International Journal of Pharmacology

ISSN 1811-7775

science alert

ansinet
Asian Network for Scientific Information

OPEN ACCESS International Journal of Pharmacology

ISSN 1811-7775
DOI: 10.3923/ijp.2017.438.447

Research Article
Evaluation of Anti-diabetic Activity of *Acacia tortilis* (Forssk.) Hayne Leaf Extract in Streptozotocin-induced Diabetic Rats

[1]Mohammed Hasan Mukhtar, [2]Waleed Hassan Almalki, [3]Aisha Azmat, [2]Mohammad Raafat Abdalla and [2]Muhammad Ahmed

[1]Department of Biochemistry, Faculty of Medicine, Umm-Al Qura University, Makkah, Saudi Arabia
[2]Department of Pharmacology, Faculty of Pharmacy, Umm-Al Qura University, Makkah, Saudi Arabia
[3]Department of Physiology, Faculty of Medicine, Umm-Al Qura University, Makkah, Saudi Arabia

Abstract

Background and Objective: In folkloric medicine from Asia, *Acacia tortilis* (Forssk.) Hayne is used for the treatment of Diabetes Mellitus (DM). This study aimed to investigate the antidiabetic effect of ethanolic extracts of *Acacia tortilis* leaves (ELAT) and its protective effect in preventing the secondary complications of diabetes mellitus. **Materials and Methods:** Different doses of ELAT (50, 100 and 150 mg kg^{-1}) were administered orally and their effects were studied in normal, glucose-loaded and STZ-induced diabetic rats. Data obtained from results was compared using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison tests. **Results:** In all experiments, ELAT caused a significant reduction ($p<0.05$) in blood glucose levels. The effect was pronounced at the doses of 50, 100 and 150 mg kg^{-1} and also showed improved activity as compared to glibenclamide used as a reference drug. The ELAT was found to be safe at the dose of 2000 mg kg^{-1}, as no mortality was observed. For hepatic function test, marker enzymes were not changed markedly in ELAT-treated rats. The lipid profile showed a significant reduction ($p<0.05$) in the levels of serum cholesterol, LDL and triglyceride. **Conclusion:** It is concluded that the leaf ethanolic extract of *Acacia tortilis* has antidiabetic activity. It also decreased the lipid profile in rats. This justifies the traditional use of plant. It serve as a natural source for antidiabetic drugs in whom hyperglycemia and hypercholesterolemia quite often coexist.

Key words: Anti-diabetic activity, streptozotocin, *Acacia tortilis*, acute toxicity

Received: March 02, 2017 Accepted: April 28, 2017 Published: June 15, 2017

Citation: Mohammed Hasan Mukhtar, Waleed Hassan Almalki, Aisha Azmat, Mohammad Raafat Abdalla and Muhammad Ahmed, 2017. Evaluation of anti-diabetic activity of *Acacia tortilis* (Forssk.) Hayne leaf extract in streptozotocin-induced diabetic rats. Int. J. Pharmacol., 13: 438-447.

Corresponding Author: Muhammad Ahmed, Department of Pharmacology, Faculty of Pharmacy, Umm-Al Qura University, P.O. Box 13578, Taif Road, Alabidyyah, Makkah Al Mukarrama, Kingdom of Saudi Arabia Tel: 00966556618257

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Diabetes Mellitus (DM) is a large health problem across the world and the prevalence of DM is expeditiously rising[1], for many reasons such as aging, physical inactivity and obesity. In, 2010, an estimated 285 million people had diabetes and by 2030, there is projected to be a 69% increase in the number of adults with diabetes[2]. The ratio of DM in adults in the Kingdom of Saudi Arabia is 23.7%. The KSA ranks second, in the Middle East and seventh in the world, for diabetes prevalence[3]. In the KSA, diabetes burdens not only the individual, but has also evoked a financial crisis for the Saudi healthcare system[4]. Diabetes mellitus doubles the risk of cardiovascular disease, retinopathy, nephropathy and neuropathy[5]. Management of DM concentrates on healthy diet, exercise, weight loss and use of appropriate medications. Synthetic drugs are available for the treatment of DM but diabetes has also been treated with herbs for a long time. Many of these plant-based medicines have already been investigated for their side effects and efficacy. Now, all over the world herbal preparation and extracts are scrutinized with renewed interest due to their relatively non-toxic effects[6]. Since 1980, World Health Organization (WHO), expert committees have also favored more studies on botanical treatment of diabetes[7].

Acacia tortilis (Forssk.) Hayne or umbrella thorn acacia is considered one of the most important tree and shrub groups in the Mimosoideae sub-family and is commonly available in Saudi Arabia[8]. As a good source of tannin, its bark is used as a disinfectant and as an anthelmintic, to treat asthma and diarrhea[8]. *Acacia tortilis* has anticonvulsant and neuroprotective effects[9] and possesses hypoglycemic activity[10]. Different species of *Acacia* possess hypoglycemic and antidiabetic activities like *Acacia nilotica*[11], *Acacia catechu*, *Acacia suma* and *Acacia senegal*[12], *Acacia arabica*, *Acacia mollissima* and *Acacia polyacantha*[13-15]. Further, in folkloric medicine, *Acacia tortilis* is useful for the treatment of various diseases like skin allergy, diabetes, hypertension and as diuretic[16]. The seed extract of *Acacia tortilis* has also been found to have anti-hyperglycemic activity[17]. Bhateja[18] reported that gum exudates from the stem and branches of *Acacia tortilis* exhibit anti-diabetic activity on streptozotocin-nicotinamide induced diabetic rats. Until now, there have been no extensive studies on the possible antidiabetic properties of *Acacia tortilis* leaves.

Hence the objective of this study was to assess the antidiabetic activity of ethanolic extracts of *Acacia tortilis* leaves (ELAT) in streptozotocin-induced (STZ) diabetic rats.

MATERIALS AND METHODS

Chemicals and drugs: Streptozotocin (STZ: S0130-500MG) was purchased from SIGMA-Aldrich and glibenclamide was acquired locally. Streptozotocin (STZ) solvent was prepared in cold citrate buffer (pH 4.5). Glibenclamide (Glib) and ELAT was prepared in distilled water for oral use.

Dose (mg kg^{-1})	Concentration (mg mL^{-1})	Volume (mL)
ELAT (50)	50	0.2-0.25
ELAT (100)	100	0.2-0.25
ELAT (150)	150	0.2-0.25
Glib (10)	10	0.2-0.25

Plant material and extraction: *Acacia tortilis* was collected from wastelands of Umm-Al Qura University, Makkah, KSA, during the month of October, 2014 and authenticated by an expert taxonomist Dr. Ibrahim Abd-Elhady, Associate Professor, Department of Pharmacognosy, Faculty of Pharmacy, Umm-Al Qura University. A voucher specimen number PHG128 was deposited. Leaves were separated from shoots and wood. Leaves were drenched by using tap water to wipe off the apparent pollutants. For extraction, 200 g of the leaves were immersed in ethanol (95%) for 24 h in a percolator. After 1 day, a dark green extract was collected in petri dishes[19]. Later this dark green extract was concentrated in a vacuum using a rotary flash evaporator. After concentration, the net yield of concentrated extract was only 32.6 g (16.3%).

Experimental animals: Mature and healthy male and female albino Sprague-Dawley rats (200-250 g) were used in this present study. The animals were obtained from the animal house of King Abdulaziz University Medical Research Centre, Jeddah, Kingdom of Saudi Arabia. Six rats were accommodated in polypropylene cages with husk. The rats were fed on a standard pellet diet *ad libitum* and had access to water. The experimental protocol was granted from the Institutional and Departmental Animal Ethics Committee Faculty of Pharmacy Umm-Al Qura University (Ethical approval number UQU-COP-EA#14341).

Acute oral toxicity study: Acute oral toxicity of ELAT was performed by using healthy rats, according to Organization for Economic Cooperation and Development (OECD) Guideline 423[20]. Rats were divided into two groups with three rats in each group.

Group I:	Control	5 mL distilled water orally (p.o.)
Group II:	Treated	Single dose of ELAT (2 g kg^{-1} mL^{-1}) p.o.

After administration of the single dose, the animals were continuously monitored for any toxic effects (behavioral and neurological) for the first 2 h, then after 24 h and then daily for fourteen days[21]. Food expenditure was screened on alternate days and weekly body weights were documented. After the 14th day, the rats were executed and vital organs examined for any sign of toxicity.

Toxicity study: For toxicity studies, 12 (six male, six female) Sprague-Dawley rats (225-250 g) were divided into two groups with six rats in each group (three male and three female).

Group I:	Control	Distilled water orally, once daily, for 14 consecutive days
Group II:		ELAT (100 mg kg^{-1} mL^{-1}) orally, once daily, for 14 consecutive days

Biochemical analysis: At the 14th day, after 2 h of dosing, rats (control and treated) were anaesthetized with pentothal sodium 40 mg kg^{-1} i.p. and 4-8 mL of blood samples were collected directly from cardiac puncture for all rats[22]. Blood samples were centrifuged at 2500 rpm for 20 min. Serum was collected and used for biochemical analysis.

Biochemical analysis was done by using commercial assay kit methods[10]. Kits for the analysis of the serum levels of liver function test included bilirubin, gamma-glutamyl transferase (γGT), alkaline phosphate (ALP), liver transaminases aspartate transaminase (AST) and alanine aminotransferase (ALT). The tests for kidney function were serum total protein (TP), urea, uric acid and creatinine (CR). Lipid profile tests, Total Cholesterol (TC), low density lipoprotein cholesterol (LDL), triglycerides (TG) and high-density lipoprotein cholesterol (HDL) were purchased from Human Diagnostica (Germany). HumaLyzer 3000 was used to measure the absorbance of light.

Autopsy: After blood collection, the rats were dissected for autopsy and the organs were thoroughly examined.

Estimation of hypoglycemic activity of ELAT in normoglycemic rats: Hypoglycemic activity of ELAT was carried out on normoglycemic rats[23]. After 16 h of fasting, the time was assumed as 0 h. Blood glucose was measured by using a glucometer (Bayer Contour Blood Glucose Meter, Germany), using drop of blood drawn from the tail. Twenty four rats were randomly separated in to four groups with six rats in each. All rats were treated orally.

Group I:	Control	Distilled water (10 mL kg^{-1})
Groups II:	Treated	ELAT (50 mg kg^{-1})
Group III:	Treated	ELAT (100 mg kg^{-1})
Group IV:	Treated	ELAT (150 mg kg^{-1})

Antidiabetic activity: Hypoglycemic and antidiabetic activity of ELAT was checked in the rats with glucose-administered hyperglycemia and rats with streptozotocin-induced diabetes. In all studies, fasted rats (overnight, 16 h), with free access to water only were used for experiments.

Blood glucose levels were continuously monitored for 1-4 h after the ELAT administration.

Evaluation of ELAT in oral glucose tolerance test (OGTT): Oral glucose tolerance test (OGTT) was performed in rats[24]. For OGTT, 24 rats were subdivided into 4 groups (6 animals each).

Group I:	Control vehicle (distilled water: 10 mL kg^{-1}) orally
Groups II, III and IV:	ELAT 50, 100 and 150 mg kg^{-1}, respectively

After 60 min of ELAT dosing, 2 g kg^{-1} glucose solution was given by intra-gastric intubation to all rats. Blood samples were drawn from the tail for the evaluation of blood glucose levels at different time intervals, upto 2 h after the glucose administration[25].

Anti-diabetic activity of ELAT in STZ-induced diabetic rats: For the induction of experimental diabetes freshly prepared a single dose of streptozotocin (STZ) in cold citrate buffer (pH 4.5), was injected intraperitoneally to rats. For control rats inject citrate buffer only. After 5 days of STZ treatment, rats with fasting blood glucose level (FBS) 250 mg dL^{-1} or more were marked and used for further study[26].

Control and diabetic animal (FBS>250 mg dL^{-1}) were divided into 6 groups of six rats each and treated as follows:

Group I:	Normal control	FBS<250 mg dL^{-1}	Distilled water
Group II:	Diabetic control	FBS>250 mg dL^{-1}	Distilled water
Group III:	Diabetic	FBS>250 mg dL^{-1}	ELAT (50 mg kg^{-1})
Group IV:	Diabetic	FBS>250 mg dL^{-1}	ELAT (100 mg kg^{-1})
Group V:	Diabetic	FBS>250 mg dL^{-1}	ELAT (150 mg kg^{-1})
Group VI:	Positive control	FBS>250 mg dL^{-1}	Glibenclamide (10 mg kg^{-1})

Fresh solutions of extracts and drugs were prepared before dosing. The ELAT and glibenclamide were administered orally for 21 consecutive days, on a daily basis. Body weights and blood glucose levels were monitored on weekly basis.

Statistical analysis: Data were presented as Mean±SEM. One-way analysis of variance (ANOVA) followed by Tukey's

multiple comparison tests were performed by using Minitab 17 for statistical analysis[9]. The significance level was set at under p = 0.05.

RESULTS

Acute oral toxicity study: The limited dose of 2 g kg^{-1} did not cause any demise in rats. A single oral dose of ELAT (2000 mg kg^{-1}) in rats did not result in any change in their gross behavioral patterns. Non-significant variations were monitored in food intake (Fig. 1) and body weight (Fig. 2) in contrast to the control group. In the treated rats, no pathological alterations were noticed at the dose of 2000 mg kg^{-1}.

Autopsy: Autopsy results confessed that any abnormal lumps and lesions were not witnessed after examining the whole body. The texture of all body organs was normal. All vital organs such as liver (Fig. 3a, b), heart (Fig. 3c, d) and kidneys (Fig. 3e, f) were intact and did not show any sign of toxicity. The ELAT did not cause any internal body hemorrhage or accumulation of fluid in the abdominal cavity.

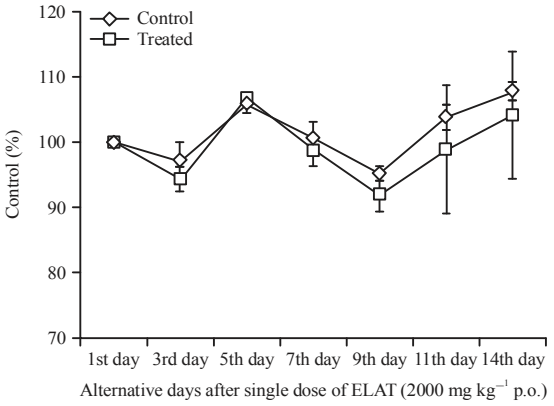

Fig. 1: Food consumption in control and ELAT (2000 mg kg^{-1}) treated rats

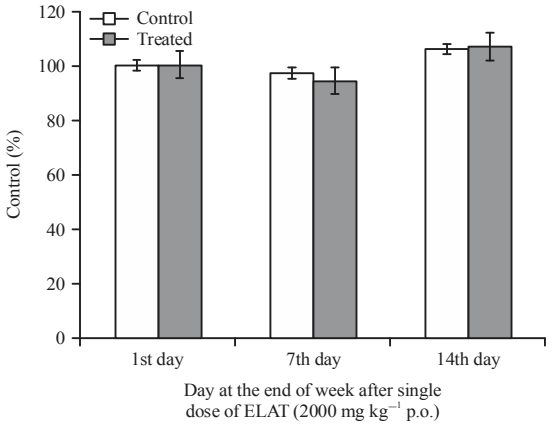

Fig. 2: Body weight in control and ELAT (2000 mg kg^{-1}) treated rats

Effect of ELAT on different biochemical parameters: The effects of ELAT (100 mg kg^{-1}) were observed on different biochemical parameters of rats. Oral administration of 100 mg kg^{-1} dose of ELAT (100 mg kg^{-1}) for 14 consecutive days was not found to alter liver and kidney functions significantly ($p>0.05$). For the liver function tests, value of serum bilirubin, gamma-glutamyl transferase (γGT), alkaline phosphate (ALP) and liver transaminases (AST and ALT) were comparable to the control group are shown in Table 1.

For kidney function tests, non-significant ($p>0.05$) variation in the serum total protein, urea, uric acid and creatinine was noticed in rats treated with ELAT (100 mg kg^{-1}).

The results of the lipid profile at the dose of 100 mg kg^{-1} ELAT are presented in Table 1. The results indicated that there was significant diminution ($p<0.0001$) in the cholesterol, low-density lipoprotein (LDL; $p<0.018$) and TG levels ($p<0.0001$) compared to the control. However, ELAT (100 mg kg^{-1}) administration to rats caused significant ($p<0.0001$) increment in serum HDL level (Table 1).

Rats in the ELAT (100 mg kg^{-1}) group witnessed significant ($p<0.014$) decreases in blood glucose levels (Table 1).

Effect of ELAT on normoglycemic rats: Results regarding the effect of different marked doses of ELAT on blood glucose level are presented in Fig. 4.

Normoglycemic rats at all doses of ELAT showed significant ($p<0.05$) hypoglycemic effects after 1 h. The ELAT at doses of 50, 100 and 150 mg kg^{-1} induced a significant reduction ($p<0.05$) in blood glucose levels, with a maximum at 150 mg kg^{-1} at 1 h. This decrease showed dose dependence (Fig. 4). At 2 h maximum reduction was observed at 50 mg kg^{-1}. However, a significant reduction ($p<0.05$) was observed with all doses. Blood glucose levels were recovered gradually by 3 h in all ELAT treated groups as compare to control (Fig. 4).

Effect of ELAT on OGTT: All groups were subjected to OGTT. Administration of D-glucose to control and pre-ELAT treated rats elicited significant hyperglycemia after 1 h ($p<0.05$) as shown in Fig. 5. The extreme peak of hyperglycemia was observed 1 h after the oral administration of glucose (5 g kg^{-1}) and this peak gradually declined to the

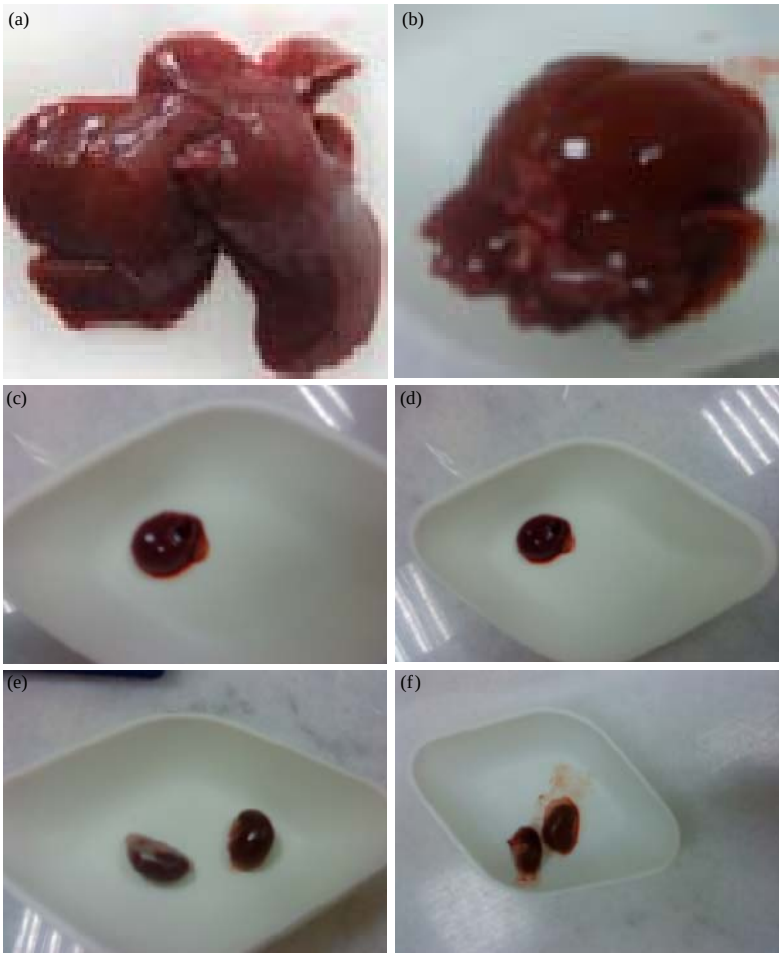

Fig. 3(a-f): Results of autopsy, (a) Control rat liver, (b) ELAT (100 mg kg^{-1}) treated liver, (c) Control rat heart, (d) ELAT (100 mg kg^{-1}) treated heart, (e) Control rat kidneys and (f) ELAT (100 mg kg^{-1}) treated kidneys

Table 1: Effect of ELAT (100 mg kg^{-1}) on different biochemical parameters

Parameters	Control	ELAT treated	p-value
Bilirubin	1.63±0.1	1.54±0.19	p>0.5
Gamma glutamyl transferase γGT	6.24±0.95	5.27±0.76	p>0.5
Alanine aminotransferase (ALT:SGPT)	15.55±5.98	12.55±1.99	p>0.5
Aspartate aminotransferase (AST:SGOT)	77.52±4.75	66.02±6.76	p>0.5
Alkaline phosphatase (ALP)	76.4±16.63	63.26±7.01	p>0.5
Total Protein (TP)	66.94±2.11	68.20±0.13	p>0.5
Urea	30.97±7.32	39.28±5.46	p>0.5
Uric acid	5.66±2.152	6.19±1.24	p>0.5
Creatinine	1.08±0.32	0. 758±0.97	p>0.5
Cholesterol	167.91±2.76	99.167±3.19	P<0.0001
High Density Lipoproteins (HDL)	44.67±1.68	69.76±2.17	p<0.0001
Low Density Lipoproteins (LDL)	104.85±1.68	78.76±2.17	p<0.018
Triglycerides (TG)	256.82±9.32	155.73±2.03	p<0.0001
Glucose	114.27±1.16	91.5±2.23	p<0.014

All values are presented as Mean±SEM (n = 12)

pre-glucose load level (Fig. 5). The ELAT extract at all three doses (50, 100 and 150 mg kg^{-1}) exhibited an inhibition of hyperglycemia induced by glucose at 2 h and blood glucose levels returned to normal. The ELAT (100 mg kg^{-1}) caused a

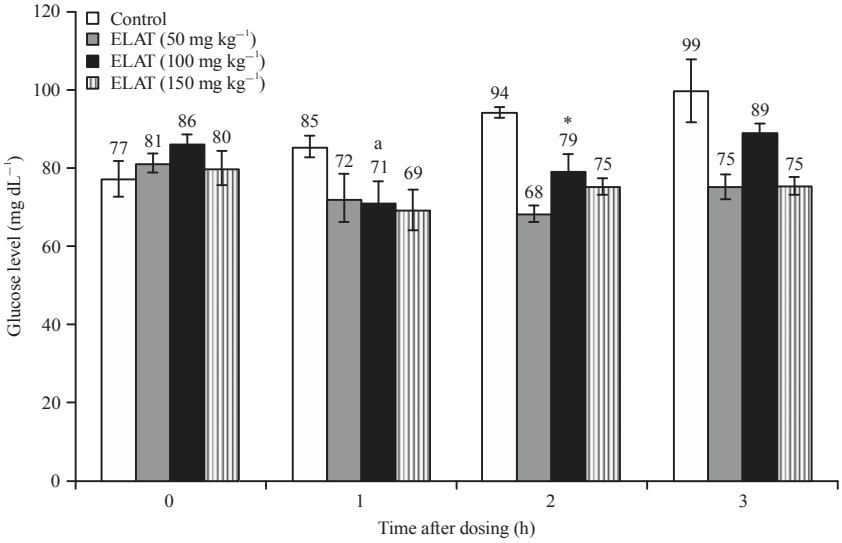

Fig. 4: Hypoglycemic activity of ELAT in normoglycemic rats

[a,]*Indicate a significant difference (p<0.05) between control and ELAT treated rats at 1 and 2 h

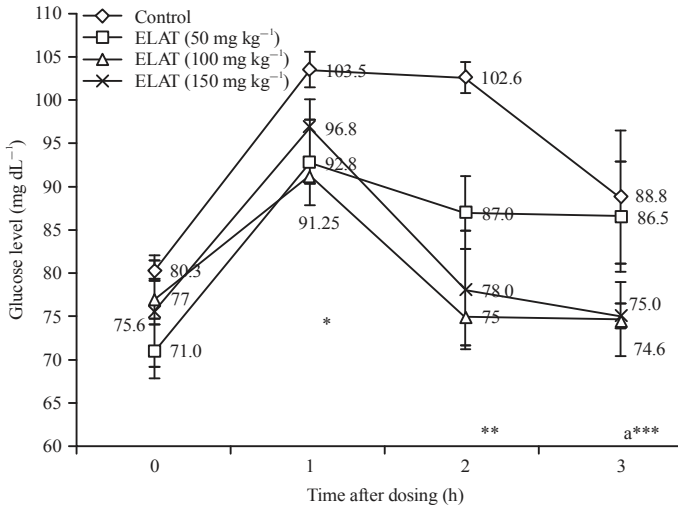

Fig. 5: Effect of different doses of ELAT on OGTT in rats

*, **, ***Indicate a significant difference (p<0.05) between control and ELAT treated rats at 1, 2 and 3 h respectively, [a]Indicates a significant difference (p<0.05) between ELAT (50 mg kg^{-1}) and ELAT (100 and 150 mg kg^{-1})

significant (p<0.05) decrease in the blood glucose at 3 h in glucose-loaded animals, when compared to the control group. All doses of ELAT 50, 100 and 150 mg kg^{-1} exhibited a significant reduction (p<0.05) in hyperglycemia induced by an oral glucose load. The ELAT (100 and 150 mg kg^{-1}) indicated the maximum and significant (p<0.05) effect in OGTT at 3 h when compared to low dose ELAT (50 mg kg^{-1}) as shown in Fig. 5.

Anti-hyperglycemic activity of ELAT in STZ-induced diabetic rats: The results regarding the daily administration of the ELAT at a different dose for 21 days in STZ-diabetics are presented in Fig. 6. For 21 days, nonsignificant (p>0.05) variations in blood glucose level was observed in control rats. However, after STZ injection in reference control rats, the level of glucose significantly (p<0.05) increased on the 7th day and remained high in all diabetic rats during the study as compared to the control rats as shown in Fig. 6. All doses of ELAT in treated rats provoked a significant (p<0.01) decrease in the fasting blood glucose level when compared with the reference control (p<0.01) rats and day zero value (p<0.05). The maximum antidiabetic effect was noticed after the treatment with ELAT at the dose of 100 mg kg^{-1}. The time-dependent significant fall in blood glucose level was

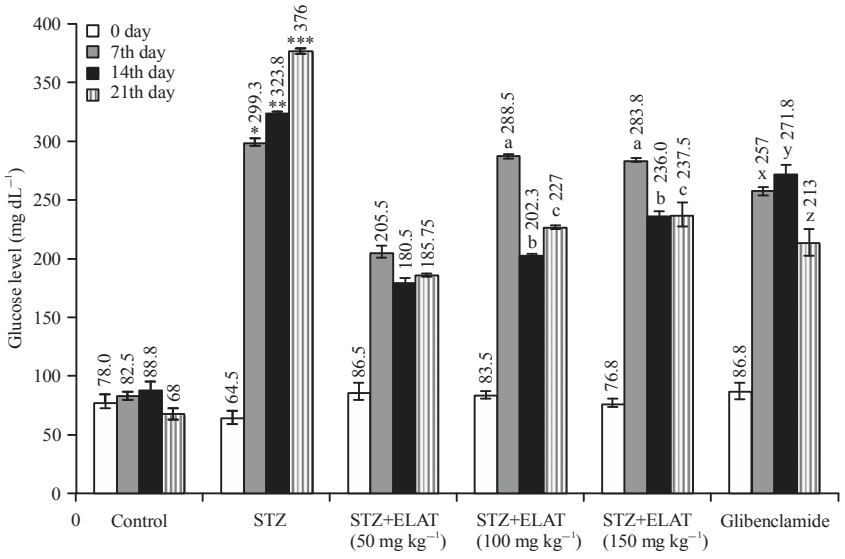

Fig. 6: Comparative effect of ELAT on blood glucose level in STZ induced diabetes in rats

*,**,***Indicate a significant difference ($p<0.05$) between control and STZ induced diabetic rats at 7th day, 14 day and 21st day, respectively, [a-c] Indicate a significant difference ($p<0.05$) between STZ diabetic control and STZ+ELAT treated rats at 7th day, 14 day and 21st day, respectively, [x-z] Indicate a significant difference ($p<0.05$) between STZ diabetic control and glibenclamide treated rats at 7th day, 14 day and 21st day, respectively

observed at all doses of ELAT. Analogously, continual administration of glibenclamide (10 mg kg^{-1} day^{-1}) for 21 days caused a significant fall ($p<0.01$) in the blood glucose level in STZ-diabetic rats. The ELAT (50 mg kg^{-1}) indicated a more pronounced antidiabetic effect than glibenclamide (Fig. 6).

DISCUSSION

Diabetes Mellitus (DM) is globally the largest growing disorder with increased risk of mortality so it demands extensive research for more suitable therapy[27]. Traditionally, conventional herbal therapy has been used globally for diabetic disorders without scientific study. At present, the study of such available herbal medicines is necessary because it might provide a natural key for diabetologists in the future. Different species of *Acacia* are used traditionally as a regimen of DM[28]. In light of previous rationale, the ethanolic leaf extract of *Acacia tortilis* was assessed. The results of this study validate the traditional use of the plant.

For the present study, the hypoglycemic activity of ELAT in normal, glucose-loaded hyperglycemic and STZ-induced diabetic rats were tested. To show antidiabetic activity, DM was induced in rats by injecting STZ. This releases the nitric oxide and provokes cytotoxicity of selective pancreatic islet β-cell, leading to diabetic complications[29]. In the present study, synthetic antidiabetic drug sulfonylurea (glibenclamide) was used as a standard drug in STZ-induced diabetes to analyze the effectivity of anti-hyperglycemic ELAT[30].

In normoglycemic rats, ELAT manifested significant hypoglycemic activity at 1 h. The hypoglycemic effect was more pronounced at 50 and 100 mg kg^{-1} as compared to 150 mg kg^{-1}. Al Dawish *et al.*[3] finding was in agreement with the present results confirming the hypoglycemic effect of ELAT (Fig. 4).

From OGTT, results showed that ELAT 50 mg kg^{-1} exhibited the maximum outcome regarding glucose tolerance. The OGTT is used to assess insulin release and insulin sensitivity[31]. In OGTT test, ELAT showed significant diminution ($p<0.05$) in blood glucose level in normoglycemic rats. It also significantly ($p<0.05$) reduces the initial ascending phase in plasma glucose levels and the zone under the plasma glucose curve as observed by Zheng *et al.*[32]. On the basis of the present results, it is proposed that ELAT might involve insulin-like activity, probably acting via increased secretion of insulin or increased sensitivity to insulin.

Streptozotocin (STZ) significantly ($p<0.05$) increases the blood glucose level or hyperglycemia. The mechanisms were discussed earlier by Goud *et al.*[29]. Orally, ELAT treatment for 21 days influenced the blood glucose level and caused a significant reduction ($p<0.05$) in blood glucose levels. The suggested mechanism by which ELAT facilitates an antidiabetic effect is an acceleration of the pancreatic

secretion of insulin from surviving β-cells of islets. This was evidenced by the significant decrease ($p<0.05$) in the level of glucose (OGTT) in ELAT-treated rats[33]. The antidiabetic activity of ELAT was compared with positive control (glibenclamide). Moreover, the present results indicated that the potent antidiabetic action in rats could be due to the multiple actions of active principles of *Acacia*. *Acacia tortilis* was also reported to possess flavonoids, which reduce hyperglycemia and increase the process of glycosylation in animals and so might show similar activity in the present study[34,35].

The results obtained from toxicological evaluation demonstrated that ELAT caused non-significant variations in food and water consumption but did not produce any significant changes in gross behavior, autopsy and biochemical and parameters of rats. The administration of ELAT (2000 mg kg^{-1}) was safe as no mortality was observed. The acute oral LD_{50} in rats treated with ELAT has been demonstrated to be greater than 2000 mg kg^{-1} of body weight[36]. Non-significant effects on liver and the kidney profile of ELAT-treated rats also confirm the margin of safety.

The lipid profile showed significant changes in ELAT-treated rats. It was observed that ELAT significantly lowered ($p<0.05$) the level of cholesterol, TG and LDL and significantly increased ($p<0.05$) the HDL as shown in Table 1. The mechanism(s) of hypolipidemic effect of the ELAT may be similar to some of those proposed by Alharbi and Azmat[10]. It is suggested that *Acacia* is rich in essential fatty acids and is said to be very beneficial for good coronary health. The β-sitosterol (β-sitosterol) and phytosterol which compete with dietary cholesterol for absorption are thought to help reduce blood cholesterol levels.

CONCLUSION AND FUTURE RECOMMENDATION

It is concluded that there is no difference between the action of plant extract ELAT in comparison to the antidiabetic drug glibenclamide. The current study implies that ELAT produced hypoglycemic and antihyperglycemic effects. It can also decrease the complications of lipid profile seen in some diabetics in whom hyperglycemia and hypercholesterolemia quite often coexist.

It is proposed that ELAT might involve insulin-like activity probably acting via increased secretion of insulin or increased sensitivity to insulin. Flavonoids content in ELAT reduced the hyperglycemia and also increased the process of glycosylation in animals and might explain the hypoglycemic and antidiabetic activity.

Future research should address some of the limitations of this study (e.g. lack of HbA1c information, pathological and biochemical results for diabetic and diabetic+ELAT treated groups).

SIGNIFICANCE STATEMENTS

- In present study, oral administration of different doses of ELAT produced hypoglycemic and antidiabetic activity significantly ($p<0.05$) comparable to glibenclamide
- The administration of ELAT (2000 mg kg^{-1}) was safe as it did not cause any side effect or death in animals
- ELAT not only produced an antidiabetic activity against STZ-induced DM in experimental rats, but also appeared to be effective in managing the major crises coupled with diabetes mellitus, such as hyperlipidemia

ACKNOWLEDGMENT

The authors would like to thank the Institute of Scientific Research and Revival of Islamic Heritage for providing financial support through grant No. 43310006 Umm-Al Qura University, Makkah, KSA to allow this research to be conducted.

REFERENCES

1. Maruthur, N.M., M.O. Gribble, W.L. Bennett, S. Bolen and L.M. Wilson *et al*., 2014. The pharmacogenetics of type 2 diabetes: A systematic review. Diabetes Care, 37: 876-886.
2. Shaw, J.E., R.A. Sicree and P.Z. Zimmet, 2010. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res. Clin. Pract., 87: 4-14.
3. Al Dawish, M.A., A.A. Robert, R. Braham, A.A. Al Hayek, A. Al Saeed, R.A. Ahmed and F.S. Al Sabaan, 2016. Diabetes mellitus in Saudi Arabia: A review of the recent literature. Curr. Diabetes Rev., 12: 359-368.
4. Alhowaish, A.K., 2013. Economic costs of diabetes in Saudi Arabia. J. Family Commun. Med., 20: 1-7.
5. The Emerging Risk Factors Collaboration, 2010. Diabetes mellitus, fasting blood glucose concentration and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies. Lancet, 375: 2215-2222.
6. Vishwakarma, S.L., R.D. Sonawane, M. Rajani and R.K. Goyal, 2010. Evaluation of effect of aqueous extract of *Enicostemma littorale* Blume in streptozotocin-induced type 1 diabetic rats. Indian J. Exp. Biol., 48: 26-30.

7. Palsamy, P. and R. Malathi, 2007. Evaluation of hypoglycemic and hypolipidemic activity of methanolic extract of *Cocculus hirsutus* (L.) diels leaves in streptozotocin-induced diabetes mellitus rats. Int. J. Biol. Chem., 1: 205-212.
8. Waly, N.M. -and H.M. Emad, 2012. Taxonomical Studies of Some Acacia spp. Growing in Saudi Arabia. Bull. Environ. Pharmacol. Life Sci., 1: 55-62.
9. Alharbi, W.D.M. and A. Azmat, 2015. Anticonvulsant and neuroprotective effects of the *Acacia tortilis* growing in KSA. Pak. J. Pharm. Sci., 28: 531-540.
10. Alharbi, W.D.M. and A. Azmat, 2011. Hypoglycemic and hypocholesterolemic effects of *Acacia tortilis* (Fabaceae) growing in Makkah. Pak. J. Pharmacol., 28: 1-8.
11. Auwal, M.S., S. Saka, A. Shuaibu, A.I. Mairiga and A.K. Sanda *et al*., 2013. Phytochemical properties and hypoglycemic activity of the aqueous and fractionated portions of *Acacia nilotica* (Fabaceae) pod extracts on blood glucose level in Normoglycemic wistar albino rats. J. Med. Sci., 13: 111-117.
12. Jarald, E., S.B. Joshi and D.C. Jain, 2009. Biochemical study on the hypoglycemic effects of extract and fraction of *Acacia catechu* wild in alloxan-induced diabetic rats. Int. J. Diabetes Metab., 17: 63-69.
13. Ikarashi, N., T. Toda, T. Okaniwa, K. Ito, W. Ochiai and K. Sugiyama, 2011. Anti-obesity and anti-diabetic effects of acacia polyphenol in obese diabetic KKAy mice fed high-fat diet. Evidence-Based Complement. Altern. Med. 10.1093/ecam/nep241.
14. Okpanachi, A.O., A.B. Adelaiye, A.A.U. Dikko, M. Kabiru and A. Mohammed *et al*., 2010. Evaluation of the Effect of Aqueous-methanolic Stem Bark Extract of *Acacia polyacantha* on Blood Glucose Levels of Alloxan Induced Diabetic Wistar Rats. Int. J. Anim. Vet. Adv., 2: 59-62.
15. Yasir, M., P. Jain, D. Debajyoti and M.D. Kharya, 2010. Hypoglycemic and antihyperglycemic effect of different extracts of *Acacia arabica* lam k bark in normal and alloxan induced diabetic rats. Int. J. Phytomed., 2: 133-138.
16. Yadav, P., R. Kant and P. Kothiyal, 2017. A review on *Acacia tortilis*. Int. J. Pharm. Phytopharmacol. Res., 3: 93-96.
17. Jagtap, A.G. and P.B. Patil, 2010. Antihyperglycemic activity and inhibition of advanced glycation end product formation by *Cuminum cyminum* in streptozotocin induced diabetic rats. Food Chem. Toxicol., 48: 2030-2036.
18. Bhateja, P.K. and R. Singh, 2014. Antidiabetic activity of *Acacia tortilis* (Forssk.) Hayne ssp. raddiana polysaccharide on streptozotocin-nicotinamide induced diabetic rats. BioMed Res. Int., Vol. 2014. 10.1155/2014/572013.
19. Das, S. and L. Kanodia, 2013. Effect of ethanolic extract of leaves of *Vitex negundo* L. on acetic acid induced colitis in albino rats. Asian J. Pharm. Clin. Res., 6: 138-141.
20. OECD., 2008. OECD guidelines for the testing of chemicals, acute oral toxicity-up-and-down-procedure (UDP). Section 425, October 3, 2008.
21. Nath, P. and A.K. Yadav, 2015. Acute and sub-acute oral toxicity assessment of the methanolic extract from leaves of *Hibiscus rosa-sinensis* L. in mice. J. Int. Ethnopharmacol., 4: 70-73.
22. Ahmed, M., A. Azmat, M.A.A. Navaid-ul-Zafar and S.I. Ahmad, 2013. Hepatoprotective effect of Barrisal (herbal drug) on carbon tetrachloride induced hepatic damage in rats. Afr. J. Pharm. Pharmacol., 7: 776-784.
23. Kar, D.M., L. Maharana, S. Pattnaik and G.K. Dash, 2006. Studies on hypoglycemic activity of *Solanum xanthocarpum* Schrad. & Wendl. fruit extract in rats. J. Ethnopharmacol., 108: 251-256.
24. Sikarwar, M. and M. Patil, 2010. Antidiabetic activity of *Pongamia pinnata* leaf extracts in alloxan-induced diabetic rats. Int. J. Ayurveda Res., 1: 199-204.
25. Arunachalam, K. and T. Parimelazhagan, 2013. Antidiabetic activity of *Ficus amplissima* Smith. bark extract in streptozotocin induced diabetic rats. J. Ethnopharmacol., 147: 302-310.
26. Arulselvan, P. and S.P. Subramanian, 2007. Beneficial effects of *Murraya koenigii* leaves on antioxidant defense system and ultra structural changes of pancreatic β-cells in experimental diabetes in rats. Chem. Biol. Interact., 165: 155-164.
27. Patterson, C.C., G. Dahlquist, V. Harjutsalo, G. Joner and R.G. Feltbower *et al*., 2007. Early mortality in EURODIAB population-based cohorts of type 1 diabetes diagnosed in childhood since 1989. Diabetologia, 50: 2439-2442.
28. Pal, R., M.S. Hooda, A. Bhandari and J. Singh, 2013. Antidiabetic activity of Acacia senegal pod extract in streptozotocin-induced diabetic rats. Int. J. Indigen Med. Plants, 46: 1400-1404.
29. Goud, B.J., V. Dwarakanath and B.K. Chikka Swamy, 2015. Streptozotocin-a diabetogenic agent in animal models. IJPPR Hum., 3: 253-269.
30. Arulmozhi, S., P.M. Mazumder, S. Lohidasan and P.A. Thakurdesai, 2010. Antidiabetic and antihyperlipidemic activity of leaves of *Alstonia scholaris* Linn. R.Br. Eur. J. Integr. Med., 2: 23-32.
31. Mollar-Puchades, M.A., V. Pallares-Carratala, M.S.N. de Solis and F. Pinon-Selles, 2006. Fasting glucose versus oral glucose tolerance testing in the diagnosis of diabetes mellitus. Revista Espanola de Cardiologia, 59: 1349-1350.
32. Zheng, X.K., L. Zhang, W.W. Wang, Y.Y. Wu, Q.B. Zhang and W.S. Feng, 2011. Anti-diabetic activity and potential mechanism of total flavonoids of *Selaginella tamariscina* (Beauv.) Spring in rats induced by high fat diet and low dose STZ. J. Ethnopharmacol., 137: 662-668.

33. Lokman, F.E., H.F. Gu, W.N. Wan Mohamud, M.M. Yusoff, K.L. Chia and C.G. Ostenson, 2013. Antidiabetic effect of oral borapetol B compound, isolated from the plant *Tinospora crispa*, by stimulating insulin release. Evidence-Based Complementary Alter. Med., Vol. 2013. 10.1155/2013/727602.
34. Vinayagam, R. and B. Xu, 2015. Antidiabetic properties of dietary flavonoids: A cellular mechanism review. Nutr. Metab., Vol. 12. 10.1186/s12986-015-0057-7.
35. Niwa, A., T. Tajiri and H. Higashino, 2011. *Ipomoea batatas* and *Agaricus blazei* ameliorate diabetic disorders with therapeutic antioxidant potential in streptozotocin-induced diabetic rats. J. Clin. Biochem. Nutr., 48: 194-202.
36. Schmitt, D., N. Tran, S. Riefler, J. Jacoby, D. Merkel, P. Marone and N. Naouli, 2008. Toxicologic evaluation of modified gum acacia: Mutagenicity, acute and subchronic toxicity. Food Chem. Toxicol., 46: 1048-1054.