30 minutes after drug administration. The animals were allowed to drink 5% glucose solution to overcome the drug induced hypoglycemia (13,14). Three days after alloxan injection, plasma blood glucose level of each animal was determined and animals with a fasting blood glucose range above 250 mg/dl were included in the study. The blood samples were collected from fasted rats using red capillary tubes introduced into the medial retro-orbital venous plexus under light ether anesthesia and with 0.1 M EDTA as anticoagulant.

Experimental Design: Fifty male Swiss albino rats (Rattus norvegicus UJ-1) weighing 212 ± 15 g of each used in this research. Rats were maintained with free access to water and a standard pellet diet (containing protein (24%), fiber (5%), ash (8%), calcium (1%) and phosphorus (0.75%), Experimental animals were divided into five groups (10 rats each) : **Healthy group**: Rats were orally administered (using a feeding needle to the esophagus) with a daily dose of 0.5ml distilled water for 4 weeks; **Diabetic untreated group**: Rats were intraperitoneally injected with a single dose of alloxan (150 mg/kg b. w). **Diabetic plant-treated group**: Rats were rendered diabetic via i.p. injection with alloxan as in group 2, and each animal received a daily oral dose (0.5ml) of the plant extract for 4 weeks. Treatment with plant extracts started 72 hours after alloxan injection. **Diabetic group treated with Metformin** (100mg/kg b.w) Rats were rendered diabetic via i.p. injection with alloxan as in group 2, and each animal received a daily oral dose (100mg/ kg b. wt.) of Metformin for 4 weeks. **Healthy group treated with extract**: rats were treated with methanolic extract of *Anastatica hierochuntica (*100 mg / kg b. w) in 0.5 ml distilled water using a gavage daily for 4 weeks.

Biochemical and histological studies: Blood samples were drawn from tail tip of rat at weekly intervals till the end of study (i.e., 4 weeks). Fasting blood glucose estimation and body weight measurement were done on day 1, 7, 14 21 and 28 of the study (15). Blood glucose estimation can be done by one touch electronic glucometer using glucose test strips. On day 28, blood was collected from retro-orbital plexus under mild ether anesthesia from overnight fasted rats .Serum was separated and analyzed for serum cholesterol (16), serum triglycerides by enzymatic DHBS colorimetric method (17), serum HDL (18), serum LDL (19) and serum GOT, GPT (20), and serum alkaline phosphatase hydrolyzed by phenol amino antipyrine method estimated (21).
The activities of hepatic marker enzymes (GPx and SOD) were assayed in blood using standard kits: RANSEL kit (22, RANSOD kit for determination of the glutathione peroxidase and superoxide dismutase activities respectively (23) glutathione. The whole pancreas from each animal was removed after sacrificing the animal and was collected in 10% formalin solution, and immediately processed by the paraffin technique. Sections of 5 thickness were cut and stained by Hematoxylin and eosin (H & E) for histological examination (24), then frozen until used for determination of the other biochemical assays.

Statistical Analysis: All the values of body weight, fasting blood sugar, and biochemical estimations were expressed as mean ± standard error of mean (S.E.M.) and analyzed for ANOVA and post hoc Dunnet's -test. Differences between groups were considered significant at $P < 0.05$ levels.

Results and discussion

Effect of *Anastatica hierochuntica* extract intake on blood glucose in healthy and alloxan induced diabetic rats.

The daily oral treatment with alloxan in a dose 150 mg/kg resulted in the development of diabetes after three days of administration, the effect gradually increasing over four week period to reach a rise of about three times % over initial values compared with healthy rats The methanolic extract residue of *Anastatica hierochuntica* was administrated orally at increased dose levels of 50mg, 100mg, and 200mg/kg b.w. to diabetic rats to assess the effective dose of the plant extracts. The highest increment was recorded at 100 mg dose level (74 % reduction). The increased serum glucose recorded in diabetic rats as compared with healthy rats (Table 1) may have derived from glycogenolysis and/or gluconeogenesis in the former. These mechanisms have been

extensively reported to be the causative reasons eventually leading to hyperglycemia in different diabetic states (25).The intake of *Anastatica hierochuntica* extract (100 mg/ kg.b.w) for 28 days caused a reduction in glucose levels by 74% in comparison with the basal levels in control. The results showed antihyperglycemic effects of the *Anastatica hierochuntica* extracts. This finding may indicate the presence of some hypoglycemic agents in the whole plant of *Anastatica hierochuntica* which have been concentrated in the crude extracts. The hypoglycemic effects of plants may be due to the presence of insulin-like substance in plants (26), stimulation of ß cells to produce more insulin (27) and increasing glucose metabolism or regenerative effect of plants on pancreatic tissue (28).

Plants with antihyperglycemic activities may contain one or more chemical constituents. Classes of chemical compounds isolated from plants including alkaloids, flavonoids, tannin, etc. are documented to have the potential to decrease the blood glucose level (29). Thus, the significant antidiabetic effect of crude methanolic extracts of *Anastatica hierochuntica* could be due to the possible presence of the aforementioned constituents in the part of the plant used in this particular study, which could act synergistically or independently enhancing the activity of glycolytic and gluconeogenic enzymes. In this study, the pancreatic ß cells were destroyed with the help of alloxan. Alloxan is one of the usual substances used for the induction of diabetes mellitus apart from streptozotocin. Alloxan has a destructive effect on the beta cells of the pancreas (12). The pancreas is the primary organ involved in sensing organism dietary.

Table 1: Effect *of oral administration of methanolic extract of Anastatica hierochuntica on glucose levels of healthy and alloxan induced diabetic rats (Values are M ±SD*)

Groups	n	Blood glucose levels (mg/dl)				
		0 day	7day	14 day	21 day	28 day
Healthy	10	112 ± 16	108±11	112 ± 12	118 ± 10	111±13
Diabetic	10	295 ±15**	300 ±13**	310 ± 15**	312 ± 14**	320±14**
Diabetic + Extract	10	300 ± 14	258±11*	210 ±13*	183 ± 14**	163±15**
Diabetic + Metformin	10	310 ± 16	256±12*	200 ± 13*	163 ± 13**	126±14**
Healthy + Extract	10	100 ± 18	102±10	110 ± 12	110 ± 16	109±14

Values are expressed as mean (mg/dl) ± SD, Diabetic control was compared with healthy group. Experimental groups were compared with diabetic control * it referred to P< 0.05, ** it mean p<0.001

Effect of *Anastatica hierochuntica* extract intake on body weight in healthy and alloxan induced diabetic rats

In the present study, we have demonstrated that diabetes induced experimentally by alloxan produced a significant decrease in body weight (170±14 gm in diabetic rats compared with 249±13 gm in healthy rats. Body weight of normal and diabetic rats was measured during the study and as shown in Table 2.

Alcoholic extract did not cause any significant change in body weight after four weeks of treatment in normal rats (239±14 gm) compared with (249±13 gm) in healthy animals, while in alloxan diabetic rats it might be remain body weight near the healthy animals at the end of treatment period (p<0.01).

Table 2: Effect of oral administration of methanolic *Anastatica hierochuntica* plant extract on body weight (gm.b.w) in healthy and alloxan induced diabetic rats during 4 weeks. (Mean ± SD)

Groups	n	Body weight (gm)				
		0 day	7day	14 day	21 day	28 day
Healthy	10	212 ± 16	219±11	227 ± 12	232 ± 10	249±13
Diabetic	10	215 ± 15	200±13	195 ± 15*	183± 15*	170±14**
Diabetic + Extract	10	218 ± 14	200±11	210 ± 14	208 ± 14	207±15
Diabetic + metformin	10	213 ± 16	210±12	209± 13	213 ± 13	216±14
Healthy + Extract	10	217 ± 12	220 ±10	227 ± 12	235± 16	239±14

Effect of *Anastatica hierochuntica* extract intake on Lipid profile activity in healthy and alloxan induced diabetic rats.

Induced diabetes by alloxan lead after four weeks to a significant increase in levels cholesterol,triglyceride,lowdensity lipoprotein, and total lipids, while high density lipoprotein was significantly decreased) (Table 3). Administration of 100 mg/kg b.w daily of *Anastatica hierochuntica* plant extract to diabetic groups (Group 3) resulted in a significant reduction in levels of, triglyceride, low density lipoprotein, total cholesterol after four week . Diabetes affects both glucose and lipid metabolism (25). In the post prandial state elevated serum insulin increases lipoprotein lipase activity in adipose tissue and promotes fuel storage as triglycerides in normal metabolism (26). The insulin deficiency depletes the activity level of lipoprotein lipase, thus leading to deranged lipoprotein metabolism during diabetes (27). The lipoprotein levels in the alloxan induced diabetics of the present study reveal a significant alter in lipoprotein metabolism. The serum total cholesterol content increased significantly in diabetic rats.

The elevated hypertryglycerdemia was increased in the synthesis of triglyceride rich lipoprotein particles (very low density lipoprotein, VLDL) in liver diminished catabolism in diabetic (28) Since insulin has a potent inhibitory effect on lipolysis in adipocytes, insulin deficiency is associated with excess lipolysis and increased influx of free fatty acids to the liver (29).

The increased levels of low-density lipoprotein (LDL) and very low density lipoprotein (VLDL) in the diabetic animals might be due to over production of LDL and VLDL by the liver due to the stimulation of hepatic triglyceride synthesis as a result of free fatty acid influx (6). The high density lipoprotein (HDL) was significantly reduced in the diabetic s which indicates a positive risk factor for atherosclerosis.

The lipoprotein levels in the alloxan induced diabetics of the present study reveal a significant alter in lipoprotein metabolism. The serum total cholesterol content increased significantly in diabetic animals.. The levels of serum TC, TG, LDL, and VLDL were found to be significantly reduced in the plant extracts treated diabetic animals. This might be due to the reduced hepatic triglyceride synthesis and or reduced lipolysis that might be due to the increase in serum insulin levels in the animals extract treated (30).The HDL increased significantly in the plant extract treated rats indicating a reversed atherogenic risk. On the basis of the aforementioned results, we concluded that *Anastatica hierochuntica* have a significant hypoglycemic effect in diabetics and that their effect was comparable to that of metformin therefore, these medicinal plants are considered to be effective and alternative treatment for diabetes. On the other hand, *Anastatica hierochuntica* has a greater antihyperlipidemic effect than antidiabetic effect.

Table 3: Effect of oral administration methanolic extract of *Anastatica hierochuntica* on serum lipid profile in healthy and alloxan induced diabetic rats.

Groups	n	Lipid profile mg/dl				
		T.Ch	TG	HDL-c	LDL-c	VLDL
Healthy	10	70± 10	80 ± 8.3	17 ± 1.1	34 ± 3.2	14 ± 2.2
Diabetic	10	97 ±14*	132± 12**	13 ± 1.1*	48 ± 4.4*	28 ±4.4*
Diabetic + Extract	10	73 ±10*	82 ± 9.4**	16 ±1.2 *	35 ±3.6*	14 ± 1.8*
Diabetic + Metformin	10	75 ± 11*	80 ± 10*	15 ± 1.9	34 ± 3.5*	14 ±1.7*
Healthy + Extract	10	74± 12*	82 ± 13*	15 ± 1.0	33 ± 3.7*	13 ± 1.8*

Values are expressed as mean (mg/dl) ± SD, Diabetic control was compared with healthy group. Experimental groups were compared with diabetic control P< 0.05

Effect of methanolic *Anastatica hierochuntica* extract intake on liver enzymes (S.GOT, S.GPT and S.ALP) activity in healthy and alloxan induced diabetic rats

Activities of S.GOT and S.GPT are cytotolic marker enzymes reflecting hepato-cellular necrosis as they are released into the blood after cell membrane damage. Therefore, we used the activities of S.GOT, S.GPT and S.ALP in the circulation as indicators of hepatic damage. In the present study, all treatment groups with experimental plant extract effectively reduced plasma. S. GOT, S. GPT and S. ALP activities in diabetic rats, suggesting that the methanolic extracts of experimental plants may prevent hepatic injury associated with diabetes. There are a significant rise in S. GOT (129 ± 12 U/L) and S. GPT (80 ± 9U/L) levels in diabetic rats compared with (83 ± 7 U/L) and (40 ± 7 U/L) in healthy animals for S.GOT and S.GPT respectively (Table 3-6), which could relate to excessive accumulation of amino acids (glutamate and alanine) in the serum of diabetic animals as a result of amino acids mobilization from protein stores (25).

The higher levels of S.GOT and S.GPT, may give rise to a high concentration of glucose. In providing new supplies of glucose from other sources such as amino acids. Following oral administration extract of Anstatica hierochuntica, S.GOT and S.GPT levels significantly restored to normal levels.

The other words, the gluconeogenic action of GOT and GPT plays the role of the effect of prolonged oral administration of plant extracts for 4 weeks on serum activity of transaminases and ALP was observed in figure (1).

The obtained results showed significant decrease in the activity of transaminases and ALP in alloxan diabetic rat's intake 100 mg/Kg b.w daily for 4 weeks, when compared to the healthy group or their basal values. So we concluded that Anastatica extract have a hepatoprotective effect in diabetic animals.

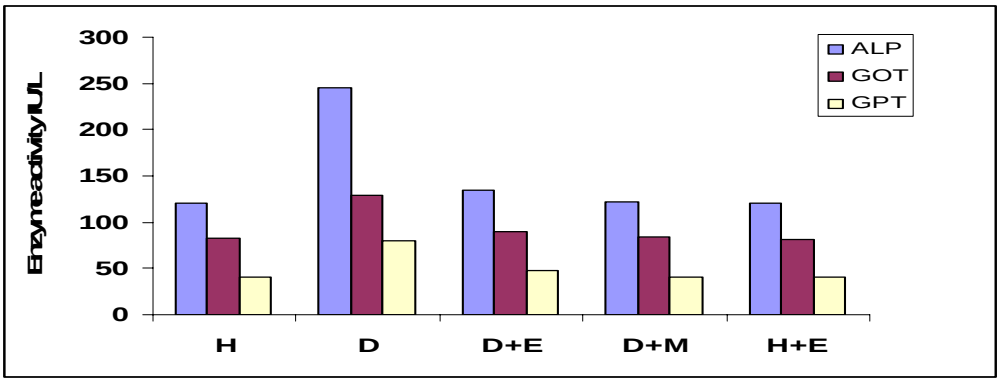


Figure 1: Effect of oral administration of methanolic *Anastatica hierochuntica* plant extract on liver enzymes (GOT, GPT and ALP) activity in healthy and alloxan induced diabetic rats after 4 weeks.

Effect of methanolic *Anastatica hierochuntica* extract intake on histomorphologic changes of Liver

Histopathology of the liver in healthy rats showed normal hepatic cells with well preserved cytoplasm, nucleus, nucleolus, and central vein (Figure 2-a). In diabetic animals, liver sections showed that the lobular architecture was maintained, but there was also severe fatty change, sinusoidal dilation and congestion, mild periportal inflammation, fibrosis; sever feathery degeneration, and necrosis (Figure 2-b).

In diabetic rats treated with methanolic *Anastatica hierochuntica* plant extract (100 mg/kg/Body weight), liver sections maintained lobular architecture and had mild fatty change, mild sinusoidal dilation and congestion mild periportal inflammation an mild feathery degeneration (Figure2-c), while in healthy animals treated with extract, liver sections showed normal hepatic cells with well preserved cytoplasm; nucleus, nucleolus and central vein, in which normal hepatic structure was maintained (Figure 2-d).

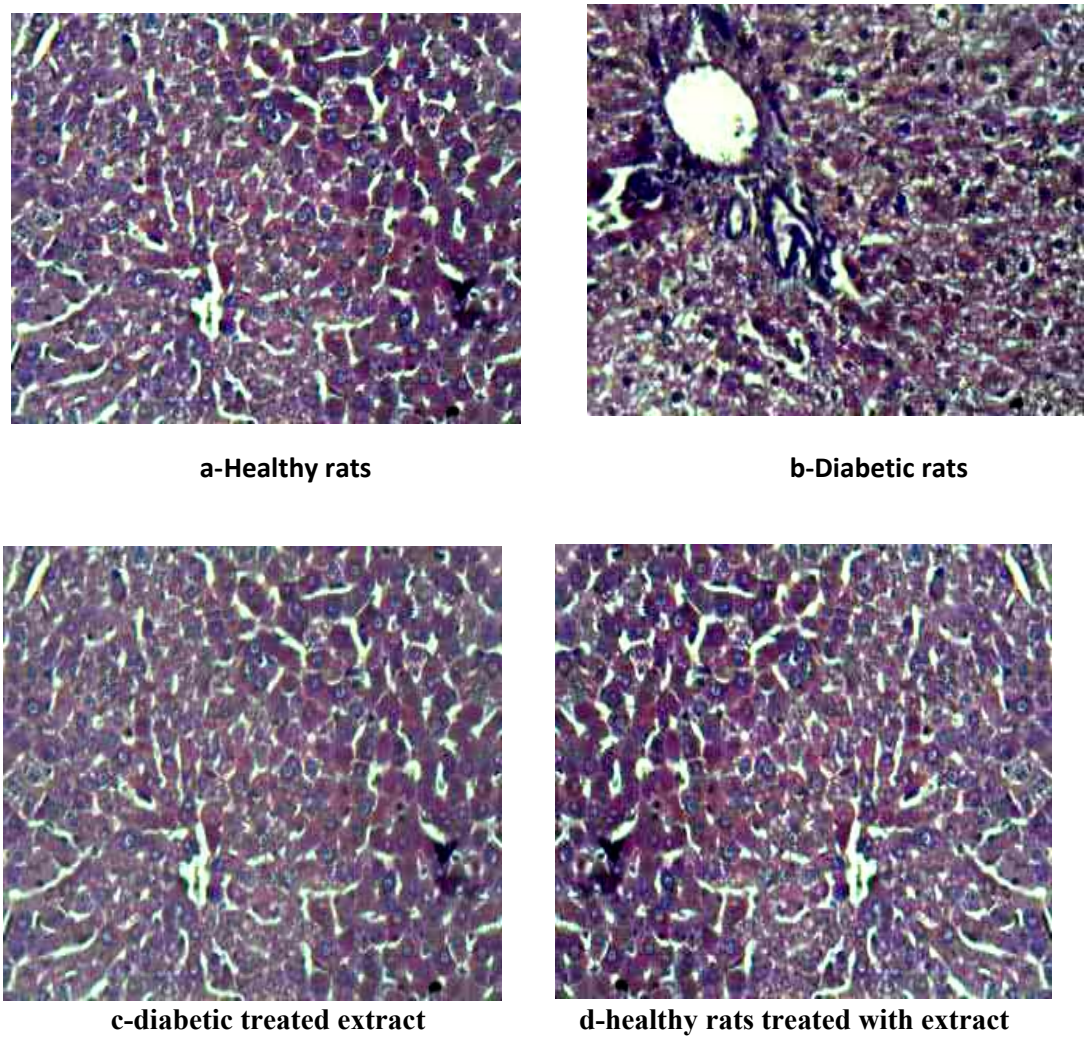
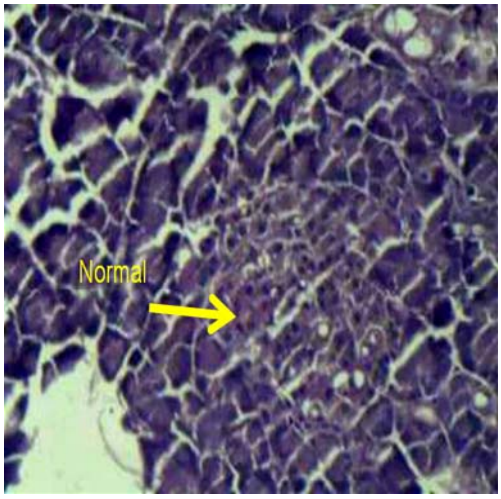


Figure 2: a-Histopathology of healthy rat liver showing normal hepatic structure (H&E 200X). b - Diabetic rat liver showing severe fatty changes, sinusoidal feathery degeneration and necrosis (H&E 200X). c- *Diabetic* rat liver treated with methanolic Anastatica hierochuntica plant extract (100 mg/Kg.b.w) showing mild fatty change, mild sinusoidal dilation and congestion (H&E 200X *and* d-healthy rat liver treated with methanolic anstatica hierochuntica plant extract (100 mg/Kg.b.w) normal hepatic structure (H&E 200X).

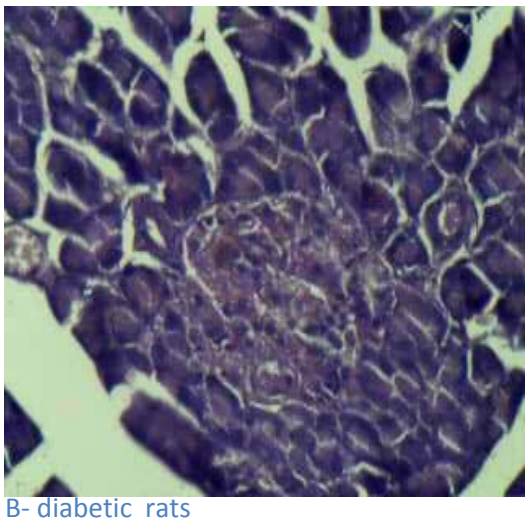
Effect of Anastatica extract intake on Histopathology of Pancreas: histomorphologic Changes of Pancreas

Control islets: The cellular integrity and architecture were intact in the healthy animals group .Animals of the control group did not appear to have any histological changes during the stages of experiment, since all the islets of the control animals appeared regular in shape with no marked differences between them, small islets of about (21µ) in diameter and reached (38 µ) in large islets. Islets of control animals had well defined boundaries. Most of the cells were of the β-type. β-cells were small polygonal arranged in groups & cords fine capillaries (Fig 3-a).

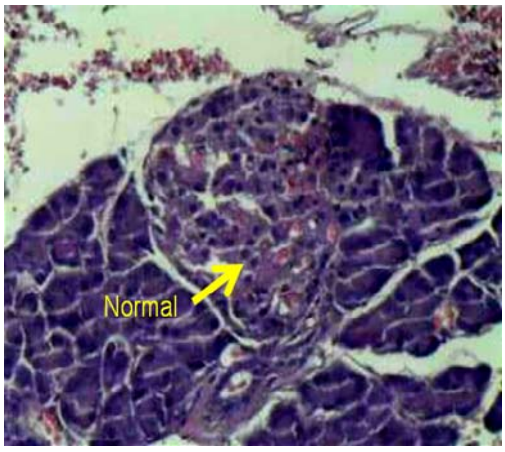
Diabetic islets: The histological studies of the endocrine region of pancreas of the diabetics revealed that shrinkage of β-cells of islets of Langerhans in the diabetic animals, while the plant extracts treated s revealed restoration of β cells. The restorations of the β-cells in diabetic treated (extract fed) s Anastatica the increased serum insulin levels in treated animals. Histopathological study of diabetic untreated rats showed degeneration of pancreatic islet cells, which was due to alloxan used in this study.(figure 3-b).Alloxan is a toxic glucose analogue, which selectively destroys insulin-producing cells in the pancreas when administered to rodents and many other animal species. This causes an insulin-dependent diabetes mellitus (called "Alloxan Diabetes") in these animals, with



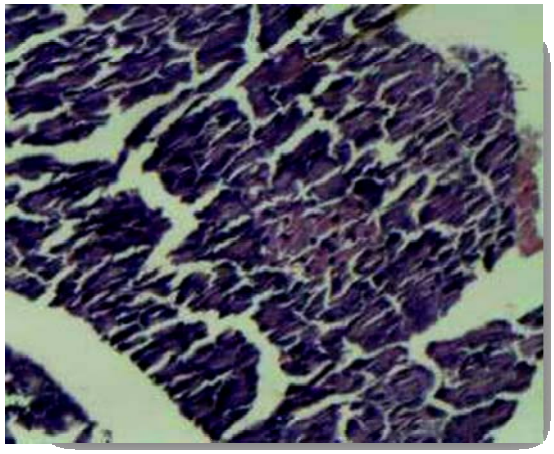
A- Healthy rats



B- diabetic rats



C- Diabetic rats treated with extract



d-Healthy rats treated with extract

Figure 3: (a) Histopathology of Pancreas of:(a) Normal rat showing normal histology, islet of Langerhans surrounded by exocrine Portion of pancreatic tissue (H&E X 200). (b) Diabetic rat showing severe congestion of pancreatic parenchyma cells, infiltration of inflammatory cells and hyperplasia of islet cells (H&E X200). Diabetic rat treated with methanolic anstatica hierochuntica plant extract showing improvement in the histological structure of Langerhans (H&E 200X). (d)Healthy rat treated with methanolic anstatica hierochuntica plant extract showing normal histology (H&E 200X).

Characteristics similar to type 1 diabetes in humans. Alloxan is selectively toxic to insulin-producing pancreatic beta cells because it preferentially accumulates in beta cells through uptake via the GLUT2 glucose transporter. Alloxan, in the presence of intracellular thiols, generates reactive oxygen species (ROS) in a cyclic reaction with its reduction product, dialuric acid. The beta cell toxic action of alloxan is initiated by free radicals formed in this redox reaction. Others show some correlation between alloxan plasma levels and diabetes Type 1 in children. Alloxan is a strong oxidizing agent and it forms a hemiacetal with its reduced reaction product dialuric acid (in which a carbonyl group is reduced to a hydroxyl group which is called alloxantin. This probably gave rise to insulin deficiency. Insulin deficiency (or diabetes mellitus) causes excessive elevation of blood glucose and underutilization leading to hyperglycemia (25). The histopathological study of diabetic treated group indicated increased volume density of islets(figure 3-c) and increased percentage of beta cells, in the diabetic rats that received the extracts, which may be a sign of regeneration. Signs of regeneration of ß cells, potentiation of insulin secretion from surviving ß cells of the islets of Langerhans and decrease of blood glucose have been reported following consumption of some plant extracts (30). *Anastatica hierochuntica* may have some chemical components that exert regenerative effects on ß cells, stimulate these cells to produce more insulin (pancreatotrophic action) or may have some insulinlike substances. Induction of regenerative stimulus in diabetic state triggers pancreatic regenerative processes, thereby restoring functional activities of the pancreas (30). A higher dose of the extract has a greater restorative effect on the islet cells of diabetic s than a lower dose of extract. The hypoglycemic effect was more pronounced in alloxan-diabetics than in normals after the administration of the aqueous extract to the alloxan induced diabetic rats revealed augmented serum insulin levels. The increment of serum insulin levels might be due to increased secretion of the hormone, which might reflect the probable 'repair' of the damaged beta cells of the endocrine of the pancreas due to alloxan. The whole plant extracts show a consistent effect on normal blood sugar levels and it effectively reversed the alloxan-induced changes in the blood sugar level and the beta-cell population in the pancreas. It also showed a protective effect when it was given prior to alloxan administration. The action of whole plant extracts on the pancreatic beta-cells and absence of acute toxicity may offer a new hope to the diabetics in future. From the above discussion it concludes that alcoholic plant extracts of *Anastatica hierochuntica* at dose100 mg/kg) exhibited significant antihyperglycemic activity similar to metformin at dose (100 mg/kg in alloxan-induced diabetic rats. These extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of cells of pancreas and so might be of value in diabetes treatment. Further investigation is necessary to determine the exact phytoconstituents(s responsible for antidiabetic effect.

Conclusion

The new findings of this study indicate that consumption of the of *Anastatica hierochuntica* extracts exerts significant hypoglycemic and hypolipidmic effects in diabetics. Histopathological studies of the pancreas of diabetic treated show evidence of signs of regeneration of ß cells in groups receiving *Anastatica hierochuntica* extracts. These findings support the traditional use of *Anastatica hierochuntica* extracts for controlling hyperglycemia in diabetics, in view of the responsive protective effects of the extract on pancreatic islet cells. Further investigation with longer period of higher doses may show clearer features of these findings. The present study suggests for the first time that the *Anastatica hierochuntica* extract had synergetic hypoglycemic, hypolipidmic effect in addition to antioxidant activity, therefore attribute to therapeutic value of the plant.

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