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Anti-Diabetic Effect of Some Herbs and Fruit Against Streptozotocin Induced Diabetic Rats

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Abstract: Experimental *Salvia officinalis* and *Cichorium intybus* herbs *and Citrullus colocynthis* fruit were exposed to hot air oven at 60°C then crushed to fine powder. Five rats from thirty male rats of Sprague Dawley strain were served as normal control while the other rats were injected (i.p) with streptozotocin (55mg/kg b.w) to induce diabetes. Then, diabetic rats were randomly classified into non-treated (received standard diet and tap water *ad-libtum)* and treated groups which were SO, CI, CC and Mix powder groups that received 10% of *Salvia officinalis, Cichorium intybus, Citrullus colocynthis* and mixture of powders, respectively. After 60 days, rats were anaesthetized by diethyl ether and sacrificed. Blood and spleen samples of each rat were collected. SO, CI, CC and Mix powder groups showed a significant increase in weight gain, weight gain percent, food intake and FER in diabetic rat groups compared to non-treated diabetic rat group. Blood analyses illustrated that SO, CI and Mix powder treatment groups showed significant lower of glucose and higher levels of insulin and PCV compared to non treated group. SO, CI, CC and Mix powder groups showed significant decrease in lipid parameters and cholesterol/high density lipoprotein cholesterol (HDLc) levels but showed significant increase in HDLc. Moreover, they showed significant decrease in liver enzymes function and albumin to globulin ratio and significant increase in total protein and globulin in compared to non-treated diabetic rat group. It is concluded that the examined herbs and fruit play role in lowering diabetes in rats.

Key words: *Cichorium intybus* · *Citrullus colocynthis* · Diabetes · Rats · *Salvia officinalis*

INTRODUCTION

Diabetes mellitus is a syndrome characterized by hyperglycemia and disturbance in carbohydrate, lipid and protein metabolism. It is associated with the specific micro vascular complications and non-specific macro vascular diseases [1]. Diabetes mellitus is a multifaceted disease state described by an elevated blood glucose level with reduced insulin levels and has been observed to be frequently associated with insulin resistance, obesity, dyslipidemia and high blood pressure [2]. Medicinal plants constitute the main source of new pharmaceuticals and healthcare products, including medications for ethno veterinary medicine. A whole range of plant-derived dietary supplements, phytochemicals and pro-vitamins that assist in maintaining good health and combating disease are now being described as functional foods and nutraceuticals. The roles of herbal tea in disease prevention and cure have been attributed, in part, to antioxidant properties of their constituents' liposoluble vitamins A and E, the water soluble vitamin C and a wide range of amphipathic molecules, broadly termed phenolic compounds [3]. *Salvia officinalis* L. (sage), a member of the family of Lamiaceae, has been reported to have wide range of biological activities. It has been proposed as effective against cardiovascular diseases, brain and nervous disorders, various infections (such as throat infections, dental abscesses and mouth ulcers) and digestion problems [4]. Chicory (*Cichorium intybus* L.) is a root vegetable and a perennial plant with blue or white flowers. Green leafy part of chicory is often used in cooking or in salads. It has been prescribed in various forms for the treatment of gastrointestinal disorders including gastric ulcers. Chicory roots or leaves extracts revealed that they produce hepatoprotective, antihyperglycemic and antioxidant effects [5]. *Citrullus colcynthis* L. *Schrad* is a member of the family Cucurbitaceae. The dried pulp of *C. colcynthis* fruit was

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used as a traditional medicine in the Sudan, mostly for skin infections, edema and in some instances, for diabetes. It has been also used for constipation worldwide [6, 7]. Thus, it is expected that the inclusion of these herbs in the diet would help in the management of diabetes mellitus and reducing its complications.

MATERIALS AND METHODS

Materials: *Salvia officinalis* herb*, Chicorium intybus* herb and *Citrullus colocynthis* fruit were purchased from the local market, Cairo city, Egypt. Streptozotocin was obtained from Sigma Chemical Co. (USA) Products. Thirty male rats of Sprague Dawley strain were purchased from the Agricultural Research Center, Giza, Egypt. The mean weight of male rats ranged from 120 ± 7g. The standard diet was formulated according to NRC [8].

Methods: Experimental herbs and fruit were exposed to hot air oven at 60°C then crushed to fine powder. After five days of adaptation, five rats served as normal control while the other rats were injected (i.p) with streptozotocin (55mg/kg b.w) dissolved in 0.1 M citrate buffer of pH 4.5 then supplied with 5% glucose solution for 48 h after injection in order to prevent hypoglycemia [9]. Seven days after streptozotocin administration, blood was collected from the rat eye canthus by means of haematocrit tubes. Animals showing fasting blood glucose higher than 200 mg/dl were selected and used as diabetic rats. Then, diabetic rats were randomly classified into non-treated control (received standard diet and tap *water ad-libtum)* and treated groups which were SO, CI, CC and Mix powder groups that received 10% *Salvia officinalis, Cichorium intybus, Citrullus colocynthis* and mixture of powders, respectively. Food intake was recorded daily and body weight of rats was measured once weekly. After 60 days, rats were anaesthetized by diethyl ether and sacrificed. Blood samples of each rat were withdrawn in test tubes. The tubes of blood were left for coagulation then centrifuged at 3000 rpm for 15 minutes to obtain serum for further analysis. Glucose, insulin, hemoglobin and pack cell volume (PCV) levels of different blood samples were determined by an enzymatic method according to Siest *et al.* [10], Wilson and Miles [11], Drabkin [12] and Mc-Inory [13], respectively. Serum alanine and aspartate aminotransferase (ALT & AST) and alkaline phosphatase (ALP) enzymes activity, total protein, albumin and total bilirubin were determined according to the method of Reitman and Frankel [14], Kind and King [15], Henry [16], Bartholomev and Delany [17] and Jendrassik [18], respectively. Serum total cholesterol, triglyceride (TG), high density lipoprotein cholesterol (HDLc) were estimated by using the spinreact enzymatic kits according to Richmond [19], Buccolo and David [20] and Grodon and Amer [21], respectively. Low density lipoprotein cholesterol (LDLc), very low density lipoprotein cholesterol (VLDLc), food efficiency ratio (FER) and athrogenic index (cholesterol/HDL-c) were calculated according to Lee and Nieman [22] and Castelli and Levitar [23]. Pancreas was collected from every rat and immersed in 10 % neutral buffered formalin as fixative and then sent to Pathological Department of Veterinary Medicine, Cairo University for histopathological examination according to Carleton [24].

Statistical Analysis: All the obtained data were statistically analyzed by SPSS16.0 student software. Hypothesis testing method included one way analysis of variance (ANOVA) followed by past hoc testing performed with least significant difference test (LSD). The *p* value of less than 0.05 was considered to indicate statistical significance according to Artimage and Berry [25].

RESULTS AND DISSCUSION

Data in Table 1 showed that non treated diabetic rat group and SO, CI, CC and Mix treated rat groups showed significant decrease in final weight, weight gain, weight gain percent, FER at $p< 0.001$ and food intake at $p< 0.05.0.01$ & 0.001 in comparing with control group. There was a significant increase in weight gain, weight gain percent, food intake and FER in diabetic rat groups which treated with *Salvia officinalis, Chicorium intybus, Citrullus colocynthis* and mixture of experimental herbs powder compared to non-treated diabetic rat group. It is known that, Streptozotocin is particularly toxic to the insulin-producing beta cells of the pancreas in mammals. Streptozotocin induced diabetic mouse is one of the animal models of human insulin dependent diabetic mellitus or type I diabetes mellitus. As expected the administration of streptozotocin to mice, resulted in reduction in body weight [26]. The improvement of nutritional values and growth performance in treatment groups may be due to their constituents of the experimental herbs. Pranav *et al.* [27] recorded that the leaves of *Salvia officinalis* L. (sage), from the family Lamiaceae are used widely as food flavouring.

Table 1: Mean ± SD of final weight, body weight gain, body weight gain %, food intake and FER of experimental diabetic rat groups.

Variables

Groups	Final Weight (g)	Weight gain (g)	Weight gain (%)	Food intake (g)	FER
Control	196.00±2.35^{a}	73.60±4.16^{a}	60.19±4.48^{a}	15.78±0.43^{a}	0.077±0.004^{a}
Non treated	159.60±1.52^{f***}	34.40±3.65^{d***}	27.58±3.83^{d***}	14.24±0.30^{d***}	0.040±0.007^{d***}
SO powder	183.00±1.23^{e***}	61.20±4.09^{b***}	50.34±5.57^{b***}	15.22±0.24^{bc*}	0.067±0.005^{b***}
CI powder	179.20±1.30^{d***}	54.60±1.67^{c***}	43.84±2.03^{c***}	15.19±0.49^{bc**}	0.060±0.002^{c***}
C.C. powder	175.60±3.36^{e***}	53.00±2.24^{c***}	43.08±1.82^{c***}	14.77±0.20^{c***}	0.059±0.002^{c***}
Mix powder	185.80±1.64^{b***}	62.40±1.67^{b***}	50.58±1.70^{b***}	15.28±0.36^{b*}	0.068±0.003^{b***}

Significant with normal control group * P < 0.05 * * P < 0.01 * * * P < 0.001

abcd Mean values in each raw having similar letters were not significantly different

Table 2: Mean ± SD of glucose, insulin, haemoglobin and PCV of the experimental diabetic rat groups.

Variables

Groups	Glucose (mg/dl)	Insulin (µ/l)	Haemoglobin (g/dl)	PCV (%)
Control	60.10±4.03^{c}	14.14±5.60^{a}	16.65±3.03^{a}	46.98±7.56^{a}
Non treated	150.60±57.68^{a***}	8.88±0.41^{b**}	11.64±0.68^{b**}	30.32±1.83^{c***}
SO powder	84.80±14.03^{bc}	12.16±1.08^{a}	12.75±0.75^{b**}	38.25±2.25^{b*}
CI powder	75.00±8.28^{c}	13.48±1.54^{a}	13.42±1.07^{b*}	40.26±3.20^{ab}
C.C. powder	121.14±24.04^{ab**}	13.20±1.41^{a}	13.58±2.61^{b*}	40.73±7.82^{ab}
Mix powder	91.00±7.42^{bc}	12.72±0.61^{a}	14.07±2.67^{ab}	38.50±3.36^{b*}

Significant with normal control group * P < 0.05 * * P < 0.01 * * * P < 0.001

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Urias-Silvas *et al.* [28] and Soheir [29] concluded that inulin (fructans) extracted from chicory regulate appetite and has a promising effect on the body weight. Food intake and growth performance of rat group administered cichorium intybus and chromium were in non-significant difference compared to control negative group. [30, 31] Shaheen and Hamed [30] and Meena and Patni [31] recorded that the protein content of seeds of colocynthis (transitional weed) was found to be 8.25% and rich in lysine, leucine and sulfo-amino acids viz., methionine. Colocynthis kernels contain oil (52%), protein (28.4%), fiber (2.7%), ash (3.6%) and carbohydrate (8.2%). These are good sources of essential amino acids (such as arginine, tryptophan and methionine) and vitamins (B1, B2 and Niacin) and minerals (Ca, Mg, Mn, K, P, Fe and Zn). Flavonoid quercetin was isolated from *in vivo* (leaf, stem, fruit and root) and *in vitro* callus of the species. Gurudeeban *et al.* [32] recorded that the content of essential amino acids in the proteins of the Citrullus colocynthis fruit flour makes it a good vegetable protein ingredient. Bitter Apple (*Citrullus colocynthis* seed flour is rich in micronutrients (vitamins and minerals). *Citrullus colocynthis* effectively ameliorated streptozotocin -induced weight loss. Table 2 showed that diabetic non treated group showed significant increase in glucose at p<0.001 and significant decrease in serum insulin, haemoglobin and PCV at p<0.01 &0.001 compared to control group. SO powder group showed non significant increase in glucose and non significant decrease in insulin at p>0.05 and significant decrease in haemoglobin and PCV at p<0.01 &0.05, respectively while SI powder group showed non significant increase in glucose and non significant decrease in insulin and PCV at p>0.05 and significant decrease in haemoglobin at p<0.05, respectively compared to control group. C.C. powder group showed significant increase in glucose at p<0.01 and non significant decrease in insulin and PCV at p>0.05 and significant decrease in haemoglobin at p<0.05 while Mix powder group showed non significant increase in glucose and non significant decrease in insulin and haemoglobin at p>0.05 and significant decrease in PCV at p<0.05 compared to control group. From the same table, the treatment groups which consumed *Salvia officinalis, Chicorium intybus* and mixture of experimental herbs powder showed significant lower of glucose and higher levels of insulin and PCV but non significant difference in haemoglobin compared to non treated group. C.C powder group showed significant increase in insulin and PCV but showed non-significant difference in glucose and haemoglobin compared to non treated diabetic rat group. These results were in agreement with those obtained by Elsner *et al.* [33] and Palmieri *et al.* [34], who reported that administration of streptozotocin destroys β-cells of the islets of Langerhans in pancreas. Destruction of β-cells in pancreas causes marked decrease in serum insulin levels. PCV (packed cell volume) and WBC

(White Blood Cell Count) counts were lower in diabetes than in non-diabetic individuals. The decreased level of haemoglobin in diabetic rats is mainly due to the increased formation of glycosylated hemoglobin or glycosylated hemoglobin (HbA1C). Also, the excess glucose present in blood reacts with hemoglobin (Hb) to form HbA1C. HbA1C is used as a marker for estimating the degree of protein glycosylation in diabetes mellitus. Huang *et al.* [35] recorded that an investigation was made to evaluate the therapeutic potential of the total polyphenolic acids fraction from *Salvia miltiorrhiza* Bunge in the type 2 diabetes mellitus rats model with an oral dose of 187mg/kg for 28 days. The total polyphenolic acids induced a significant decrease in fasting blood glucose, fasting blood insulin, total cholesterol, triglyceride and blood urea nitrogen and an obvious increase in insulin sensitivity index in diabetic rats induced by a high fat diet and a low dose of streptozocin. Steiner [36] and Ahmed [37] found that the diabetogenic effect of streptozotocin which leads to destruction and decreased number of β-cells in the islets of Langerhans and serum insulin concentration was increased markedly as a result of treating diabetic rats with *Esculetin* and *Cichorium intybus.* Presence of esculetin in *Cichorium intybus* potentially increased the levels of insulin and C-peptide in streptozotocin-induced diabetic rats. Welihinda *et al.*[38] and Sebbagh *et al.*[39] suggested that the mechanism responsible for the serum glucose lowering effect of bitter melon (*Citrullus colocynthis*) are attributed to an inhibitory effect of glucose absorption, an increased incorporation of circulating glucose as hepatic glycogen or an enhanced secretion of insulin.

Supplementation with *Citrullus colocynthis* oil, which provided linoleic acid, also had a protective or regenerative effect on the endocrine pancreas compared with both olive and sunflower oils against the toxic effects of streptozotocin. Jayaraman *et al.* [40] revealed that petroleum ether extract of *Citrullus colocynthis* has shown significant pharmacological activity towards lowering blood glucose in diabetes and reduced the glycosylation of Hb and thus reduces the level of HbA1C thereby increasing the level of Hb. Data in Table 3 illustrated that non-treated diabetic rat group showed significant increase in cholesterol, triglyceride, LDLc, VLDLc and cholesterol/HDLc but showed significant decrease in HDLc at $p<0.001$ in comparing with control group. SO powder rat group showed significant decrease in cholesterol and LDLc at $p<0.05$ & $p<0.01$, respectively and showed significant increase in serum triglyceride and VLDLc at $p<0.05$ but showed non-significant difference in high density lipoprotein cholesterol (HDLc) at $p> 0.05$ while CI powder group showed significant increase in cholesterol, LDLc and cholesterol/HDLc at $p<0.05$ & $p<0.01$ and showed non-significant difference in triglyceride, HDLc and VLDLc at $p> 0.05$ in comparing with control group. CC powder rat group showed significant increase in cholesterol, TG, LDLc, VLDLc and cholesterol/HDLc levels at $p<0.001$ and showed significant decrease in HDLc at $p<0.001$ while Mix powder rat group showed significant decrease in serum TG and VLDLc levels at $p< 0.05$ and showed significant increase in cholesterol, LDLc and cholesterol/HDLc at $p<0.001$ & 0.01 but showed non-significant difference in HDLc at $p> 0.05$ in comparing with control group. Diabetic rat groups which treated with *Salvia officinalis, Chicorium intybus, Citrullus colocynthis* and mixture of experimental herbs powder showed significant decrease in cholesterol, TG, LDLc, VLDLc and cholesterol/HDLc levels but showed significant increase in HDLc in compared to non-treated diabetic rat group. These results were agreement with those obtained Trautwein *et al.* [41], who established that the decrease in serum HDL cholesterol is a potential risk factor involved in atherosclerosis development. This lipoprotein has an important role in reverse cholesterol transport, from peripheral tissues to liver where is metabolize into bile acids. Cuvelier *et al.* [42] and Baricevic and Bartol [43] recognized that *Salvia officinalis L.* (common sage) is a

Table 3: Mean ± SD of some serum lipids parameters of the experimental diabetic rat groups.

Variables						
Groups	Cholesterol (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDLc (mg/dl)	Cholesterol/ HDLc
Control	88.20±12.66 ^{c}	78.60±9.69 ^{d}	38.60±2.30 ^{a}	33.88±10.98^{c}	15.72±1.94^{d}	2.28±0.29 ^{d}
Non treated	158.20±1.92 ^{a***}	190.80±3.70 ^{a***}	28.60±2.30 ^{c***}	91.44±3.19 ^{a***}	38.16±0.74 ^{a***}	5.56±0.46 ^{a***}
SO powder	70.60±12.38 ^{d*}	89.80±2.59 ^{e*}	36.40±3.78 ^{a}	16.24±9.31 ^{d**}	17.96±0.52 ^{c*}	1.93±0.18 ^{d}
CI powder	105.60±8.76 ^{b*}	88.20±14.30 ^{cd}	35.40±2.70 ^{a}	52.56±9.61 ^{b**}	17.64±2.86 ^{cd}	3.00±0.34 ^{c**}
C.C. powder	117.60±5.60 ^{b***}	111.40±1.82 ^{b***}	32.00±1.58 ^{b***}	63.32±5.84 ^{b***}	22.28±0.36 ^{b***}	3.68±0.29 ^{b***}
Mix powder	116.80±15.55 ^{b***}	68.20±7.23 ^{e*}	37.60±1.52 ^{a}	65.56±14.91 ^{b***}	13.64±1.45 ^{e*}	3.11±0.47 ^{c**}

Significant with normal control group * P < 0.05 * * P < 0.01 * * * P < 0.001

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medicinal plant well known for its strong antioxidant properties attributed to its constitution in phenolic compounds (rosmarinic acid being the most representative). Behall *et al.* [44] found that chicory has several health benefits, the short-chain fatty acids produced through the fermentation of soluble fiber in the large intestine serve to stabilize blood glucose levels, lower LDL in the blood and increase the production of immune cells. Brosnahan and Mony [45] reported that inulin in herbs and a fruit lowers serum cholesterol when added to the diet of rats. That may decrease cholesterol synthesis by inhibiting hydroxyl methylglutaryl-CoA reductase. A mechanism of action of oligofructose was associated with the modulation of *de novo* cholesterol synthesis by short chain fatty acids produced by the gut microflora during the fermentation process. Nehal [46] reported that feeding experimental diets supplemented with celery, chicory and barley plant powder, alone and combined, for four weeks to rats significantly decreased levels of total cholesterol, LDLc, VLDLc and triglycerides but significantly increased the levels of HDLc in the serum, as compared to the control positive group. Waffa [47] showed that values of serum cholesterol, triglyceride, LDLc and cholesterol/HDLc ratio were significantly decreased in all treated groups with cichorium powder group (CP), cichorium extract group (CE), cichorium powder with vanadium group (CPV) and cichorium extract with vanadium group (CEV). Kianbakht *et al.* [48] recorded that the extract of *Salvia officinalis* lowered the blood levels of total cholesterol, triglyceride, LDL and VLDL, but increased the blood HDL levels without any significant effects on the blood levels of ALT, AST and creatinine compared with the placebo group at the endpoint. Data in Table 4 illustrated that non-treated diabetic rat group showed significant increase in ALT, AST, ALP and total bilirubin at $p< 0.001$ in comparing with control group. SO powder rat group showed significant increase in AST and ALP at $p<0.001$ but showed non-significant difference in ALT and total bilirubin at $p> 0.05$ while CI powder rat group showed significant increase in AST and ALP at $p<0.001$ but showed non-significant difference in ALT and total bilirubin at $p> 0.05$ in comparing with control group. CC powder rat group showed significant increase in ALT, AST, ALP and total bilirubin at $p<0.01$ & $p<0.001$ while Mix powder rat group showed significant increase in AST and ALP at $p< 0.001$ and non-significant difference in comparing with control group. Diabetic rat groups which treated with *Salvia officinalis, Chicorium intybus, Citrullus colocynthis* and mixture of experimental herbs powder showed significant decrease in ALT, AST, alkaline phosphatase and total bilirubin in compared to non-treated diabetic rat group. The elevation of ALT and AST enzyme activities is considered as an evidence for hepatic damage. An increase of these enzyme activities is also associated with fatty liver disease and decreased hepatic insulin sensitivity in type 2 diabetes [49]. The administration of chicory supplemented diet resulted

Table 4: Mean ±SD of ALT, AST, ALP and total bilirubin of the experimental diabetic rat groups.

Control	ALT(µ/l)	AST(µ/l)	ALP (µ/l)	Bilirubin (mg/dl)
Control	60.00±22.28 ^{c}	80.61±7.64^{e}	93.71±3.51 ^{e}	0.45±0.04 ^{c}
Non treated	144.20±2.95^{a***}	191.20±22.82^{a***}	164.00±8.01^{a***}	1.51±0.07 ^{a***}
SO powder	44.00±17.72 ^{c}	116.60±2.41^{cd**}	119.41±2.30^{bc***}	0.54±0.15 ^{bc}
CI powder	52.40±19.17 ^{c}	125.60±2.41^{c***}	124.38±2.41^{b***}	0.57±0.13 ^{bc}
CC powder	90.00±15.18^{b**}	140.80±3.56^{b***}	113.20±2.39^{d***}	0.62±0.02^{b**}
Mix powder	49.80±3.03 ^{c}	109.40±2.07^{d***}	118.30±1.95^{cd***}	0.54±0.04 ^{bc}

Significant with normal control group * P < 0.05 * * P < 0.01 * * * P < 0.001

abcd Mean values in each raw having similar letters were not significantly different

Table 5: Mean ±SD of total protein, albumin, globulin and A/G ratio of the experimental diabetic rat groups.

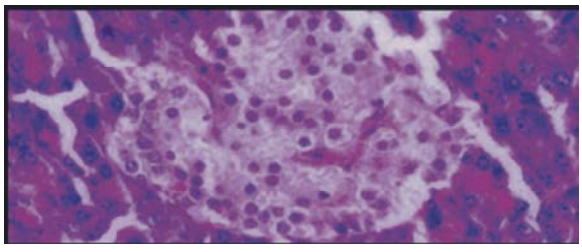
Control	Total Protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)	A/G Ratio
Control	8.86±0.92 ^{a}	4.04±0.34 ^{a}	4.82±0.36 ^{a}	0.84±0.12 ^{b}
Non treated	5.28±1.57 ^{c***}	3.01±0.31 ^{b***}	2.27±0.11 ^{d***}	1.33±0.18 ^{a***}
SO powder	7.34±0.11 ^{b**}	3.17±0.22 ^{b***}	4.18±0.30 ^{b**}	0.76±0.08 ^{b}
CI powder	7.14±0.39 ^{b**}	3.18±0.31 ^{b***}	3.96±0.29 ^{bc***}	0.80±0.06 ^{b}
CC powder	6.62±0.16 ^{b***}	3.06±0.39 ^{b***}	3.62±0.50 ^{c***}	0.86±0.17 ^{b}
Mix powder	7.10±0.62 ^{b**}	3.17±0.22 ^{b***}	3.94±0.31 ^{bc***}	0.81±0.11 ^{b}

Significant with normal control group * P < 0.05 * * P < 0.01 * * * P < 0.001

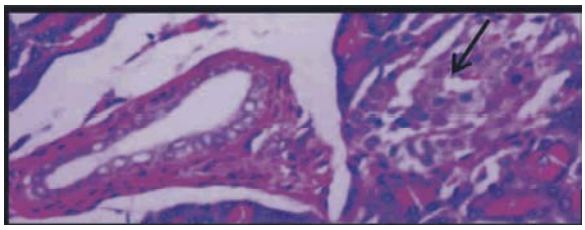
abcd Mean values in each raw having similar letters were not significantly different

in an improvement of protein pattern by preventing protein oxidation and improves liver and other organs functions which synthesized plasma protein [50]. The *Citrullus colocynthis* treated rats showed a significant elevating tendency in the serum ALT, AST and ALP [51]. Data in Table 5 illustrated that the non-treated diabetic rat group showed significant decrease in total protein, albumin and globulin at $p< 0.001$ and showed significant increase in A/G ratio at $p< 0.001$ in comparing with control group. Diabetic rat groups which treated with *Salvia officinalis, Chicorium intybus, Citrullus colocynthis* and mixture of experimental herbs powder showed significant decrease in total protein, albumin and globulin ($p<0.01$ & $p<0.001$) but showed non-significant difference in A/G ratio at $p> 0.05$ in comparing with control group. However, they showed significant decrease in A/G ratio and significant increase in total protein and globulin in diabetic rat groups compared to non-treated diabetic rat group. These results were agreed with Abd El-Ghany *et al.* [52] who cleared that the alteration in A/G ratio may occur due to the reduction in albumin and or elevation of globulin. However the ratio may be increased in some cases of biliary cirrhos. Akram and Eidi [53] reported that Oral administration of 0.2 and 0.4 g/kg body wt. of the sage extract for 14 days exhibited a significant reduction in serum glucose, triglycerides, total cholesterol, urea, uric acid, creatinine, AST, ALT and increased plasma insulin in streptozotocin-induced diabetic rats. Kiran *et al.* [54] showed that the treatment with *Cichorium intybus* at doses, 200 and 400mg/kg b.w. resulted in significant decrease in serum AST, ALT and ALP levels and rise in total protein levels which clearly depicts its hepatoprotective action.

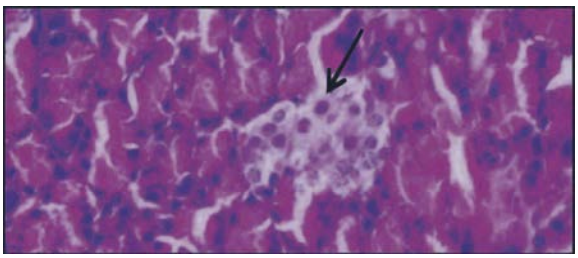
Pancreas Histopathology: Pancreas of control rats revealed the normal histological structure (picture 1). Pancreas of rat from diabetic non treated group revealed vacuolations of B cells of islets of Langerhans (picture 2). Meanwhile pancreas from diabetic rat group treated with *Salvia officinalis* powder showed atrophy of B cells of



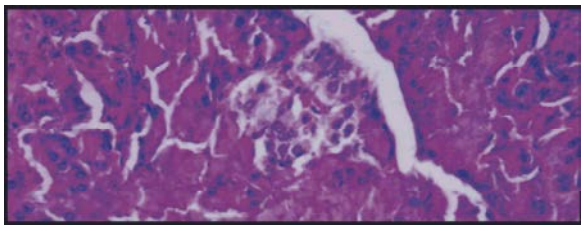
Picture 1: Pancreas of normal control rat showing no histopathological changes(H and E × 400).



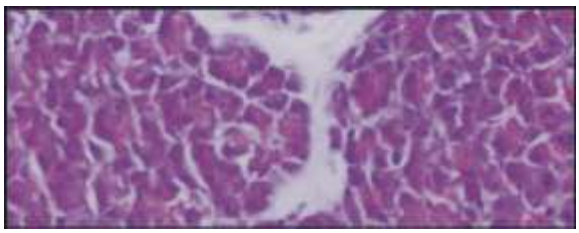
Picture 2: Pancreas of non-treated rat showing vacuolations of B cells of islets of Langerhan's (H and E × 400)



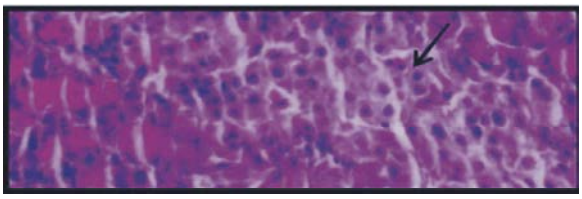
Picture 3: Pancreas of rat treated with *Salvia officinalis* powder showing atrophy of B cells of islets of Langerhan's. (H and E × 400).



Picture 4: Pancreas of rat treated with *Chicorium intybus* powder showing no histopathological changes. (H and E × 400).



Picture 5: Pancreas of rat treated with *Citrullus colocynthis* powder showing no histopathological changes. (H and E × 400).



Picture 6: Pancreas of rat treated with mixture powder showing necrosis of B cells of islets of Langerhan's. (H and E × 400).

islets of Langerhans (picture 3). Examined sections of diabetic rat groups treated with *Chicorium intybus* and *Citrullus colocynthis* powder showed no histopathological changes (picture 4 & 5). However, pancreas of diabetic rat group treated with mixture of experimental herbs powder revealed necrosis of B cells of islets of Langerhans (pict.6). The histopathological results were agreed with Hanaa *et al.* [55] reported that streptozotocin, selectively destruct β cells of the islets of langerhans in the pancreas. Ahmed *et al.* [56] reported that the treatment with *Cichorium intybus* and *Sonchus oleraceus* infusions and esculetin administration stimulates recovery of islets. At the end of the experiment, the islets regain their normal architecture with fewer hydropic vacuolated cells in the treated groups as compared with the diabetic control rats. Alpha and delta cells appeared more intact and are granulated. There are still few necrotic areas and vacuolations. Zupko *et al.* [57] cleared that *Salvia officinalis* L. has the antioxidant properties of sage and some of its constituents, mainly phenolic compounds such as carnosic, rosmarinic, caffeic and salvianolic acids as well as other phenolic structure-based compounds. Ahmad *et al.* [58] showed that the pancreases and livers of the treated rats with *Citrullus colocynthis* an improvement in their histological architecture. The pancreas of the treated animals with *Citrullus colocynthis* showed an increase in the size of the islets, with hyperchromic nucleus and regeneration of the B cells. It is advised to prepare diets fortified with the examined herbs as regimen for diabetic patients.

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