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The effect of herbal tea from *Balanites aegyptiaca* fruits on streptozotocin-induced diabetes mellitus in rats

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Abstract : Diabetes mellitus and its complication are a worldwide health problem. Many plants have been used to improve glucose tolerance and insulin sensitivity in treatment strategies of diabetes mellitus. The present study investigated the potential therapeutic effects of herbal tea from *Balanites aegyptiaca* fruits on certain biochemical markers in streptozotocin-induced diabetes mellitus in rats. Diabetes was induced in rats by single intraperitoneal injection of streptozotocin (STZ) with concentration of 60 mg/kg body weight. Herbal tea solutions of *B. aegyptiaca* fruits with different concentration 0.25, 0.5, and 1.0% were given to diabetic rats in replacement of drinking water. Diabetic control and normal control groups were given drinking water without herbal tea. The effects of *B. aegyptiaca* tea on blood glucose, total cholesterol, triglyceride, total protein, urea, creatinine and the activities of liver marker enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), and antioxidants markers were examined in the plasma of control and treated rats. After four weeks of treatment with *B. aegyptiaca* tea; blood glucose, urea, creatinine, AST, ALT, total cholesterol and triglyceride was significantly reduced in diabetic rats. However, the levels of total protein and selected antioxidant enzymes activity were increased compared to diabetic control. Total antioxidant capacity was restored to near normal levels. The present results shown that herbal tea of *B. aegyptiaca* fruit has an anti-hyperglycemic effect and subsequently may improve hepatics and renal damage associated with STZ- induced diabetes mellitus in rats. Hence, the use of *B. aegyptiaca* fruit tea is applicable to approach health-promoting.
Key words: *Balanites aegyptiaca*; Streptozotocin; Hypoglycemia; Antioxidant enzyme; Diabetes.

Introduction

The prevalence of diabetes is increasing rapidly worldwide; about 422 million people have diabetes[1]. The World Health Organization[1] has predicted that this number will be doubled in the next twenty years. There are two types of diabetes. Type 1 diabetes is an auto-immune disorder which the immune system mistakenly aggression pancreatic beta cell and this causes insulin deficiency subsequently high blood glucose[2]. Type 2 diabetes is resulted from inadequate insulin secretion and/or tissue responses reduction of insulin[3]. Some drugs have side effect[4], therefore, plants have become targets for alternative medicine[5]. *B. aegyptiaca* is a tree known

as 'desert date' distributed in drier parts of Africa and South Asia. It contains a wide variety of compounds such as essential amino acids, saponins, flavonoids, alkaloids and carbohydrates[6,7,8]. *B. aegyptiaca* (heglig; Egyptian name) has been used in the Egyptian folk medicine as anti-diabetic agents. In recent reports, the edible and non-edible parts of *B. aegyptiaca* showed anti-diabetic properties in rats. *B. aegyptiaca* kernel extract (a dose of 50 mg/kg body weight) was found to have anti-hyperglycemic effect comparable to glibenclamide drug[9]. The extraction of *B. aegyptiaca* cortex delays the diabetic nephropathy[10]. The administrated water extract of *B. aegyptiaca* fruits (1.5 g/kg body weight) have anti-diabetic and antioxidant effects as well in diabetic rats [11]. Also, ethyl ether extract of *B. aegyptiaca* fruit reveled hypoglycemic and anti-inflammatory impact in a dose-dependent manner[12]. *B. aegyptiaca* has promising application in terms of supplementation and drug development. Hence, we investigated the effect of *B. aegyptiaca* fruits as herbal tea against streptozotocin-induced diabetes mellitus in rats.

Materials and Methods

Chemicals:

Streptozotocin was purchased from Sigma (St. Louis, MO, U.S.A.).

Plant material:

Fruits of *B. aegyptiaca* (L.) Del were collected from the western desert of Egypt from Wadi El-Gedid city. Fruits were sliced and dried in a hot air oven at 40ºC then ground to a fine powder.

Preparation of herbal tea:

Herbal tea solutions were prepared by adding 0.25, 0.5 or 1.0 g of powdered *B. aegyptiaca* fruit to 100 ml boiling water and intermittent stirring for 10 min then cooled for 15 min. Thereafter, *B. aegyptiaca* fruit tea was filtered using a Millipore filter (Millipore 0.2 mm) to remove particulate matter then poured into clean drinking bottles and were given to three groups of rats. The herbal tea solutions were prepared daily.

Animal and Diet:

Animal Male Sprague Dawley rats (150-160 g) were obtained from the Animal Unit of National Research Centre, Cairo, Egypt. Animal were housed under a controlled environmental conditions (23 ± 1ºC, 55 ± 5% humidity and 12-h light: 12- h dark cycle). Animals were fed a standard chow diet composed of 61% wheat starch, 14% casein, 4% sunflower oil, 10% sucrose, 5% cellulose, 3.5% mineral mixture and 1% vitamin mixture. Food and water/herbal tea were given *ad-libtium.*

Induction of diabetes:

Diabetes was induced by an intraperitoneal injection of streptozotocin at a dose of 60 mg/kg body weight dissolved in a citrate buffer (0.1 M, pH 4.5)[13]. After 3 days rats with fasting blood-glucose levels more than 200 mg/dL were considered as diabetic and selected for the study.

Experimental design:

The animals were randomly divided into five groups of 6 rats each. Group 1 (untreated control): normal rats receiving water and fed *ad libitum* and served as a normal control group. Group2 (untreated control): diabetic rats receiving water and fed *ad libitum* and served as diabetic control rats. Group3 (treated diabetics): diabetic rats receiving *B. aegyptiaca* fruit tea (0.25 g / 100 ml) in replacement of drinking water and fed *ad libitum*. Group4 (treated diabetics): diabetic rats receiving *B. aegyptiaca* fruit tea (0.5 g/ 100 ml) in replacement of drinking water and fed *ad libitum*. Group 5 (treated diabetics): diabetic rats receiving *B. aegyptiaca* fruit tea (1.0 g / 100 ml) in replacement of drinking water and fed *ad libitum.* Their daily consumption of water or herbal tea was measured. After 4 weeks from treatments, rats were fasted and subsequently anaesthetized and blood samples were collected on heparinized tubes. Plasma was separated and used for determination of blood glucose, total cholesterol, triglyceride, liver and kidney functions and antioxidant biomarkers. The RBCs were washed several times with cold saline solution for determination of glutathione peroxidase. Plasma and packed RBCs were stored at -20°C.

Biochemical Assays:

All assays were carried out by a colorimetric method using a commercial kit (Bio-diagnostic kit, Giza, Egypt). Blood glucose, total cholesterol and triglyceride were measured using standard procedures as described by Trinder (1969)[14], Richmond (1973)[15] and Fossati & Prencipe (1982)[16]. The specific activities of catalase (CAT), superoxide dismutase (SOD), cellular glutathione peroxidase (GPx) and total antioxidant capacity (TAC) levels in the plasma were measured using colorimetric method according to the methods of Aebi (1948)[17], Beauchamp & Fridovich (1971)[18], Paglin & Valentine (1967)[19], Koracevic, et al. (2001)[20]. Total protein, alanine amino transferase (ALT), aspartate amino transferase (AST) were carried out by using assay kits[21, 22] (Gornallet al,. 1949; Reitman & Frankel, 1957). Kidney function (creatinine and urea) was evaluated according to the methods of Bartles et al. (1972)[23] and Fawcett & Soctt (1960)[24].

Statistical study

The data presented in the study were statistically evaluated as mean ± SD for each group. Statistical evaluation of the difference between the group mean values was carried out by analysis of variance (ANOVA) analysis. *P* values less than 0.05 were considered significant[25.]

Results

The body weight gain did not differ among all groups. The consumption volume of *B. aegyptiaca* tea solutions did not significantly differ in treated diabetics groups compared to the volume of drinking water consumed by diabetic control and normal control groups.

Plasma glucose levels

The blood glucose level was significantly ($P< 0.01$) higher in diabetic control rats than in normal control rats. *B. aegyptiaca* tea caused a significant decrease in the glucose levels of diabetic rats (Table 1). *B. aegyptiaca* tea with concentration of 1.0 g/100 ml has achieved the main decline in the level of blood sugar compared to other tea solutions (0.25 and 0.5 g/100 ml).

Lipid profile

Total cholesterol and triglyceride were elevated in plasma of diabetic control rats compared to normal control rats (Table 1). *B. aegyptiaca* fruit tea significantly reduced ($P< 0.01$) the total cholesterol and triglyceride in comparison to diabetic control rats. The value of total cholesterol and triglyceride in plasma of rats drinking herbal tea solution (0.5 and 1.0 g /100 ml) restored to normal values (Table 1).

Table 1. Effect of *B. aegyptiaca* fruit tea solutions on glucose, total cholesterol and triglyceride in plasma of diabetic rats

Groups	Glucose	Total cholesterol	Triglyceride
	mg/dl		
Normal control	86±4.44[a]	180±9.50[a]	197±12.33[a]
Diabetic control	550±20.33[b]	249±29.11[b]	297±28.44[b]
Diabetic rats treated with herbal tea solutions :			
Herbal tea (0.25 g/ 100 ml)	438±19.44[c]	196±9.66[a]	234±19.35[ab]
Herbal tea (0.5 g/ 100 ml)	240±12.55[c]	176±10.66[a]	200±16.46[ac]
Herbal tea (1.0g/ 100 ml)	107±3.22[d]	188±11.87[a]	199±15.67[ac]

Values are given as mean ± SD (n= 6 rats). Mean values in the same column with same letters are not-significantly different; different letters are significantly different at 0.05 probability.

Liver and kidney function

Plasma ALT, AST, urea, and creatinine were significant decreased ($P < 0.01$) in diabetic rats treated with *B. aegyptiaca* fruit tea compared to diabetic control rats (Table 2). Total protein concentrations were comparable in diabetic rats treated with different doses of *B. aegyptiaca* fruit tea to a normal level of normal control rats. Plasma total protein was significant increased ($P< 0.01$) in diabetic control rats when compared to normal control rats (Table 2).

Table 2. Effect of *B. aegyptiaca* fruit tea solutions on liver and kidney functions parameters in plasma of diabetic rats

Groups	ALT	AST	Total protein	Urea	Creatinine
	U/l		mg/dl		
Normal control	69±5.0[a]	142±6.90[a]	8.5±0.50[a]	44±5.90[a]	0.39±0.02[a]
Diabetic control	81±5.0[b]	194±11.50[b]	6.9±0.50[b]	80±8.10[b]	2.8±0.16[b]
Diabetic rats treated with herbal tea solutions :					
Herbal tea (0.25 g/ 100 ml)	70±5.3[a]	148±12.40[a]	8.5±0.70[a]	50±5.10[a]	0.54±0.2[a]
Herbal tea (0.5 g/ 100 ml)	72±5.7[a]	149±13.50[a]	8.1±0.40[a]	51±10.60[a]	0.36±0.17[a]
Herbal tea (1.0g/ 100 ml)	75±5.1[a]	150±15.50[a]	8.6±0.80 [a]	40±5.30[a]	0.32±0.02[a]

Values are given as mean ± SD (n= 6 rats). Mean values in the same column with same letters are not-significantly different; different letters are significantly different at 0.05 probability.

Antioxidant effect

STZ induction was associated with a reduction in the antioxidant enzyme activity (GP-x, CAT and SOD) and TAC in diabetic control group (Table 3). *B. aegyptiaca* tea treatments significantly increased the activities of the selected antioxidant enzymes and TAC compared to diabetic control rats. *B. aegyptiaca* tea with concentration of 1.0 g/100 ml had the highest effect on GP-x, CAT and SOD activity and TAC compared to the other doses in diabetic rats.

Table 3. Effect of *B. aegyptiaca* fruit tea solutions on antioxidant biomarkers in plasma of diabetic rats

Groups	GP-x	CAT	SOD	TAC
	U/ml			mmol/L
Normal control	1092±100[a]	25.58±3.90[a]	199±21.0[a]	1.67±0.14[a]
Diabetic control	707±53[b]	22.57±2.60[b]	139±24[b]	0.73±0.19[b]
Diabetic rats treated with herbal tea solutions :				
Herbal tea (0.25 g/ 100 ml)	843±4[c]	25.69±3.70[a]	145±26.11[b]	1.77±0.13[a]
Herbal tea (0.5 g/ 100 ml)	943±54[c]	27.46±3.10[c]	171±25.33[c]	1.92±0.1[c]
Herbal tea (1.0g/ 100 ml)	955±50[c]	34.80±4.0[c]	191±22.11[c]	1.93±0.13[c]

Values are given as mean ± SD (n= 6 rats). Mean values in the same column with same letters are not-significantly different; different letters are significantly different at 0.05 probability.

Discussion

Medicinal plants will remain to offer a source for generating novel drug compounds. There is a continuous need to develop new therapies with better effects and lower side effects to treat diabetes mellitus[26]. Plants are rich sources of anti-diabetic, anti-hyperlipidemic and anti-oxidant agents such as flavonoids, gallotannins, amino acids, and other related polyphenols[27]. *B. aegyptiaca* fruit contents a high amount of bioactive compounds[28,7,29,8]. Demonstration of flavonoids isolated from different plant sources exposed anti-

diabetic activity in animal models[30]. Six different flavonoids were detected in *B. aegyptiaca*[31]. Ojo et al. (2006)[32] reported that leaves, steam bark and root extracts of *B. aegyptiaca* content more than 100 mg/kg of saponins, steroids or alkaloids. The saponin extracted from *B.aegyptiaca* fruits was reported to have a hypoglycemic effect in diabetic rats[33]. Our results revealed that, rats treated for 4 weeks with herbal tea of *B. aegyptiaca* resulted in a significant reduction ($p<0.01$) in the blood glucose levels of diabetic rats, when compared to control group. This result in agreement with many previous studies[34,35,12,11]. Ghanem et al. (2008)[29] reported that carvacrol and cinnamyl alcohol were presented in fruit extract of *B. aegyptiaca* (14.49 % and 9.31% of total volatile compounds). Cinnamyl alcohol is oxidized to cinnamaldehyde. Plaisier et al. (2010)[36] showed that cinnamaldehyde have effects on the glucose transport activity and enhance insulin action. Umasankar et al. (2015)[37] showed that carvacrol possess significant anti-hyperglycemic and anti-hyperlipidemic effects in HFD/STZ-induced type 2 diabetic rats. The hypoglycemic effect of *B. aegyptiaca* might be related to the presence of bioactive components such as flavonoids, saponin, carvacrol and/or cinnamyl alcohol. These latter compounds may be enhanced pancreatic secretion of insulin from beta cell and enhanced the glucose homeostasis.

The treatment of diabetic rats with *B. aegyptiaca* fruit in this study exerted a hypoglycemic effect as we elucidated and that was concomitant with improvement on the antioxidant status. Recent studies demonstrated[10, 12,11,9] that *B. aegyptiaca* elevating the antioxidant enzymes activity and decreased lipid oxidation in diabetic rats. STZ is partial damages pancreatic beta cells by generated reactive oxygen species and reduces the tissue antioxidant enzyme activity[38,39]. The radical scavenging activity of *B. aegyptiaca* that was detected in this investigation may be attributed to its content from antioxidant agents. It is well known that essential oils, which are rich in carvacrol, exerts antioxidant properties equivalent to those of ascorbic acid, butyl hydroxyltoluene and vitamin E[40, 41]. Ghanem et al. (2008)[29] stated that the fruit extract of *B. aegyptiaca* content polyphenol with concentration of 2.34 % in dry matter. Phenolic compounds are well known to exhibit antioxidant activity through a variety of mechanisms, including free radical-scavenging, lipid peroxidation and chelating of metal ions[42, 43].

Morsya et al., (2010)[35] demonstrated that the dose of 5.4g per week from *B. aegyptiaca* can decrease the level of total cholesterol and triglyceride in diabetic rats. Our results revealed that *B. aegyptiaca* significantly reduced ($p<0.01$) the blood total cholesterol and triglyceride levels of diabetic rats, when compared to control group. The reduction in the cholesterol biosynthesis enzyme activity and lipolysis inhibition under the regulator of insulin may cause the reduction in total cholesterol and triglyceride[44,45]. An elevation in serum creatinine and urea levels indicates an impaired renal function of diabetic animals[46,47,10].The results of the present study demonstrated that the treatment of diabetic rats with *B aegyptiaca* caused a noticeable significant elevation in plasma total protein and a reduction in the plasma creatinine and urea as compared with diabetic control rats. Thus, it would appear that the *B. aegyptiaca* supplement enhanced the renal function that is generally impaired in diabetic rats. The ALT and AST levels have been shown to be improved in Alloxan-induced diabetic rats[48,49]. In this investigation *B aegyptiaca* significantly ($p<0.05$) reduced levels of ALT and AST in diabetic rats thus enhancing the liver functions. Our results are in agreement with Nadro & Samson (2014)[50] which demonstrated that the *B aegyptiaca* kernel cake supplement has achieved the largest decline in the plasma biomarkers parameters level compared with normal levels.

In conclusion, *B. aegyptiaca* fruits as herbal tea showed hypoglycemic, anti-hyperlipidemic, and anti-oxidant effect. Moreover, ameliorated liver and kidney function associated with diabetes mellitus. All the different concentration of *B. aegyptiaca* fruits tea improved biomarker parameters compared to diabetic control and some biochemical parameter return to normal value. The most efficient concentration *B. aegyptiaca* fruits tea was 1.0 g/100 ml. This make *B. aegyptiaca* fruits applicable health product for treatment diabetes mellitus. In future study we will investigate the anti-diabetic effect of *B. aegyptiaca* fruits on human.

Conflict of Interest: Authors declare that they have no conflict of interest.

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