The Egyptian Journal of Hospital Medicine (July 2013) Vol. 52, Page 725–739

Antidiabetic and Antihyperlipidemic Effect of *Balanites aegyptiaca* Seeds (Aqueous Extract) on Diabetic Rats

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ABSTRACT:

Objectives: Type II diabetes mellitus is increasing health problems that negatively affect health care systems worldwide. There is a constant urge to develop new therapies with better effects, lower side effects at lower prices to treat this disease. Therefore, the present study carried out to investigate whether *Balanites aegyptiaca* (seeds) could treat the hyperglycemic, dislipidemic, liver, and kidney toxicity and the pancreatic damage in diabetic rats.

Material and method: fifteen adult male albino rats were divided into two groups; group 1: control group, group 2: alloxan induced diabetic rats that divided into two subgroups; subgroup1: diabetic untreated rats, subgroup2: diabetic treated with aqueous extract of *B. aegyptiaca* (seeds). After thirty days of treatment, all rats were sacrificed. Blood sample were collected to estimate some hematological and biochemical parameters. Liver samples were collected to determine their glycogen content and pancreatic samples were obtained and processed for microscopic and quantitative evaluation of α, β & δ-cells number.

Results: diabetic group recorded reduction in body weight's gained, hyperglycemia, hypoinsulinemia, significant increase in some parameters of liver and kidney functions, dislipidemia, changes in proteins level and decreased liver glycogen content. While, treatment with *B. aegyptiaca* (seeds) was ameliorated most of the toxic effects of alloxan and showed partially improvement in histological changes produced by alloxan.

Conclusion: The aqueous extract of *B. aegyptiaca* (seeds) has hypoglycemic, hypolipidemic effects, increasing insulin level, and decreasing insulin resistance. Moreover, ameliorate the most complication associated with diabetes mellitus.

Key words: Alloxan; Hypoglycemia; Diabetic; *Balanites aegyptiaca*.

Introduction:

The importance of human diabetes mellitus as a world health problem is attributes to the fact that at least 150 million people are affected, thus the necessity to seek new drugs [1]. Nature is an extraordinary source of antidiabetic medicines. Where, many herbal products have recommended for the treatment of diabetes mellitus since antiquity [2].

Alloxan causes severe necrosis of pancreatic β-cells [3] with the consequent lack of insulin secretion. For this reason, it has been widely used to induce experimental diabetes mellitus, and many studies have performed using this model to explore pancreatic damage [1].

B. aegyptiaca Del. (Zygophyllaceae) has traditional roles and values known for thousands of years as fruits were found in tombs of the12th Egyptian dynasty [4]. The tree is using for food and fodder [5] as agro forestry tree [6] and has a wide range of medicinal uses. The seed kernel contains high amount of oil and protein that varies among different sources [7].

It known as ‘desert date’ widely distributed in dry land areas of Africa and South Asia. It contains protein, lipid, carbohydrate, alkaloid, saponin, flavor-noids, and organic acid. The traditional claims, phytochemistry, and pharmacology of *B. aegyptiaca* Del reported [8].

The present study was designed to evaluate the antihyperglycemic and antihyperlipidemic effect of *B. aegyptiaca* (seeds), as we discovered that it ameliorated glucose intolerance and reduce body weight in a previous study.

DOI:0000610/10.12816

Material and Methods:

Fifteen adult male albino rats of local strain with body weight ranging between (120-140 gm.) were divided into two groups as following**: group I**= control non diabetic rats; **Group II** = alloxan-induced diabetic rats which divided also into two subgroups; **subgroup1**: diabetic untreated rats, **subgroup2**: diabetic treated with aqueous extract of *B. aegyptiaca* seeds (4.2mg/ 100gm. b.wt. dally) by gastric intubation.

Induction of diabetes mellitus by giving s.c freshly prepared alloxan solution 120 mg/ kg dissolved in 0.5 ml acetate buffer (pH 5.5) to overnight fasting animals. After 48 hours of alloxan injection, rats were fasted overnight (8-10hrs) and administered glucose (3gm/kg b.wt.) by gastric intubation. After 2 hours of glucose administration, blood glucose level was determined by glocometer. The rats with blood glucose levels above 200mg/dl were used for the study [9].

Preparation of aqueous extract of *B. aegyptiaca* seeds by finely grounded seedsand boiling 3 gm. of their powder in 200 ml water then filtered.The extract was given to animals (4.2mg/100gm. b.wt orally as used in the Egyption folk medicine) by oral tube once daily for one month.

Body weight of rats determined at the beginning and the end of the experiment. Blood samples were collected from the orbital plexus using heparinized capillary tubes [10] after a month of treatment. Part of blood was collected on EDTA for hematological studies and the other part collected in clean centrifuge tubes to separate the serum by centrifugation for 10 min. for 5000 rpm, and the supernatant serum was immediately separated for biochemical analysis. Livers were taken for glycogen determination. Samples from the pancreases were also taken and processed for the stain with Heamatoxylin and Eosin (HX & E) and modified aldhyde fuchsin [11] for histological study.

Blood cells count were performed with an automatic cell counter, liver glycogen content was determined by an acid-hydrolysis method as described by **Joseph** [12], serum insulin level determined by using an ELISA (Enzyme Linked Immunosorbent Assay) kit, assay principle according to **Reeves** [13], serum glucose was estimated by the enzymatic colorimetric method described by **Burtis** [14]. HOMA-IR estimated by using the euglycemic clamp method (r= 0.88) according to **Matthews *et al.*** [15], ASAT and ALAT determined according to the method described by **Schumann** and **Klauken** [16], serum urea and creatinine estimated according to the method of **Burtis** [14] and **Tietz** [17]respectively. Serum total protein and albumin estimated according to **Young** [18]. Serum total lipid, triglycerides, cholesterol, HDL-cholesterol, and VLDL-cholesterol were determined according to the method of **Knight *et al.*** [19], **McGowam** [20], **Schettler** and **Nussel,** [21], **Warnick *et al.*** [22] and **Finley** [23]. While, LDL-cholesterol calculated by the following equation:

LDL= cholesterol– HDL – (triglyceride/5) according to **Demacker *et al.*** [24].

Statistical analyses:

Data were analyzed using student (t) test [25]. Data at ($P \leq 0.05$) considered significant.

Results:

Body weights change:

Treatment with alloxan only led to significant decrease in percentage of body weight gain ($P \leq 0.01$) and the diabetic rats treated with *B. aegyptiaca* seed extract recorded significant decrease ($P \leq 0.01$) when compared with both diabetic and control groups.

Parameters associated with type II diabetes mellitus:

The present study recorded significant decrease ($P \leq 0.01$) in liver glycogen content and serum insulin level and significant increase ($P \leq 0.01$) in blood glucose level and HOMA-IR in diabetic untreated as compared with control rats. While, the treatment with water extract of *B. aegyptiaca* (seed) showed no significant change in serum glucose and insulin levels, and liver glycogen content, while

HOMA-IR recorded significant decrease (P≤0.01) when compared with control group (table, 2).

Lipids profile:

Dislipidemia records in diabetic untreated rats showed highly significant increase (P≤ 0.01) in all serum lipids profile except HDL-C and HDL-C/LDL-C where recorded significant decrease (P≤0.01) when compared with the control. On the other hand, *B. aegyptiaca* treated group recorded no significant change in all lipids parameters when compared with the control group.

Proteins level:

Diabetic untreated rats recorded significant decrease (P≤0.01) in all serum protein levels when compared to the control group except serum globulin level, which was recorded significant increase (P≤0.05). While, *B. aegyptiaca* treated rats showed no significant change in all of these parameters when compared to the control rats.

Liver function tests:

There is significant increase (P≤0.01) in ALAT and ASAT activities as a result to toxic effect of alloxan on rats' liver tissues when compared to the control group. The treatment with *B. aegyptiaca* ameliorates this toxic effect where it was recorded no significant change in both parameters when compared to control group.

Kidney function tests:

Hyperglycemia associated by increasing serum creatinine and urea levels, as recorded in diabetic untreated rats compared with the control (table, 6). Otherwise, *B. aegyptiaca* treated group showed no significant change in both of them when compared with the control group.

Some hematological parameters:

RBCs count and Hct (percentage) recorded no significant change in diabetic and treated groups. WBCs and lymphocytes which play a pivotal role in initiating immunity showed significant decrease (P≤0.05 and P≤0.01 respectively) in diabetic rats when compared with normal group. These abnormalities in the defense mechanisms returned to nearly normal by treatment with *B. aegyptiaca*.

Some Histological changes:

Microscopic examinations of the control rats' pancreatic tissues display three main types of pancreatic islet cells (alpha, beta, and delta) by the modified aldehyde fuchsin stain. Where, β-cells are occupying the central portion of the islet and contained numerous granules, α-cells occupied the periphery of the islet (granular and polygonal with central spherical nuclei) and δ-cells were usually adjacent to alpha cells (and larger) as clearly observed in plate (2).

On the other hand, pancreatic tissues of diabetic rats display islets shrinkage, cytoplasmic vacuolation in β-cells with pyknotic nuclei. While, *B. aegyptiaca* treated rats showed nearly normal architecture of the pancreatic islets. Where, most of the cytoplasm of β-cells became granulated with less vacuole.

Number of α, β and δ cells recorded significant decrease (P≤0.01) in diabetic untreated rats when compared with control group. While, *B. aegyptiaca* treated group showed no significant change in β-cells and recorded significant decrease (P≤0.01) in α-cell and δ-cell numbers when compared with control group.

DISCUSSION:

The rapidly increasing incidence of diabetes millets is becoming a serious threat to humankind's health in all parts of the world [26]. There is a constant urge to develop new therapies with better effects, lower side effects at lower prices to treat this disease [2].

Traditional antidiabetic plants might provide a useful source of new oral hypoglycemic compounds for development as pharmaceutical entities, or as simple dietary adjuncts to existing therapies [27]. Where, plants are rich sources of antidiabetic, antihyperlipidemic and antioxidant agents such as flavonoids, gallotannins, amino acids, and other related polyphenols [28]. *B. aegyptiaca* is a plant commonly used in

Egyptian folk medicine as a hypoglycemic agent [29]. However, there are very few studies concerning the effect of the seeds as antidiabetic agent.

The results recorded significant decrease in body weight gain and liver glycogen content and sever hyperglycemia in diabetic untreated rats as a result to sever hypoinsulinemia and increasing insulin resistance. Where, the defect in insulin level or function leads to alteration in carbohydrates metabolism causing hyperglycemia and decreasing liver glycogen content. These may be due to the effect of insulin on hepatic cells by stimulating glycogenolysis and gluconeogenesis and inhibition of its effect on peripheral utilization of glucose. Which in agreement with **Defronzo** and **Goodman** [30], who attributed hyperglycemia to increase hepatic glucose production, a decrease in peripheral glucose uptake, and significant decrease in the conversion of glucose to glycogen in the liver.

While, this sever serum hypoinsulinemic level recorded in diabetic rats may be attributed to reduction in β-cells mass or β-cells' cytoplasmic vacuolation. Where, microscopic examination showed reduction in β-cells mass, which may be due to the selective destructive cytotoxic effect of alloxan on the β-cells. Where, alloxan has direct effect on β-cells membrane permeability by causing failure of ionic pumps and increasing cell size which inhibits intra cellular energy generation by inhibiting enzymes of tricarboxylic acid cycle and Ca^{+2} dependants dehydrogenises in their mitochondrion, causing ATP deficiency, cessation of insulin production and cell necrosis [3&31]. In addition, may be due to its sudden activation of quiescent cell for a high level of protein synthesis and produced rapid and massive β-cell death which, leading to a decrement in β-cells number [32]. Moreover, showed β-cells' cytoplasmic vacuolation which may be attributed to the diabetogenic action of alloxan where, it induced highly reactive oxygen radicals whom have cytotoxic effect on β-cells as explained by **Fischer** and **Homburger** [33]. These results are in agreement with finding of **Kessler *et al.*** [34] who reported that vacuolation of the islet in the most prominent with lesion associated with functional islet abnormality and development of hyperglycemia.

Otherwise, the improvement of general diabetic conditions in rats treated by the extract of *B. aegyptiaca* (seeds) is possibly due to recovered endocrine pancreatic tissue at both structural and functional levels. Where, the present results showed regeneration in β-cells structure and number. This can lead to elevated insulin level and improved insulin sensitivity that lowers the concentration of glucose in blood. Where, insulin inhibits hepatic glucose production, stimulates both of glucose uptake and of metabolism by muscle and adipose tissues and increases liver glycogen content. In addition, *B. aegyptiaca* (seeds) containing diosgenin [35], which may be useful for ameliorating the glucose metabolic disorder, associated with diabetes and obesity. Where, diosgenin can be absorbed through the gut and plays an important role in the control of metabolic diseases such as diabetes and obesity as reported by **Ulbricht *et al.*** [36]. Furthermore, *in vitro* experiment showed that diosgenin promoted 3T3-L1 adipocyte differentiation to enhance insulin-dependent glucose uptake [37]. While, **Abdel Motaal *et al.*** [38] attributed the antihyperglycemic activity of *B. aegyptiaca* fruits to increase muscle basal glucose uptake significant insulin-like and partly glitazone-like activities in peripheral tissues.

According to the increase in the number of β-cells, insulin level and decrease insulin resistance recorded in *B. aegyptiaca* treated rats we suggested that, this plant might be inducing betatrophin secretion from the liver and adipose tissues where this hormone is secreted into the blood stream to signal β-cells in the pancreas to reproduce [39]. The new β-cells only produce insulin when called for by the body, offering the potential for the natural in the complication associated with diabetes [40].

Nevertheless, the significant reduction in the percentage of body weight gain after treatment with the aqueous seed extract of *B. aegyptiaca* though it increases insulin level and sensitivity may be due to loss of appetite. Where, **Matter** and **Helal** [41] reported that, *B. aegyptiaca* seed extract stimulates secretion of leptin, which induce loss of appetite through repression of the hypothalamic neuropeptide Y (NPY) production. In addition, may be rise from its claim to result in nutrient partitioning so that ingested calories directed to muscle, rather than fat and/or attempt to affect gastric satiety by filling the stomach [42]. Moreover, possibly spring from its anti water retention action [43].

Hypoinsulinemia clearly showed in diabetic untreated rats considered the main cause of dislipidemia recorded. Where, hypertriglyceridemia and hypercholesterolemia associated with increased production of VLDL and decreased HDL level. These findings are in agreement with **Abdel-Moneim *et al.*** [44] who found marked increase of serum triglycerides, cholesterol, and LDL-cholesterol levels in the diabetic animals. This increase may be due to the decrease in lipoprotein lipase (LPL) activity secondary to insulin deficiency [45].

In addition, **Goodman** and **Gilman's** [46] who explained the same result by inhibition of the transcription of lipoprotein lipase in the capillary endothelium as a result to deficiency of insulin which lead to elevate the plasma chylomicron and VLDL levels, resulting in hypertriacylglycerolemia and associated with low HDL levels. And also, agreement with **Harvey** and **Ferrier** [31] who reported that, the metabolic abnormalities of type II diabetes area result of insulin resistance which lead to dislipidemia in the liver where, fatty acids are converted to triacylglycerol which are packaged and secreted in VLDL. Both lipid accumulations particularly triglycerides and reduction in antioxidant activity are contributed to the development of oxidative stress in diabetic rats [47]. In addition, agrees with **Osman** and **Kandil** [48] who demonstrated marked decrease of HDL-cholesterol in serum of IDDM patients and alloxan diabetic rats. These abnormalities certainly play a role in the increased risk of cardiovascular disease. While, increased serum LDL-cholesterol level may be due to overproduction of VLDL by the liver or decreased removal of VLDL and LDL from the circulation [49]. Moreover, **Stanfield** [50] reported that, diabetes increases the number of LDLs that transport lipids including cholesterol to the cells and decreases the number of HDLs that transport lipids and cholesterol to the liver.

At the same time, the elevated level of serum triglycerides in diabetic animals of the present study may be attribute to decreased clearance and increased production of the major transporters of endogenously synthesized triglycerides [51]. In addition, the expansion of cholesterol pool in diabetes might be explain by a higher input into system through acceleration of intestinal cholesterol synthesis or an increment of the rate of intestinal cholesterol absorption [52].

On the other hand, the improvement in dislipidemia by *B. aegyptiaca* treatment may attribute to the increase insulin level and sensitivity. The present results are in agreement with **Matter** and **Helal** [41] who reported that, the level of serum triglycerides and cholesterol was not significantly different when compared with control after treatment with *B. aegyptiaca* seeds extract. In agreement with **Abd El-Rahman** and **Al-ahmari** [53], returned the amelioration of lipid profile to presence of saponins in its extract which show antihypercholester-emic and hypoglycemic. Where, diosgenin in *B. aegyptiaca* seeds kernels plays an important role in the control of cholesterol metabolism [54].

In untreated diabetic rats, the decrement of total protein, albumin, and A/G ratio may be attribute to enhance rate of gluconeogenesis, which is a secondary

effect of insulin deficiency, and increase insulin resistance. This process associated with increased production and excretion of urea. These results are in agreement with **Helal**[27]and **Abdel-Moneim** [44] who found marked decrease in serum total proteins and albumin in diabetic animals. This decrease in total serum protein content of diabetic rats may be due to the decreased of amino acids uptake [55]. In addition, increased conversion rate of glycogenic amino acids to CO_2 and H_2O [9].

In addition, reduction in protein synthesis which in turn may be due to a decrease in the amount and availability of mRNA [56] and also, a reduction in ribosomal protein synthesis as a result of insulin deficiency [57]. While, **Shafrir** [3] explained the decrease of total proteins and albumin in alloxan diabetic rats to enhanced proteolysis in tissues, which lead to reduce production of growth factors and increase growth factor binding protein by a rapid mechanism and slow, long-losing activations of a myofbrillar protease.

Otherwise, treatment with aqueous seeds extract of *B. aegyptiaca* showed insignificant change in all of these parameters when compared with the control group. This result is in agreement with **Matter** and **Helal** [41] who recorded statistically no significant low values in total protein and albumin levels in animals treated with drenched water or ethanol extracts of *B. aegyptiaca* as compared to control group. This improvement in all of these parameters may be because of improving the glycemic condition, insulin level and insulin sensitivity. Where, insulin plays an important role in amino acids transport and augmenting incorporation of certain amino acids into protein [58]. Moreover, **Aquilani** [59] reported that, the inhibition of proteolysis and enhanced protein synthesis gradually abolished by insulin.

The elevation of serum ASAT and ALAT activities in diabetic untreated rats recorded in the present work may be attribute to the excessive release of such enzymes from the damaged liver cells into the blood circulation. Where, there is an inverse relationship between the liver activity and the level of enzymes in serum [60]. This may be consistent with their greater need for gluconeogenesis substrates or may reflect damage of the hepatic cells due to hepatotoxic effect of alloxan [27&61].

On the other hand, rats treated with *B. aegyptiaca* seed extract recorded improvement in ALAT and ASAT activities, which are suggesting hepatoprotective effects of the present treatment. Where, improved liver functions may be resulted from return gluconeogenesis process towards their normal levels and to the insulinogenic effect of these agents as claimed by **Hough *et al.*** [62] who indicated that, enzymes activity were completely normalized following insulin administration.

The significant increase of serum urea and creatinine levels recorded in diabetic group may be resulted from failure of the body to excrete the metabolic products of proteins [63]. This increased in diabetic group because of increasing gluconeogenesis rate. In addition, this may because by the hyperglycemia, hyper-tension, or hyperlipidemia that occurs with diabetes [50]. Where, serum creatinine often rises in type II diabetes due to renal arterial disease and/or cardiac failure rather than to diabetic nephropathy [63]. Where, hyperglycemia causes kidney damage through glycosylation, activation of protein kinase C, release of several cytokines, and increase activity of the polyol pathway [50].

The improvement of serum urea and creatinine levels in rats treated with aqueous seeds extract of *B. aegyptiaca* reflected improvement effect of kidney functions and stops the destructive effect of alloxan. This may be due to the sapogenin effect, which decreased serum urea and creatinine as reported by **Abd El-Rahman** and **Al-ahmari** [53]. Where, *B. aegyptiaca* seeds contain a good amount of sapogenin [53].

Abnormalities in the defense mechanisms of diabetic rats in the present results where, WBCs and lymphocyte,

which play a pivotal role for initiating immunity, showed significant decrease ($p \leq 0.05$ and $p \leq 0.01$ respectively). This is may be due to decrease proliferative response of lymphocyte, which, owing to high glucose concentration concomitancy, inhibited the DNA synthesis of mitogen-stimulated lymphocytes. Therefore, high glycemic in addition to the lack of insulin may participate in the reduced proliferation capacity of lymphocytes from diabetic rats [64].

B. aegyptiaca seed extract treatment ameliorates these defects may be due to increase insulin level, which stimulates DNA synthesis and amino acids uptake in human fibroblasts [65]. In addition, insulin may be enhancing the response of lymphocytes to Concanavalin A (Con. A), these cells were activated with short-term pulse of Con. A. Insulin was capable of replacing the requirement of Con. A for the continuation of the proliferative response [66].

Conclusion:

From the above discussion, it concluded that, treatment with water extract of *B. aegyptiaca* seeds could ameliorate most β-cells dysfunction and increasing the insulin's receptors sensitivity that associated by improvement in general diabetic conditions. Other doses and periods of experiments must be studied, and its relationship with betatrophin secretion.

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Table (1): Body weight changes in control, diabetic and *B. aegyptiaca* treated rats.

	Control	Diabetic	*B. aegyptiaca*
%Body weight change	**21.89+0.93**	**13.26+1.03**	**6.56 +2.63**
a		**	**
b			**

Data expressed as:

Mean + standard error,
*=P≤0.05, **= P≤0.01,
(+) = Increased from control,
(a) = compared to control,
% = percentage of change,
n.s. = non significant,
(-) = Decreased from control.
(b) = compared to diabetic.

Table (2): Parameters associated with DM in normal, diabetic and *B. aegyptiaca* treated male albino rats.

	Control	Diabetic	*B. aegyptiaca*
Glucose (mg/dl)	**121.8+1.11**	**286.4+3.36**	**117.6+2.5**
%a		**+135.14**%**	**-3.45$^{n.s}$%**
%b			**-58.94**%**
Insulin (µu/l)	**4.06+0.04**	**3.01+0.09**	**3.63+0.039**
%a		**-25.86** %**	**-10.59$^{n.s}$%**
%b			**-20.59$^{n.s}$%**
Glycogen content (mg/dl)	**18.18+0.56**	**2.45+0.16**	**15.03+0.27**
% a		**-77.27 **%**	**-17.33$^{n.s}$%**
%b			**+513.47**%**
HOMA-IR	**1.22+0.07**	**2.11+0.08**	**0.76+0.02**
%a		**+72.95** %**	**-36.7**%**
%b			**-63.98**%**

Data expressed as:

Mean + standard error,
*=P≤0.05, **= P≤0.01,
(+) = Increased from control,
(a) = compared to control,
% = percentage of change,
n.s. = non significant,
(-) = Decreased from control.
(b) = compared to diabetic.

Table (3): Lipids profile in normal, diabetic, and *B. aegyptiaca* treated male albino rats.

	Control	Diabetic	*B. aegyptiaca*
T. Lipid	**303.8+2.08**	**436.2+1.36**	**307.6+2.94**
%a		**+43.58**%**	**+1.25$^{n.s}$%**
%b			**-29.48**%**
T. cholesterol (mg/dl)	**109.4+1.96**	**199+1.87**	**111.6+1.69**
%a		**+81.9**%**	**+2.01$^{n.s}$%**
%b			**-43.92**%**
Triglycerides (mg/dl)	**85+1.37**	**92.2+1.02**	**84.2+1.46**
%a		**+8.47**%**	**-0.94$^{n.s}$ %**
%b			**-8.68**%**
HDL-C (mg/dl)	**25.2+0.73**	**19.2+0.97**	**26.4+0.51**
%a		**-23.8** %**	**+4.76$^{n.s}$ %**
%b			**+37.5 **%**
LDL-C (mg/dl)	**67.2+2.34**	**117.36**+1.2**	**71.72+0.96**
%a		**+74.64 %**	**+6.73$^{n.s}$ %**
%b			**-38.89** %**
(HDL-C)/ (LDL-C)	**0.38+ 0.02**	**0.25+ 0.01**	**0.37+0.01**
%a		**-34.21**%**	**-2.63$^{n.s}$ %**
%b			**+48**%**
VLDL-C (mg/dl)	**17+0.28**	**64.4**+1.96**	**17.74+0.5**
%a		**+278.82%**	**+4.35$^{n.s}$ %**
%b			**-72.45** %**

Data expressed as:

Mean + standard error, % = percentage of change,
*=P≤0.05, **= P≤0.01, n.s. = non significant,
(+) = Increased from control, (-) = Decreased from control.
(a) = compared to control, (b) = compared to diabetic.

Table (4): Proteins level in normal, diabetic and *B. aegyptiaca* treated male albino rats.

	Control	Diabetic	*B. aegyptiaca*
Total protein (g/dl)	**6.34+0.11**	**5.88+0.09**	**5.96+0.19**
%a		**-7.26** %**	**-5.99$^{n.s}$%**
%b			**+1.36$^{n.s}$ %**
Albumin (g/dl)	**3.54+0.13**	**2.84+0.07**	**3.36+0.17**
%a		**-19.77** %**	**-5.08$^{n.s}$%**
%b			**+18.31*%**
Globulin (g/dl)	**2.8+0.19**	**3.3+0.06**	**2.72+0.09**
%a		**+17.86* %**	**-2.86$^{n.s}$ %**
%b			**-17.58**%**
A/G ratio	**1.29+0.06**	**0.86+0.03**	**1.24+ 0.05**
%a		**-33.33** %**	**-3.88$^{n.s}$%**
%b			**+44.19**%**

Data expressed as:

Mean + standard error, % = percentage of change,
*=P≤0.05, **= P≤0.01, n.s. = non significant,
(+) = Increased from control, (-) = Decreased from control,
(a) = compared to control, (b) = compared to diabetic.

Table (5): Parameters of liver function in control, diabetic, and *B. aegyptiaca* treated male albino rats.

	Control	Diabetic	*B. aegyptiaca*
ALAT (U/ml)	**8+0.32**	**10.2+0.37**	**9 +0.55**
%a		**+27.5** %**	**+12.5$^{n.s}$%**
%b			**-11.76$^{n.s}$%**
ASAT (U/ml)	**7.4+0.51**	**11.2+0.37**	**9.4+0.93**
%a		**+ 51.35**%**	**+27.03$^{n.s}$%**
%b			**-16.07$^{n.s}$ %**

Data expressed as:

Mean + standard error, % = percentage of change,
*=P≤0.05, **= P≤0.01, n.s. = non significant,
(+) = Increased from control, (-) = Decreased from control.
(a) = compared to control, (b) = compared to diabetic.

Table (6): Parameters of kidney function in control, diabetic and *B. aegyptiaca* treated male albino rats.

	Control	Diabetic	*B. aegyptiaca*
Creatinine (mg/dl)	**0.62+0.04**	**0.82+0.04**	**0.76+0.07**
%a		**+32.25** %**	**+22.58$^{n.s}$%**
%b			**-7.32$^{n.s}$ %**
Urea (mg/dl)	**18.4+0.5**	**28.4+0.51**	**21.2+2.22**
%a		**+ 54.35** %**	**+15.22$^{n.s}$%**
%b			**-25.35$^{n.s}$ %**

Data expressed as:

Mean + standard error, % = percentage of change,
*=P≤0.05, **= P≤0.01, n.s = non significant,
(+) = Increased from control, (-) = Decreased from control.
(a) = compared to control, (b) = compared to diabetic.

Table (7): Some hematological parameters in control, diabetic, and *B. aegyptiaca* treated male albino rats.

	Control	Diabetic	*B. aegyptiaca*
RBCs count ($X10^6$/µl)	**8.94+0.29**	**8.35 +0.26**	**8.54+0.2**
%a		**-6.59$^{n.s}$ %**	**-4.47$^{n.s}$ %**
%b			**+2.28$^{n.s}$ %**
Hct%	**42.92+1.52**	**40.2 +1.71**	**41.75+2.69**
%a		**-6.34$^{n.s}$ %**	**-2.73$^{n.s}$%**
%b			**-5.54$^{n.s}$%**
WBCs ($X10^3$/µl)	**9+0.35**	**7.78+0.16**	**9.8+1.04**
%a		**-13.56 *%**	**+8.89$^{n.s}$%**
%b			**+25.96$^{n.s}$%**
Lymph ($X10^2$/µl)	**90.02+1.42**	**82.58+1.62**	**93.96+1.87**
%a		**-8.26** %**	**+4.38$^{n.s}$%**
%b			**+13.78**%**

Data expressed as:
Mean + standard error, % = percentage of change,
*=P≤0.05, **= P≤0.01, n.s. = non significant,
(+) = Increased from control, (-) = Decreased from control.
(a) = compared to control, (b) = compared to diabetic.
Lymph= Lymphocyte

Table (8): Some histological changes in control, diabetic, and *B. aegyptiaca* treated male albino rats.

	Control	Diabetic	*B. aegyptiaca*
A-cell count	**3.67+0.33**	**1.67+0.33**	**2+0.0**
%a		**-54.5** %**	**-45.5** %**
%b			**+19.76$^{n.s}$ %**
B-cell count	**91.67+0.88**	**57.33+0.88**	**88.67+3.28**
%a		**-37.46** %**	**-3.27$^{n.s}$%**
%b			**+54.67**%**
D-cell count	**4.67+0.33**	**2.33+0.33**	**3+0.0**
%a		**-50.1** %**	**-35.76** %**
%b			**+28.76$^{n.s}$ %**

Data expressed as:
Mean + standard error, % = percentage of change,
*=P≤0.05, **= P≤0.01, n.s. = non significant,
(+) = Increased from control, (-) = Decreased from control.
(a) = compared to control, (b) = compared to diabetic.

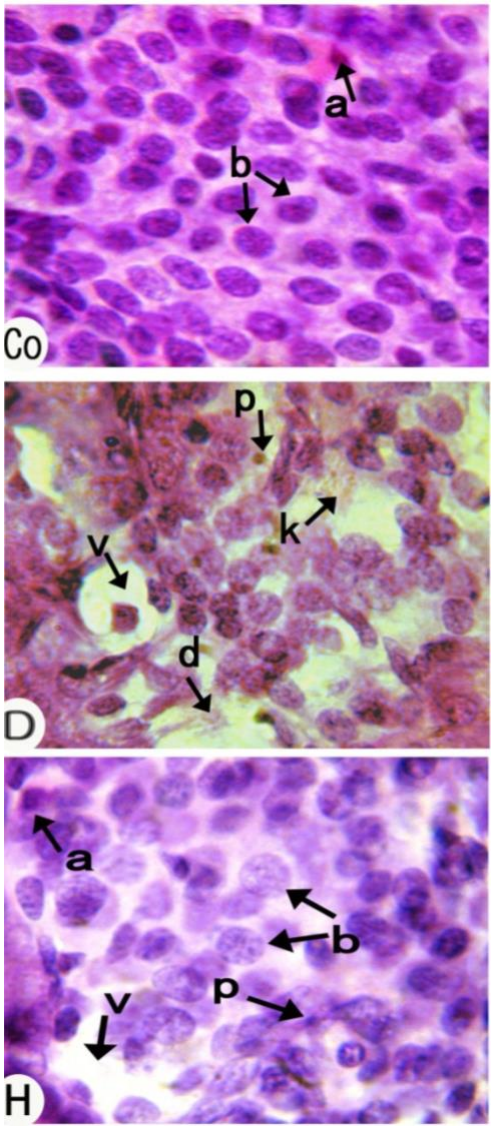

Plate (1): Photomicrograph of pancreatic islets of Control (Co.), Diabetic (D) and *B. aegyptiaca* (H) treated rats stained by heamatoxylin and eosin stain (X 1000).

Where,

a; normal alpha cell
b; normal beta cell
P; pyknotic beta cell
v; vacuolated beta cell
k; beta cell karyorrhexis
d; degenerated beta cell

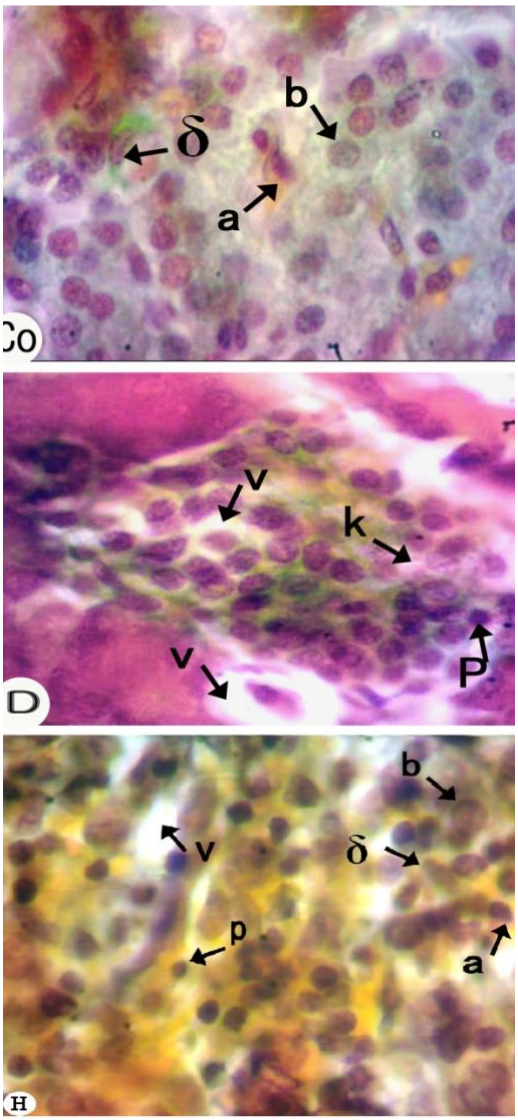

Plate (2): Photomicrograph of pancreatic islets of Control (Co.), Diabetic (D) and *B. aegyptiaca* (H) treated rats stained by Modified aldhyde Fuchsin stain (X 1000).

Where,

a; normal alpha cell
v; vacuolated beta cell
b; normal beta cell
δ; normal delta cell
k; beta cell karyorrhexis
P; pyknotic beta cell