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Original Article

ANTIDIABETIC EFFECT OF *THYMUS SATUREIOIDES* AQUEOUS EXTRACT IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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ABSTRACT

Objective: The aerial parts of *Thymus satureioides* have been traditionally used to treat diabetes mellitus and its complications in Morocco. The aim of the present study was to investigate the antidiabetic and antihyperlipidemic effects of the aqueous extract of *Thymus satureioides* aerial parts in streptozotocin (STZ) induced diabetic rats.

Methods: Experimental diabetes was induced in overnight fasted rats by intraperitoneal injection of streptozotocin (45 mg/kg). Diabetic rats were orally administered with aqueous extract of *Thymus satureioides* (500 mg/kg b.w.) for 28 d. Glibenclamide (2 mg/kg), a standard antidiabetic drug, was used as a positive control drug. Body weight and fasting blood glucose (FGB) were measured every week. Oral glucose tolerance, change in lipid parameters, urea, creatinine, aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT) levels of diabetic rats were evaluated at the end of the treatment.

Results: Administration of *Thymus satureioides* aqueous extract to diabetic rats for 28 d reduced their fasting blood glucose levels significantly compared to the diabetic control rats. The extract improved body weight and glucose tolerance in diabetic rats. The antihyperlipidemic assessment of the extract revealed a decrease in plasma total cholesterol, triglycerides, LDL levels and an increase in HDL level in the plasma of treated diabetic rats. Furthermore, the biochemical liver and kidney functional tests have shown that serum biomarkers of liver and renal dysfunction were significantly reduced in treated diabetic rats.

Conclusion: The present findings suggest that *Thymus satureioides* extract has both antidiabetic and antihyperlipidemic effects in experimental diabetic rats which can be beneficial in the management of diabetes and its complications.

Keywords: *Thymus satureioides*, Diabetes mellitus, Streptozotocin, Antidiabetic activity, Antihyperlipidemic activity, Glucose tolerance

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INTRODUCTION

Diabetes mellitus is one of the most common endocrine-metabolic disorders worldwide. It affects millions of people and has an incidence that is increasing at a striking rate [1]. Diabetes is considered as an alarming global health problem due to the high rate of morbidity and mortality which result from the associated macrovascular and microvascular complications such as retinopathy, neuropathy, nephropathy and cardiovascular complications [2]. Diabetes is also associated with profound alterations in the plasma lipid and lipoprotein metabolism. Diabetic dyslipidemia is characterized by elevated triglycerides, elevated LDL-cholesterol, low HDL-cholesterol and the predominance of small dense VLDL particles [3]. Recent studies have reported that some natural compounds have beneficial effects on dyslipidemia and diabetes [4]. In addition, the antihyperlipidemic activity of many medicinal plants has been reported in experimental studies [4]. Therefore, the use of natural compounds derived from medicinal plants, having the double effect of improving both glycemic and lipidemic profiles, may improve the management of diabetes and reduce cardiovascular risk in diabetic patients [5].

Medicinal plants have been used increasingly with greater advocacy for complementary and alternative medicine and continue to play an important role in the development of new drug formulations. The use of the medicinal plant to treat diabetes mellitus has gained growing interest in recent years since the recommendations made by WHO on diabetes mellitus, which encourage the search for safer and effective antidiabetic compounds derived from medicinal plants [6]. Considering the increasing prevalence of diabetes, investigations of the potentials offered by herbal medicines may contribute to the development of alternative therapeutic approaches towards the management and prevention of diabetes mellitus and its complications [7].

Thymus species constitute a group of aromatic plants of the Mediterranean flora belonging to the Lamiaceae family and are commonly used as spices and as traditional medicine remedies [8]. *Thymus satureioides* locally known as "Zaetra"or "Azoukni" is a perennial shrub endemic of Morocco [9]. The decoction and infusion of the aerial parts of this plant are used in the moroccan folk medicine to treat various diseases such as inflammation, hypertension, digestive ailments, cough bronchitis, whooping and rheumatism [10, 11]. Pharmacological studies have reported anti-inflammatory and analgesic effects of *Thymus satureioides* in experimental animals [12, 13]. *In vitro* studies have shown that this plant possesses antioxidant [14], anti-hemolytic [15], antibacterial [16] and anticoagulant activities [17]. Furthermore, another study demonstrated the antihyperlipidemic effect of polyphenol-rich extract from *Thymus satureioides* in Triton WR-1339-induced hyperlipidemic rats [18]. In addition, the essential oil of this plant has been investigated for its chemical composition and antibacterial activity [19].

Ethnobotanical surveys conducted in some regions of Morocco have reported the traditional use of *Thymus satureioides* in the treatment of diabetes mellitus [20-22]. The anti-diabetic effect of this plant has never been experimentally investigated. Thus, the aim of the present study was to evaluate the antidiabetic and antihyperlipidemic activities of aqueous extract from aerial parts of *Thymus satureioides* in streptozotocin-induced diabetic rats.

MATERIALS AND METHODS

Chemicals and reagents

STZ, quercetin and folin–Ciocalteu reagent were purchased from Sigma-Aldrich Co (Germany). D-glucose was purchased from Farco

Chemicals, while glibenclamide was obtained from Promopharm (Morocco). Gallic acid and aluminium chloride were purchased from VWR chemicals. All other chemicals and reagents used in this study were analytical grade.

Plant material

The aerial parts of *Thymus satureioides* were collected in April 2015 in the region of Agadir Ida-Outanane (Latitude: 30 °37', Longitude: 9 °22', Altitude: 760 m), South-west of Morocco. The plant material was taxonomically identified and authenticated, and a voucher specimen (specimen number MA-FSTF 15) was deposited in the herbarium of the Department of Biology, Faculty of Sciences and Techniques, Fez, Morocco.

Preparation of aqueous extract

The aerial parts of *Thymus satureioides* were washed well with water; air dried at room temperature and then reduced to a coarse powder using an electric grinder. The aqueous extract was prepared by infusion according to the traditional method used in Morocco [23]. The powder (40 g) was dissolved in 400 ml of boiling distilled water, and the mixture was homogenized for 60 min. The extract was then filtered through whatman filter paper and concentrated under vacuum at 50 °C using a rotary evaporator. The extract was kept in a sterile sample tube, under refrigerated conditions, until use for pharmacological investigations.

Determination of total phenol contents

Total phenolic contents in the aqueous extract were determined using the folin–ciocalteu reagent assay [24]. An aliquot (500 µl) of the extract (5 mg/ml) or standard solution was mixed with 2.5 ml of folin–ciocalteu reagent 10% (v/v). Thereafter, 2 ml of 7.5% Na2CO3 solution was added to the mixture followed by incubation at 45 °C for 15 min. The absorbance against a blank was measured at 765 nm. Gallic acid was used to prepare a standard curve (0.05–0.25 mg/ml; y = 0.009x+0.042;r2 = 0.995, where y is the absorbance and x is the standard concentration). The results were expressed as mg of gallic acid equivalents (GAE)/g of extract. Experiments were conducted in triplicate.

Determination of flavonoid content

The flavonoid content in the extract was measured by the aluminum chloride colorimetric method [25]. An aliquot (500 µl) of the extract (5 mg/ml) or standard solution of quercetin was mixed respectively with 1.5 ml of methanol and 100 µl of 10% AlCl3 solution. After 5 min, 0.5 ml of 1M NaOH solution and 2.5 ml of dH2O were added to the mixture. The solution was well mixed, and the absorbance against blank was determined at 451 nm. Quercetin was used for standard curve construction (0.05–0.3 mg/ml; y = 0.007x+0.104;r2 = 0.995). The results were expressed as mg quercetin equivalents (QE)/g of extract.

Animals

Wistar rats of either sex weighing 180–230 g were used in this study. They were obtained from the animal facility of the Biology Department (Faculty of Sciences and techniques, Fes, Morocco). The animals were housed in appropriate cages and had free access to water and laboratory rodent chow. Experiments procedures were carried out in accordance with the international guidelines for the care and use of laboratory animals [26]. All animal procedures were approved by the Institutional Ethical Committee of Sidi Mohamed Ben Abdellah University, Morocco.

Acute toxicity

Aqueous leaf extract of *Thymus satureioides* in 500 mg/kg doses was administered to the rats orally. All animals were observed for 24 h after treatment.

Evaluation of antidiabetic activity

Induction of experimental diabetes

Experimental diabetes was induced in overnight fasted rats by an intraperitoneal injection of 45 mg/kg body weight of streptozotocin (STZ). STZ was dissolved in freshly prepared citrate buffer (0.1 mol/l, pH 4.5). Fasting blood glucose was measured in rats 72 h after the injection. Rats with fasting blood glucose level>200 mg/dl were considered diabetic and included in the study [27].

Experimental design

The experimental rats were randomly divided into four groups of six rats each:

Group I: normal control rats, treated with distilled water.

Group II: diabetic control rats, treated with distilled water.

Group III: diabetic rats treated with *Thymus satureioides* aqueous extract (TS Aq Ext 500 mg/kg b.w.).

Group IV: diabetic rats treated with glibenclamide (2 mg/kg b.w.)

The selection of the effective dose (0.5 g/kg/day of b.w.) of *Thymus satureioides* aqueous extract was based on a prior preliminary short-term study. The plant extract and the drug glibenclamide were given in aqueous solution daily by intragastric gavage for 28 consecutive days. Body weight was recorded weekly. The fasting blood glucose (FGB) was measured on days 1, 7, 14, 21 and 28 of the treatment to evaluate the antidiabetic activity of the extract. Rats fasted for 12 h and the blood from tail vein was collected for FGB estimation using a glucometer (On Call plus®) in which its measurement principle is based on glucose oxydase method.

The oral glucose tolerance test (OGTT)

On the 28th day of treatment, the 12-h fasted animals were subjected to an oral glucose tolerance test. Fasting glycemia was measured and indicating zero time of the test. After this procedure, animals received their treatment orally and after a 60-minute interval, all groups received an oral load of glucose (2 g/kg b.w.). The blood sample was obtained by tail vein puncture at 30, 60, 90, and 120 min after glucose administration and blood glucose level (BGL) was determined at these time intervals using the On Call® Plus blood glucose monitoring system and compatible blood glucose test strips. Curves of BGL (mg/dl) versus the time intervals (min) were constructed, and total glycemic responses were calculated from respective areas under the curve (AUC) during the 120 min of the observation period.

Estimation of biochemical parameters

At the end of the experimental period, the animals were deprived of food overnight and then sacrificed by cervical decapitation following anesthesia. Blood was collected in tubes containing heparin for the estimation of lipid, renal function, and kidney function profiles parameters. Total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density-lipoprotein-cholesterol (HDL-C), triglycerides (TG), alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), urea and creatinine were determined using ''Cobas Integra 400 plus'' analyzer based on enzymatic/ photometric method.

Statistical analysis

Statistical analysis was performed using Graph Pad Prism version 6.0 for Windows. The difference between groups was assessed by one-way analysis of variance (ANOVA) followed by Tukey's post hoc test and values of *P* less than 0.05 were considered statistically significant. All values are expressed as the mean±SD.

RESULTS

Total phenol and flavonoids contents

The total phenolic content in *Thymus satureioides* extract was estimated to be equivalent to 121.05±4.25 mg of gallic acid equivalent/g of plant extract, and the flavonoids content was 83.52±2.12 mg of quercetin equivalent/g of plant extract.

Acute toxicity

After oral administration of the aqueous extracts of *Thymus satureioides* 500 mg/kg doses, no mortality was recorded for all

animals observed 24 h after the extract administration. There were no lethality or toxic reactions found at the dose selected until the end of the study.

Changes in body weight

The effect of aqueous extract of *Thymus satureioides* on body weight of STZ-induced diabetic rats is summarized in table 1. A progressive decrease in body weight was observed in the untreated diabetic group throughout the experimental period compared to healthy nondiabetic animals. This decrease in body weight was very significant at the end of the fourth week (P<0.001). The diabetic groups treated with *Thymus satureioides* aqueous extract and glibenclamide (2 mg/kg) for 4 w showed a significant improvement in body weight compared to the diabetic control group (P<0.01).

Table 1: Changes in the body weight of normal and diabetic rats during the experimental period of 28 d

Treatment	Body weight (g)				
	Day 1	Day 7	Day 14	Day 21	Day 28
Normal control	202.00±22.75	212.67±23.93	232.67±31.27	238.50±27.73	245.63±28.39
Diabetic control	212.14±15.44	183.45±26.91	154.34±17.54##	127.67±12.38###	124.10±31.73###
Diabetic+TS Aq Ext (500 mg/kg)	218.17±10.73	207.51±10.48	193.67±8.17**	185.35±6.58*	179.33±4.55**
Diabetic+glibenclamide (2 mg/Kg)	210.15±7.04	202.36±11.23	190.67±7.45**	184.17±5.47*	177.24±7.43**

Values are expressed as mean±SD (n = 6 rats). ##P<0.01, ###P<0.001 compared to normal control; *P<0.05, ** P<0.01 compared to diabetic control.

Effect of *Thymus satureioides* extract on glycemia in diabetic rats

The effect of repeated oral administration of *Thymus satureioides* extract (500 mg/kg per day) on fasting blood glucose levels of diabetic rats is shown in fig. 1. Fasting blood glucose was estimated on days 1, 7, 14, 21 and 28 of the treatment. At the beginning of the experiment, the FBG levels were significantly higher in the diabetic group compared to the nondiabetic control group (P<0.001). Four weeks administration of *Thymus satureioides* aqueous extract resulted in a significant reduction (p<0.001) in FBG levels of the diabetic treated rats, starting from the 14th day of treatment, compared to the diabetic control group. This reduction was maximum in the fourth week as reaching a 23% reduction, compared to day 0 and a 32% reduction compared to the control values of the untreated diabetic group. Standard drug glibenclamide also exhibited a significant reduction in FGB levels of the treated animals in comparison with the diabetic control (p<0.001).

Table 2: Effect of the aqueous extract of *Thymus satureioides* on levels of urea, creatinine, ALAT and ASAT in streptozotocin-induced diabetic rats after 28 d' experiments

Treatment	Hepatic markers		Renal markers	
	ALAT (UI/l)	ASAT (UI/l)	Urea (g/l)	Creatinine (mg/l)
Normal control	68.37±7.15	127.5±12.5	0.43±0.06	5.28±0.65
Diabetic control	127.05±10.46##	210.4±25.4##	0.64±0.07##	7.47±0.64##
Diabetic+TS Aq ext (500 mg/kg)	87.54±15.53*	159.6±12.24*	0.51±0.07*	6.24±0.85*
Diabetic+glibenclamide (2 mg/Kg)	85.31±12.50*	168.83±21.05*	0.53±0.05*	6.32±0.61*

Values are expressed as mean±SD (n = 6 rats). *P<0.05 compared to diabetic control; #P<0.05, ##P<0.01 compared to normal control.

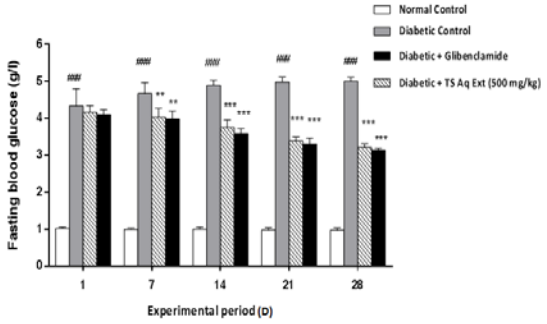

Fig. 1: Effect of aqueous extract of *Thymus satureioides* on fasting blood glucose in streptozotocin-induced diabetic rats during the experimental period of 28 d

Values are expressed as mean±SD (n = 6 rats). ###P<0.001 compared to normal control,**P<0.01, *** P<0.001 compared to diabetic control

Oral glucose tolerance test

The analysis of the glucose tolerance test and the comparison between the AUCs of glycemia during the 120 min period are presented in fig. 2. The blood glucose level in both normal and diabetic control rats showed a high peak value at 30 min after glucose load. Oral administration of aqueous extract as well as glibenclamide to diabetic rats induced a significant decrease in blood glucose concentrations at 30 min (p<0.001) and 60 (p<0.01) min when compared with the diabetic control rats. The AUCs of glucose concentration in groups treated with *Thymus satureioides* extract and glibenclamide were significantly reduced by 14 % and 15 %, respectively in comparison with the diabetic control group (fig. 3).

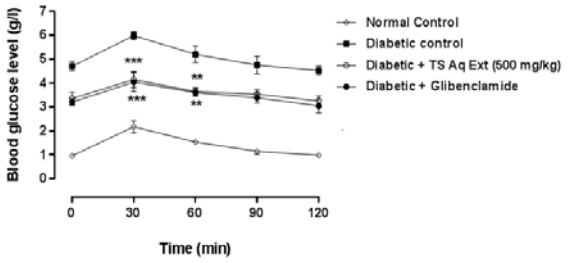

Fig. 2: Effect of the aqueous extract of *Thymus satureioides* on blood glucose level in streptozotocin-induced diabetic rats during OGTT

Values are expressed as mean±SD (n = 6 rats). **P<0.01, *** P<0.001 compared to diabetic control

Effect of *Thymus satureioides* extract on plasma lipid profile

Fig. 4 and 5 depict the levels of total cholesterol and triglycerides in control and experimental groups of rats. Results showed that the levels of total cholesterol and triglycerides were increased in the diabetic control group by 36 % and 38 % respectively, after 28 d of experiments, in comparison to the normal control rats (p<0.05). On the other hand, diabetic animals treated with glibenclamide and the aqueous extract of *Thymus satureioides* showed a significant

decrease in plasma triglycerides and total cholesterol when compared to the diabetic control rats (p<0.05).

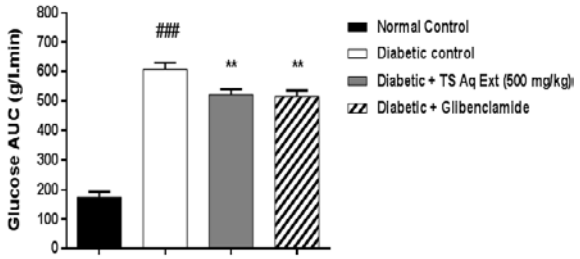

Fig. 3: Effect of *Thymus satureioides* extract on total area under the curves (AUCs) of blood glucose

Values are expressed as mean±SD (n = 6 rats). ###P<0.001 compared to normal control, **P<0.01 compared to diabetic control

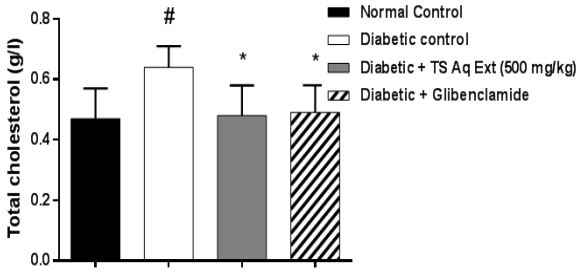

Fig. 4: Effect of the aqueous extract of *Thymus satureioides* on total cholesterol in streptozotocin-induced diabetic rats after 28 d' experiments

Values are expressed as mean±SD (n = 6 rats). #P<0.05 compared to normal control, *P<0.05 compared to diabetic control

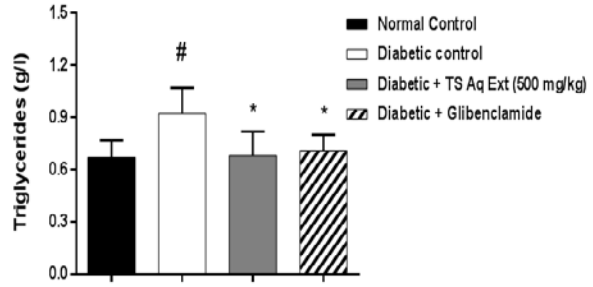

Fig. 5: Effect of the aqueous extract of *Thymus satureioides* on triglycerides in streptozotocin-induced diabetic rats after 28 d' experiments

Values are expressed as mean±SD (n = 6 rats). #P<0.05 compared to normal control,*P<0.05 compared to diabetic control

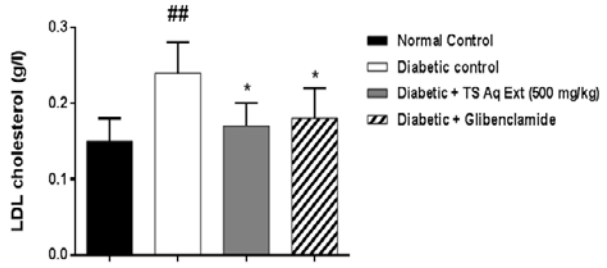

Fig. 6: Effect of the aqueous extract of *Thymus satureioides* on LDL-cholesterol in streptozotocin-induced diabetic rats after 28 d' experiments

Values are expressed as mean±SD (n = 6 rats). ##P<0.01 compared to normal control,*P<0.05 compared to diabetic control

The level of LDL-C was significantly higher in the diabetic control rats compared to the normal control rats (p<0.05). The administration of *Thymus satureioides* extract to STZ-induced diabetic rats significantly (p<0.05) decreased their plasma level of LDL-C by 30 %. Glibenclamide treated group also showed a significant reduction in LDL-C levels compared to the diabetic control group (P<0.05) (fig. 6).

The HDL-C level was significantly reduced in the diabetic control group in comparison to the values of normal control rats (p<0.05). The diabetic group treated with the aqueous extract of *Thymus satureioides* showed a significant increase in the level of HDL-C by 23 % when compared to the untreated diabetic rats. On the other hand, no significant change was observed in HDL-C level of glibenclamide treated group (fig. 7).

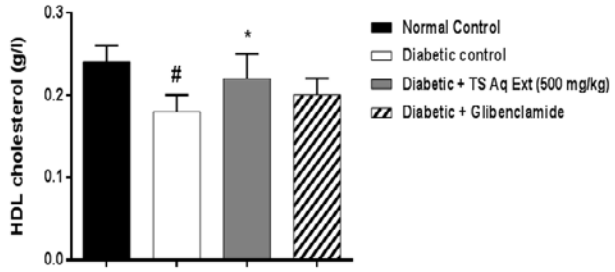

Fig. 7: Effect of the aqueous extract of *Thymus satureioides* on HDL-cholesterol in streptozotocin-induced diabetic rats after 28 d' experiments

Values are expressed as mean±SD (n = 6 rats). #P<0.05 compared to normal control, *P<0.05 compared to diabetic control

Effect of *Thymus satureioides* extract on hepatic and renal function markers

The levels of hepatic and renal functional markers of experimental rat groups are presented in table 2. There was a significant (p<0.05) elevation in the activities of ALAT and ASAT in diabetic control rats as compared with non-diabetic control group. The administration of *Thymus satureioides* extract (500 mg/kg body w. t.) to STZ-induced diabetic rats for 28 d significantly decreased the activities of these enzymes when compared to the diabetic control rats (p<0.05). Streptozotocin-induced diabetic rats displayed a significant (p<0.05) increase in urea and creatinine levels after 4 w as compared to normal control group. However, treatment of diabetic rats with aqueous extracts of *Thymus satureioides* significantly reduced their creatinine and urea levels by 18 % and 16 % respectively in comparison to the diabetic group (p<0.05). A significant decrease in the levels of urea and creatinine was also observed in diabetic rats treated with glibenclamide (p<0.05).

DISCUSSION

To the best of our knowledge, the present study represents the first assessment of the antidiabetic and antihyperlipidemic activities of the aqueous extract from aerial parts of *Thymus satureioides* on STZ induced diabetic rats. Administration of the aqueous extract of *Thymus satureioides* to diabetic rats for 4 w resulted in a significant diminution of fasting blood glucose level in respect to the untreated diabetic rats. The antidiabetic activity of the extract was similar to that obtained for glibenclamide, a standard antidiabetic drug used as a positive control in experimental diabetes studies. The effect of *Thymus satureioides* extract on glucose tolerance and tissue utilization of glucose was assessed in diabetic rats using the OGTT test which assesses the rate of tissue uptake and utilization of glucose. Diabetic rats showed a significant increase in the AUC of glucose compared to normal control rats. Impaired glucose tolerance is attributed to increased hepatic gluconeogenesis and abnormal utilization of glucose by the tissues which are caused by pancreatic dysfunction [28]. On the other hand, the significant reduction in the AUC of glucose observed in the treated group suggests that the extract is induced an increase in glucose utilization and glucose

tolerance by the body tissues in diabetic rats which indicates improved glucose homeostasis.

Diabetic rats manifested a significant reduction in body weight concomitant with hyperglycemia. Decrease in body weight of diabetic rats is attributed to the intensive catabolism of fats and structural proteins which used as an energy source due to unavailability of carbohydrates [29]. Insulin plays an important role in the regulation of protein synthesis and proteolysis in skeletal muscle. In insulin resistance or deficiency state, muscle wasting and weight loss in diabetic rats results from the excessive catabolism of protein which provides amino acids for gluconeogenesis [30]. Oral administration of *Thymus satureioides* aqueous extract and glibenclamide for 28 consecutive days to diabetic rats improved their body weight, which reflects the better control of the hyperglycemic state in these rats.

In diabetes, hyperglycemia is associated with dyslipidemia, which represents a risk factor for cardiovascular diseases [31]. The abnormally high level of serum lipids is mainly due to the uninhibited actions of lipolytic hormones on the fat depots, which are caused by the deficiency in insulin secretion or insulin sensitivity [31]. Under normal circumstances, the enzyme lipoprotein lipase is activated by insulin, which hydrolyzes triglycerides. However, in diabetic state insulin deficiency causes inactivation of lipoprotein lipase, resulting in hypertriglyceridemia and hypercholesterolemia [32]. Furthermore, in the diabetic state the secretion of very low-density lipoprotein cholesterol (VLDL) is stimulated by triglycerides and such increase in very low-density lipoprotein cholesterol particles increases the LDL-C particles and reduces the HDL-C level [33]. In our study, the altered serum lipid profile was found in diabetic rats. This finding is in correlation with the findings of previous studies [34, 35]. Alterations in serum lipid profile were attenuated after 4 w administration of *Thymus satureioides* aqueous extract to diabetic rats. The effect of *Thymus satureioides* extract on lipid metabolism might be directly attributable to the improvement in insulin. On the other hand, the antihyperlipidemic activity of the extract may also attribute to other lipid-lowing mechanisms, such as repressing some key enzymes involved in cholesterol and fatty acids biosynthesis. Regulation of plasma or tissue lipid levels led to a decrease in the risk of micro or macrovascular diseases and related complications [36]. Therefore, the extract could be beneficial in improving lipid metabolism, which can lead to preventing diabetes complications such as atherosclerosis and coronary heart diseases.

Elevated serum levels of ASAT and ALAT are indicative of cellular leakage and loss of functional integrity of the hepatic cell membranes implying hepatocellular damage [37]. In the present study, high serum levels of ASAT and ALAT were detected in the diabetic group in comparison with the normal control. This finding suggests possible damage to the liver caused by the injection of STZ, which is one of the characteristic changes in experimental diabetes induced by this compound. Liver damage in diabetic rats was evidenced. However, diabetic groups treated with *Thymus satureioides* aqueous extract for 28 d showed a significant reduction in the levels of ASAT and ALAT levels when compared to the untreated diabetic control. This result showed that aqueous extract exhibited hepatoprotective activity in diabetic rats by decreasing serum ASAT and ALAT levels, which consequently alleviated the damage caused by STZ. The high blood levels of urea and creatinine are considered as markers of renal damages [38]. Therefore, increased levels of urea and creatinine found in diabetic rats suggest impaired renal function. On the other hand, the administration of *Thymus satureioides* aqueous extract to the diabetic rats significantly reduced the levels of creatinine and urea. This suggests that the extract of *Thymus satureioides* may exhibit a preventive action against kidney damages in diabetic condition.

The results of the present study demonstrated that the aqueous extract of *Thymus satureioides* was rich in total polyphenols and flavonoids. These phytochemical compounds present in the aqueous extract may account for the observed pharmacological activities. Several studies have reported that polyphenols and flavonoids compounds bring their antidiabetic effect by various mechanisms, including inhibition of α-amylase activity, stimulation of insulin secretion and increase of peripheral glucose consumption [39]. Several flavonoid-containing plants with antidiabetic potential have also shown an antihyperlipidemic effect by modulating enzymes involved in lipid metabolism [40]. Flavonoids and polyphenols have also been reported to attenuate complications associated with diabetes in liver, kidneys and blood vessels through mechanisms such as aldose reductase inhibition, advanced glycation end-products inhibition and the decrease of oxidative stress [41].

CONCLUSION

It can be concluded that the aqueous extract of *Thymus satureioides* has potential antidiabetic effect in STZ induced diabetic rats which were as effective as glibenclamide. The aqueous extract also had the potential to reduce diabetic complications by attenuating dyslipidemia and preventing liver and kidney damages. These pharmacological activities may be attributed to the presence of secondary metabolites like polyphenols and flavonoids in *Thymus satureioides* extract which have been found to be beneficial in controlling diabetes. Further investigations are needed to isolate the bioactive components of *Thymus satureioides* involved in these pharmacological activities as well as the elucidation of their mechanism of action. In addition, toxicological studies should be performed to evaluate the innocuity of this plant.

CONFLICT OF INTERESTS

We declare that we have no conflict of interest

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