World Applied Sciences Journal 33 (12): 1940-1948, 2015
ISSN 1818-4952
© IDOSI Publications, 2015
DOI: 10.5829/idosi.wasj.2015.33.12.15637

Anti-Hyperglycemic Effect of *Tamarindus indica* Extract in Streptozotocin-Induced Diabetes in Male Rats

Maha Ahmed Al-Ahdab

Department of Food and Nutrition, Faculty of Home Economics,
King Abdul-Aziz University, Jeddah, Saudi Arabia

Abstract: The present study was conducted to evaluate the hypoglycemic effect of *Tamarindus indica* extract (*T. indica* extract) in streptozotocin (STZ)-induced diabetes in male rats. Forty adult male albino rats of Sprague-Dawley strain weighing 200±5g were divided into five groups of equal number and weight. Group I, normal control rats; group II, diabetic control rats(positive control group); and groups III, IV and V, diabetic rats given orally *T. indica* extract by tube feeding at levels of 100, 200 and 300 mg/kg of body weight, respectively. Oral administration of *T. indica* extract at the three different doses caused significant increase in body weight and serum insulin level parallel with significant reduction in blood glucose level and improvement in lipid profile as well as liver and kidney functions compared to the positive control group. Histological of that pancreas tissue section of rats from the positive control group showed hypertrophy and hyperplasia of ß-cells of islets of Langerhans associated with pyknosis of their nuclei. However, treatment with 100 mg/kg b.wt of *Tamarindus indica* extract resulted in vaculations of acinar epithelial lining in pancreas. Slight hypertrophy of islets of langerhans was demonstrated in pancreas of treated rats with 200 mg/kg b.wt. Apparently normal histological structure of ß-cells of islets of Langerhans was found in the treated rats with 300 mg/kg b.wt. In conclusion administration of *T. indica* extract reduced blood glucose level and the incidence of different diabetic complications. The antihyperglycemic effect of *T. indica* could be attributed to the presence of bioactive compounds with antioxidant properties that exert health promoting effects.

Key words: *Tamarindus indica* · Diabetes · Rats · Hyperlipidemia

INTRODUCTION

Diabetes is a chronic metabolic disorder characterized by hyperglycaemia. It is a complex and multifarious group of disorders leading to micro and macrovascular complications. Diabetes occurs when the pancreas is no longer able to synthesize insulin and is classified into two major categories, type 1 and type 2. Type 2 diabetes (T2DM) is the most prevalent form of diabetes, accounting for 90 to 95 percent of cases [1]. The prevalence of diabetes mellitus has reached epidemic proportions and has affected 6.4% of adults worldwide in 2010 [2]. The global prevalence for all age groups was estimated to be 4.4% in 2030 [3]. Applying medicinal herbs has been popular from ancient times among people and in recent years, a multilateral approach has emerged on using natural medicine and especially herbal one [4]. Tamarindus [*Tamarindus indica* L. *(T. indica*)], belongs to the family Leguminosae (Fabaceae), is one of the fruit tree species. It is widely cultivated as an ornamental tree and for its acidic fruits used in making drinks and a popular component of many decoctions that is used as traditional medicine [5]. All parts of *T. indica* plant (root, body, fruit and leaves) are rich in nutritional value and broad usage area in medicine but also has industrial and economic importance. Tamarindus fruit is an ideal source of all essential amino acids except tryptophan (82%) [6]. Also, *T. indica* is contains high carbohydrate content which provides energy. It is also rich in minerals such as potassium, phosphorus, calcium and magnesium *T. indica* can also provide smaller amounts of iron and vitamin A [6]. According to phytochemical analysis results, *T. indica* contains phenolic compounds like catenin, procyanidin B2, epicatechin, tartaric acid, mucilage, pectin, arabinose, xylose, galactose, glucose, uronic acid and triterpen [7]. The fruit pulp extract of *T. indica* has been reported for its antioxidant and hypolipidemic properties [8]. Therefore, the aim of present study was to

Corresponding Author: Maha Ahmed Al-Ahdab, Department of Food and Nutrition, Faculty of Home Economics, King Abdul-Aziz University, Jeddah, Saudi Arabia

determine the antihyperglycemic effect of oral administration of *Tamarindus indica* extract in streptozotocin-induced diabetes in male rats.

MATERIALS AND METHODS

Material

***Tamarindus indica* Plant:** *T. indica* was obtained from local herbs and medicinal plants market, Jeddah, KSA.

Chemicals and Kits: Streptozotocin was purchased from Sigma-Aldrich Chemical Company (St. Louis, MO, USA). Kits for biochemical analysis of glucose, insulin, serum triglycerides, total cholesterol, HDL-C, serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase urea nitrogen, uric acid and creatinin were purchased from Biodiagnostic Co. USA.

Rats: Forty adult male Sprague Dawley rats weighing 200±5g body weight were used in this study. Animals were obtained from Faculty of Pharmacy, King Abdul-Aziz University, Jeddah, Saudi Arabia. Rats were housed in a well ventilated laboratory room under standard conditions of 24°C temperature, 50-52% relative humidity and 12 hr light/12 hr dark cycles. Experiment was carried out according to the National regulations on animal welfare and Institutional Animal Ethical Committee (IAEC).

Diets: The basal diet (AIN-93M) was prepared according to Reeves *et al*. [9]. Diet was formulated to meet the recommended nutrients levels for rats.

Methods

Preparation of *Tamarindus indica*: The aqueous extracts of *T. indica* were prepared using 10g dried material/100ml distilled water and boiling for 5 min at 100°C. Then the extract filtrated, concentrated at 50c° under reduced pressure using a rato vapor and kept at -15°C until it was used in the experiment [10].

Induction of Diabetes Mellitus: Diabetes was induced by a single intraperitonial (i.p.) injection of freshly prepared Streptozotocin (STZ) at a dose level of 65 mg/kg of body weight dissolved in 0.02 ml of 0.05 M citrate buffer pH 4.5 in fasted rats according to Nafiu *et al*. [11]. After i.p. injection, the animals allowed to drink 5 % glucose solution overnight to overcome the death from hypoglycemia shock. Seventy-two hrs later, the blood samples were with drown from orbital plexus vein of each injected rat by a fine capillary glass tube and the blood glucose concentration was determined to confirm induction of diabetes, the non-diabetic rats excluded from the study and diabetes established with non- fasting blood glucose levels of = 300 mg/dl.

Experimental Design: Forty rats weighing 200±5 were housed in healthy condition at temperature rooms (21-25°C), with 40-60% humidity, exposed to a 12:12h light-dark cycle and fed on the basal diet and water was provided *ad libitum* for one week before starting the experimental protocol for acclimatization. After acclimatization period rats were divided into five equal groups of eight rats each as follows:

- Group (1): Served as a negative control group (normal rats) and fed on basal diet only for 4weeks.
- Group (2): Kept as a diabetic control rats (positive control group) fed on the basal diet only for 4 weeks.
- Group (3): Diabetic rats, orally given *Tamarindus indica* extract in a dose of 100 ml/kg b.wt for 4 weeks.
- Group (4): Diabetic rats, orally given *Tamarindus indica* extract in a dose of 200 ml/kg b.wt for 4 weeks.
- Group (5): Diabetic rats, orally given *Tamarindus indica* extract in a dose of 300 ml/kg b.wt for 4 weeks.

The initial and final body weights of rats were recorded and body weight gains was calculated. At the end of the experimental period (4 weeks) diets were withheld from experimental rats for 12h and then the rats were sacrificed and blood samples were collected from the portal vein into dry clean centrifuge tubes for serum separation. Serum samples were frozen at -20°C until biochemical analysis. Pancreas of sacrificed rats were kept in 10% formalin solution till processed for histopathological examination.

Biochemical Analysis: Glucose and Insulin Concentration: Blood glucose was measured using a glucose oxidase kit [12] and insulin level was measured using ELISA kit according to Clark and Hales [13].

Lipid Profile Parameters: Total cholesterol (TC), triacylglycerols (TG), high density lipoprotein cholesterol (HDL-c) were determined according to Richmond [14], Lopes-Virella *et al*. [15] and Fossati and Prenpe [16], respectively. While low density lipoprotein cholesterol (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) were calculated according to Fridewald *et al*. [17] by using the following equation:

LDL-C = TC - (HDL-C +V LDL-C). VLDL-C estimated as triglyceride/5

Liver and Kidney Functions Assay: Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and alkaline phosphatase (ALP) activities were determined using colorimetric methods as described in the kits instruction (Biodiagnostic Company).The absorption of the test samples were read at 505nm for AST and ALT and at 510 nm for ALP. Kidney function was assessed by chemical estimation of blood urea nitrogen [18]; uric acid [19] (and creatinine [20] concentrations in the serum.

Histopathological Examination: The fixed Pancreas specimens were trimmed, washed and dehydrated in ascending grades of alcohol. Specimens were then cleared in xylol, embedded in paraffin, sectioned at 4-6 microns thickness and stained with Heamtoxylin and Eosin stain for examination of the Pancreas as described by Carleton [21].

Statistical Analysis: Results were expressed as a (mean ±SD). Data were analyzed statistically by analysis of variance, for statistical significance using LSD test, one way ANOVA, post hoc multiple comparisons according to Snedecor and Cochron [22]. SPSS version 20 was used for these calculations.

RESULTS

Effect of oral administration of *Tamarindus indica* extract at doses of 100, 200,300 mg/kg b.wt on body weight in diabetic rats is recorded in Table 1. Results indicated that at the initial body weight of experiment, there was no significant difference in body weight (g) among all groups ($p<0.05$). Final body weight of positive control group was significantly ($p<0.05$) reduced compared to the negative control group. Oral administration of *T. indica* extract at the three different doses caused significant increase in body weight (g) in all treated groups compared to the positive control group. The increase in body weight in the treated groups was dose dependent. Diabetes induced by streptozotocin significantly ($P<0.05$) increased blood glucose and decreased serum insulin level in rats when compared to the negative control group. Oral administration of *T. indica* extract to diabetic rats at three dosage levels for 4 weeks significantly ($P <0.05$) lowered blood glucose and elevated insulin serum level when compared with the positive control group as depicted in Table 2. Percentages of the decrease in blood glucose level were 48.25, 59.27 and 66.32 in rats orally given *T. indica* extract at three dosage levels 100,200 and 300 mg/kg b.wt., respectively and increased insulin serum level when compared with the positive control group were 142.68, 235.37 and 268.29, respectively. Serum concentrations of TG and TC in diabetic rats are presented in Table 3. Tabulated results revealed that positive control group showed significant ($p<0.05$) increase in serum levels of TC and TG compared to the negative control group by 54.96 and 56.29% respectively. According to the results, treated rats with different doses of *T. indica* extract (100, 200 and 300 mg/kg b.wt) showed significant ($p<0.05$) decrease in serum levels of TC compared to the positive control rats by17.23, 25.12 and 33.4%, respectively. The same effect was observed in serum TG of treated groups by 22.96, 29.33 and 35.46%, respectively compared to positive control group. Treated group with 300mg/kg b. wt revealed the lowest levels of serum TC and TG, which were significantly ($p<0.05$) decreased compared to the other treated groups.

The results revealed that diabetes induced significant decrease in high density lipoprotein cholesterol (HDL-c) by 59.54% compared to the negative control group accompanied by increase in low (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) by 143.4 and 44.88%, respectively when compared to the negative control group,. Oral administration of *T. indica* extract at three dosage levels given to diabetic rats for 4 weeks significantly ($P <0.05$) increased serum HDL-c and

Table 1: Effect of oral administration *T. indica* extract on body weight (B.wt) and body weight gain percent (BWG) in diabetic rats

Parameters			
Groups	Initial B. wt (g) at week 0	Final B. wt (g) at week 4	BWG (%)
Group (1) -Ve control	205.23±2.33^{a}	255.07±2.82^{a}	24.28±1.36^{a}
Group (2) + Ve control	204.13±1.25^{a}	185.50±4.52^{d}	9.1±1.37^{d}
Group (3) *T. indica* 100 ml/kg b.wt	205.11±3.51^{a}	233.32±4.66^{c}	13.75±1.68^{c}
Group (4) *T. indica* 200 ml/kg b.wt	205.31±2.86^{a}	241.43±2.43^{b}	17.59±1.52^{b}
Group (5) *T. indica* 300 ml/kg b.wt	205.43±2.35^{a}	252.85±6.37^{a}	23.08±1.14^{a}

Mean with different letters in the same column differ significantly at $p < 0.05$ using one way ANOVA test. n=8 rats

Table 2: Effect of oral administration of *T. indica* extract on blood glucose (BG) and insulin levels in diabetic rats

Parameters		
Groups	BG (mg/dl)	Insulin (ng/ml)
Group (1) - Ve control	97.57±2.34d	3.11±0.67a
Group (2) +Ve control 20% CP	310.42±3.53a	0.82±0.43d
Group (3) *T. indica* 100 ml/kg b.wt	160.63±2.87b	1.99±0.54c
Group (4) *T. indica* 200 ml/kg b.wt	126.42±2.62c	2.75±0.63b
Group (5) *T. indica* 300 ml/kg b.wt	104.54±3.73c	3.02±0.85b

Mean with different letters in the same column differ significantly at $p < 0.05$ using one way ANOVA test. n=8 rats

Table 3: Effect of oral administration of *T. indica* extract on serum total cholesterol (TC) and triglycerides (TG) in diabetic rats

Parameters		
Groups	TC (mg/dl)	TG (mg/dl)
Group (1) - Ve control	95.37±2.42 d	79.34±1.47d
Group (2) +Ve control 20% CP	147.79±2.13 a	124.00±3.22a
Group (3) *T. indica* 100 ml/kg b.wt	122.32±2.21 b	95.53±2.11b
Group (4) *T. indica* 200 ml/kg b.wt	110.66±3.28c	87.63±2.25c
Group (5) *T. indica* 300 ml/kg b.wt	98.43±2.54d	80.03±1.03d

Mean with different letters in the same column differ significantly at $p < 0.05$ using one way ANOVA test. n=8 rats

Table 4: Effect of oral administration of *T. indica* extract on serum levels of high (HDL-c), low (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) in diabetic rats

Parameters			
Groups	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
Group (1) - Ve control	55.49±2.85a	23.57±1.52d	17.09±0.09d
Group (2) +Ve control 20% CP	22.45±1.89d	57.37±3.05a	24.76±0.06a
Group (3) *T. indica* 100 ml/kg b.wt	44.36±2.18c	45.56±1.18b	20.43±0.74b
Group (4) *T. indica* 200 ml/kg b.wt	49.50±2.27b	33.43±0.94c	19.66±0.03c
Group (5) *T. indica* 300 ml/kg b.wt	52.32±3.26a	24.47±1.03d	18.44±0.32d

Mean with different letters in the same column differ significantly at $p < 0.05$ using one way ANOVA test. n=8 rats

Table 5: Effect of oral administration of *T. indica* extract on the activity of serum aspartate aminotransferase (AST), alanine amino-transferase (ALT) and alkaline phosphatase (ALP) in diabetic rats

Parameters			
Groups	AST(U/L)	ALT(U/L)	ALP(U/L)
Group (1) - Ve control	47.24±1.67d	38.09±.32d	90.19±3.35c
Group (2) +Ve control 20% CP	76.21±2.02a	68.11±1.27a	109.32±3.43a
Group (3) *T. indica* 100 ml/kg b.wt	62.43±2.66b	57.21±2.35b	99.24±3.76b
Group (4) *T. indica* 200 ml/kg b.wt	54.23±1.09c	44.65±2.01c	95.21±2.27b
Group (5) *T. indica* 300 ml/kg b.wt	49.21±2.31d	40.98±1.43d	91.04±3.18c

Mean with different letters in the same column differ significantly at $p < 0.05$ using one way ANOVA test. n=8 rats

Table 6: Effect of oral administration of *T. indica* extract on blood urea nitrogen (BUN), uric acid (UA) and creatinine (Cr) levels in diabetic rats

Parameters			
Groups	BUN (mg/dl)	UA (mg/dl)	Cr (mg/dl)
Group (1) - Ve control	3.87±0.04d	33.41±0.32 d	0.87±0.02d
Group (2) +Ve control 20% CP	5.94±0.13 a	58.62±0.65 a	2.36±0.06 a
Group (3) *T. indica* 100 ml/kg b.wt	4.94±0.34 b	46.43±0.54 b	1.43±0.04b
Group (4) *T. indica* 200 ml/kg b.wt	4.36±0.78 c	40.43±0.71 c	1.11±0.01c
Group (5) *T. indica* 300 ml/kg b.wt	3.92 ± 2.01d	35.32 ± 0.01d	0.93 ± 0.02d

Mean with different letters in the same column differ significantly at $p < 0.05$ using one way ANOVA test. n=8 rats

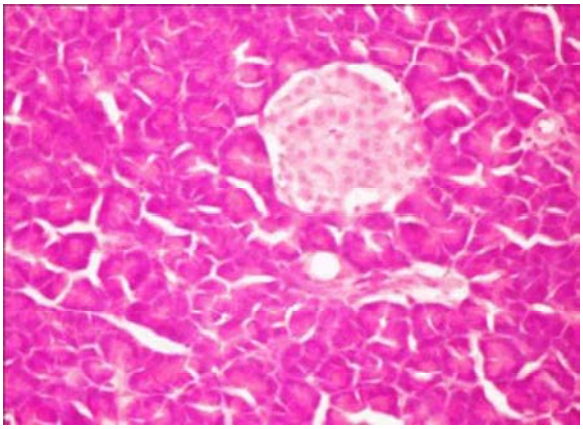

Fig. 1: Pancreas of control negative (-ve) rats showing no histopathological change (H and E stain x 400).

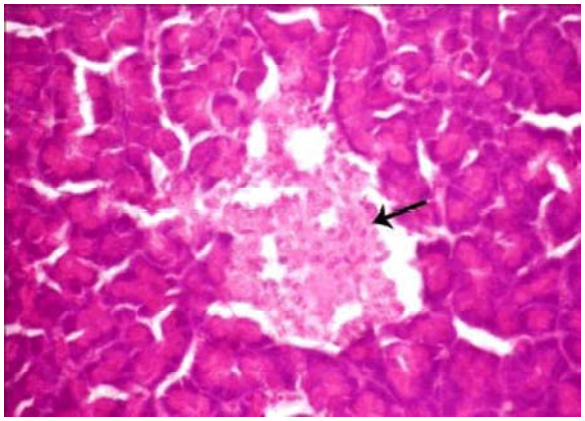

Fig. 2: Pancreas of diabetic rats showing necrosis of β-cells of islets of langerhans (H and E stain x 400).

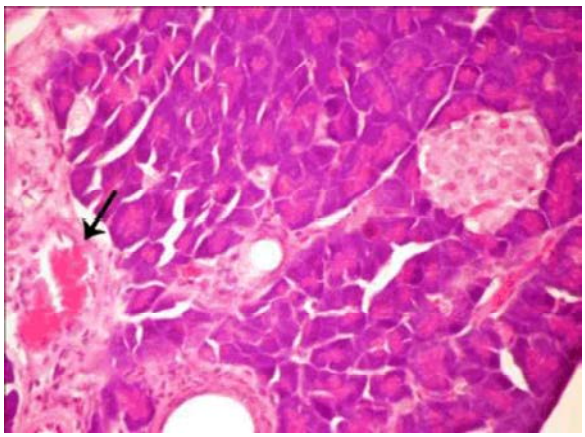

Fig. 3: Slight hypertrophy of islets of langerhans was observed in pancreas of treated rats with 200mg/kg b.wt *T. indica* extract (H and E stain x 400).

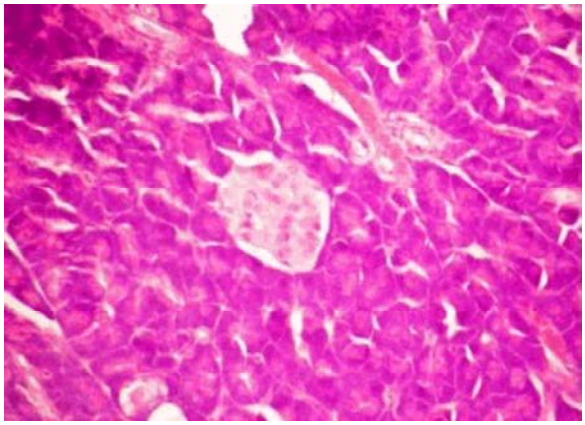

Fig. 4: Apparent normal histological structure of pancreas was showed in treated group with 300 mg/kg b. wt *T. indica* extract (H and E stain x 400).

decreased LDL-c and VLDL-c when compared with the positive control group as recorded in Table 4. The activity of AST, ALT and ALP as indicator of liver functions is recorded in Table 5. Data revealed that positive control group had significant increase ($p<0.05$) in the activity of serum AST, ALT and ALP compared to the negative control group. Oral administration of *T. indica* extract caused significant increase ($p<0.05$) in serum of AST, ALT and ALP activity compared to the positive control group. The reduction of serum of AST, ALT and ALP activity was more detectable with increasing the dose of *T. indica* extract. Data in Table 6 illustrated the effect of oral administration of *T. indica* extract on kidney functions as indicated by serum concentrations of BUN, UA and Cr. Results revealed that positive control group had significant increase in serum levels of BUN, UA and Cr ($p<0.05$) compared to the negative control group. However, oral administration of *T. indica* extract at the three different doses caused significant decrease in serum concentrations of BUN, UA and Cr compared to the positive control group.

Histopathological examination of the pancreatic tissue section of negative control group showed no histopathological changes (Fig. 1). Microscopic examination of the pancreatic tissue section of diabetic rats revealed necrosis of β-cells of islets of langerhan's and cystic dilatation of pancreatic duct and congestion of pancreatic blood vessels (Fig. 2). Slight hypertrophy of islets of langerhans showed in pancreas tissue section of treated rats with 200mg/kg b.wt *T. indica extract* (Fig. 3). Apparent normal histological structure of pancreas tissue section was noticed in treated rats with 300 mg/kg b. wt *T. indica* extract (Fig. 4).

DISCUSSION

Different parts of *T. indica* are recognized for their various medicinal properties. It has been reported that the antioxidant-rich *T. indica* fruit pulp extract was able to significantly regulate the expression of a sizable number of genes [23]. It has been recently stated that the leaves of *T. indica* possessed high phenolic contents with potent antioxidant activity in scavenging free radicals in non-cellular based assays [24]. Catechin, epicatechin and quercetin were detected in the antioxidant-rich leaf extract of *T. indica* [24]. The present study aimed to investigate the hypoglycemic effect of *T. indica* extract in diabetic male rats. The study results revealed that animals injected with STZ appeared ill-looking with loss of their body weight. Present observations are in agreement with the findings of Habibuddin *et al*. [25] and Lee *et al*. [26], who reported that these effects may be due to injurious effect of STZ which caused alkylation of DNA and produced hyperglycaemia and necrotic lesions. Kota *et al.* [27] found that there were an association between hyperglycemia and decreased body weight of diabetic animals. DM induced reduction in body weight and the body's inability to store or use glucose causes hunger and weight loss. In our study, administration of *T. indica* extract to diabetic rats resulted in increased body weight compared to the positive control group this may be due to the retained levels of glucose and insulin levels because of the antioxidant effects of *T. indica* extract.

Our results during experimental period revealed that, blood glucose level in the diabetic rats was significantly high and serum insulin level was significantly low compared to the negative control rats. Histopathological examination of pancreas sections from positive control rats is agreed with Laxmi *et al*. [28] and Yaghmoor and Khoja [29], who reported that STZ. Induced diabetes in male rats in a dose of 60 mg/kg and had a negative effect on glucose concentration and insulin levels. Diabetes syndromes characterized by increased blood glucose, altered lipids, carbohydrate and an increased risk of diabetic complications and oxidative stress [30, 31]. Moreover, STZ induced destruction of β-cells of islets of Langerhans and causing degranulation and reduction of insulin secretion as proposed by Zhang and Tan [32] and Kavalali *et al.* [33].

In the current study, it was observed that there was a significant decrease in serum glucose concentrations while insulin level demonstrated a significant increase in diabetic groups treated with *T. indica* extract as compared with the diabetic group. These results are in conformity with the results of Bhutkar and Bhise [34], who reported that this may be due to the hypoglycemic effect of *T. indica* extract bioactive compounds which may help in suppressing the free radical in diabetes, this will ultimately lead to decreased levels of blood glucose and also it has a protective effect on pancreatic β-cells and restored plasma insulin level. In the present study, diabetic rats showed a significant increase in serum TC, TG, LDL-C and VLDL-C levels accompanied by a significant decrease in serum HDL-C level when compared with negative control group. A similar result reported that STZ in a dose of 30 mg/kg had a negative effect on lipid profile when compared with normal rats [27]. In addition, Ramudu *et al.* [35] found significant increase in TC, TG and phospholipids levels in STZ-induced diabetic rats against non-diabetic rats. These effects may be attributed to the affect of diabetes on lipid metabolism. Low insulin levels are associated with high levels of chylomicrons and very-low-density lipoprotein (VLDL-C) and lipoprotein lipase deficiency resulting in hypertriglyceridaemia [36, 37, 38]. Insulin affects many sites of mammalian lipid metabolism; it stimulates synthesis of fatty acids in liver, adipose tissues in the intestine. Insulin deficiency has also been reported to increase the cholesterol synthesis and increase the activity of lipoprotein lipase in white adipose [39].

The present results revealed that the treatment of diabetic rats with *T. indica* extract caused significant decrease in plasma levels of cholesterol, LDL-C, VLDL-C, TG and an increase in HDL-C. This may be an indication of positive metabolic control of *T. indica* extract on mechanisms involved in the elimination of the lipids from the body. This effect may be due to antioxidant effect of *T. indica* extract or because *T. indica* extract may change the rate of fatty acids oxidation in the liver and reduced the rate of triglycerides biosynthesis in rats [40]. Liver functions tests in the present study included serum AST, ALT and ALP activity. The activities of AST and ALT are cytosolic marker enzymes reflecting hepatocellular necrosis as they are released into the blood after cell membrane damage. Therefore, ALT and AST are the specific markers to assess hepatocellular damage leading to liver cell necrosis [41]. Thus lowering of these enzymes content in serum is a definite indication of hepatoprotective action of a drug. In the current study data revealed that positive control group had a significant higher serum AST, ALT and ALP activity compared to

that of the negative control group. These results are in agreement with those obtained by Arkkila *et al*. [41], who reported that elevated activity of serum AST and ALT is a common sign of liver diseases and observed frequently among people with diabetes than in the general population. Ana Angelica *et al*. [42] indicated that activity of AST, ALT was increased in the serum of diabetic animals. Hamden *et al*. [43] demonstrated that increased generations of free radicals due to oxidative stress develop several adverse effects in diabetes mellitus such as hepathology and nephropathy disorders. Therefore, the oxidative stress is a common pathogenetic mechanism contributing to initiation and progression of hepatic damage in a variety of liver disorders [44]. Hyperglycemia increases the generation of free radicals by glucose auto-oxidation and the increment of free radicals may lead to liver cell damage. The increase in oxygen free radicals in diabetes could be primarily due to the increase in blood glucose levels and secondarily due to the effects of the diabetogenic agent STZ.

The present study indicated that diabetic rats had significant increase in serum levels of BUN, UA and Cr as compared to that of the negative control rats. These results are in agreement with those reported by Verma and Bordia [45], who indicated that increased kidney parameters in serum are signs of kidney dysfunctions in the diabetic disease compared to control. These results were confirmed by Uladimir [46], who revealed that hyperglycemia are associated with long-term damage, dysfunction and failure of various organs especially kidneys. Jarald *et al*. [47] showed that diabetic rats had a significant increase in creatinin and urea levels as compared to the normal animals. Kidney dysfunctions in the diabetic rats may be related to the generation of reactive oxygen species and lipid peroxidation. In addition, Shah *et al*. [48] reported that increased oxidative stress and reduced antioxidative ability in diabetes results in renal tubular injury, proteinuria and leads to gradual loss of renal function. The diabetic rats had higher values of plasma BUN than control rats [49].

The hepatoprotective and nephroprotective effects of *T. indica* extract reported in this study were evident from the significant reduction in the activity of liver enzymes (AST, ALT and ALP) and kidney function (BUN, UA and Cr) of diabetic rats. The hepatoprotective and nephroprotective effects of *T. indica* was in accordance with the those reported by Sudjaroen *et al*. [50]. The potential mechanism underlying the hepatoprotective and the nephroprotective effects of *T. indica* extract could be attributed to its antioxidant activity which possessed high phenolic contents and had potent antioxidant activities in scavenging free radicals in non-cellular based assays [24].

CONCLUSION

In conclusion, all the above complications in diabetic rats may be related to the oxidative stress resulting from the increased blood glucose level. Oxidative stress may cause oxidative damage of cellular membranes and changes in the structural and functional integrity of sub-cellular organelles and may produce effects that result in various complications in diabetes disease. This study demonstrate that *T. indica* extract significantly ameliorates hyperglycemia, hyperlipidemia due to the antioxidant effect of its phytochemicals.

REFERENCES

1. Li, Y., V.H. Tran, C.C. Duke and B.D. Roufogalis, 2012 Gingerols of *Zingiber officinale* enhance glucose uptake by increasing cell surface GLUT4 in cultured L6 myotubes. Planta Medica, 78: 1549-1555.
2. Elshater, A.E.A., Muhammad M.A. Salman and Mahrous M.A. Moussa, 2009. Effect of ginger extract consumption on levels of blood glucose, lipid profile and kidney functions in Alloxan induced-diabetic rats. Egypt. Acad. J. Biology. Sci., 2: 153-162.
3. Shanmugam, K.R., C.H. Ramakrishana, K. Mallikarjuna and R.K. Sathyavelu, 2009. The impact of ginger on kidney carbohydrate metabolic profiles in STZ induced diabetic rats. Asian J. Exp. Sci., 23: 127-134.
4. Mohajeri, D., B.A. Tabrizi, G. Mousavi and M. Mesgari, 2008. Anti-diabetic activity of *Crocus sativus* L. (Saffron) stigma ethanolic extract in alloxan-induced diabetic rats. Res. J. Biol. Sci., 3: 102-1108.
5. Kumar, C.S. and S. Bhattacharya, 2008. Tamarind Seed: Properties, Processing and Utilization. Critical Reviews in Food Science and Nutrition, 48: 1-20.
6. Shehla Imam, I. Azhar, M. Mohtasheemul Hasan, M.S. Ali and S. Waseemuddin Ahmed, 2007. Two Triterpenes Lupanone and Lupeol Isolated and Identified from *Tamarindus indica* Linn. Pak. J. Pharm. Sci., 20(2): 125-127.

7. Maiti, R.I., D. Jana, U.K. Das and D. Ghosh, 2004. Antidiabetic effect of aqueous extract of seed of Tamarindus indica in streptozotocin-induced diabetic rats. J. Ethnopharmacol., 92(1): 85-91.
8. Ursula, R.W. Chong, Puteri S. Abdul-Rahman, Azlina Abdul-Aziz, Onn H. Hashim and Sarni Mat-Junit, 2013. Effects of *Tamarindus indica* Fruit Pulp Extract on Abundance of HepG2 Cell Lysate Proteins and Their Possible Consequential Impact on Metabolism an Inflammation. Bio. Med. Research International, (1): 333-339.
9. Reevs, P.G., 1997. Components of AIN-93 diet as improvement in the AIN 76 diet. J. Nutr., 127: 838-841.
10. Kassi, E., Z. Papoutsi and N. Fokialakis, 2004. Greek plant extracts exhibit selective estrogen receptor modulator (SERM)-like Properties. J. Agric. Food Chem., 52: 6956-6961.
11. Nafiu, B.A., M.C. Maung, W. Ni, Z. Rahela and M.T. Rahman, 2011. Beneficial effects of ginger (Zingiber officinale) on carbohydrate metabolism in streptozotocin-induced diabetic rats. British J. Nut., 7: 1194-1201.
12. Trinder, P., 1969. Enzymatic method of glucose estimation. J. Clin. Path., 22: 246.
13. Clark, P.M.S. and C.N. Hales, 1994. How to measure plasma insulin, Diabet. Metab. Rev., 10: 79-90.
14. Richmond, N., 1973. Colorimetric determination of total cholesterol and high density lipoprotein cholesterol (HDL-c). Clin. Chem., 19: 1350-6.
15. Lopes-Virella, M.F., S. Stone, S. Ellis and J.A. Collwell, 1977. Cholesterol determination in high-density lipoproteins separated by three different methods, Clin. Chem., 23: 882-886.
16. Fossati, P. and L. Prenape, 1982. Serum triglycerides deter-mined colorimeterically with enzyme that produce hydrogen peroxide. Clin. Chem., 28: 2077-2080.
17. Friedewald, W.T., R.I. Levy and D.S. Frederickson, 1972. Estimation of plasma low density lipoprotein cholesterol concentration without use of the preparative ultracentrifuge. Clin. Chem., 18: 499-502.
18. Patton, C.J. and S.R. Crouch, 1977. Enzymatic colorimetric method for determination of urea in serum. Anal. Chem., 49: 464-465.
19. Fossati, P., L. Prencipe and G. Berti, 1980. Use of 3, 5-dichloro-2-hydroxybenzenesulfonic acid/4-aminophenazone chromogenic system in direct enzymic assay of uric acid in serum and urine. Clin. Chem., 26(2): 227-31.
20. Husdan, H. and A. Rapoport, 1968. Estimation of creatinine by Jaffe reaction method, Clin. Chem., 14: 222-228.
21. Carleton, H., 1979. Histological Techniques. 4th Ed., London, Oxford University Press, New York, USA, Toronto.
22. Snedecor, G.W. and W.G. Cochron, 1989. Statistical Methods. 8th Ed., Iowa State Univ. Press, Ames, Iowa., USA.
23. Razali, N., A.A. Aziz and S.M. Junit, 2010. Gene expression profiles in human HepG2 cells treated with extracts of the *Tamarindus indica* fruit pulp. Genes and Nutrition, 5(4): 331-341.
24. Razali, N., S. Mat-Junit, A.F. Abdul-Muthalib, S. Subramaniam and A. Abdul-Aziz, 2012. Effects of various solvents on the extraction of antioxidant phenolics from the leaves, seeds, veins and skins of *Tamarindus indica* L. Food Chemistry, 131(2): 441-448.
25. Habibuddin, M., H.A. Daghriri, T. Humaira, M.S. Al-Qahtani and A.A. Hefzi, 2008. Antidiabetic effect of alcoholic extract of *Caralluma sinaica* L. on streptozotocin-induced diabetic rabbits. J. Ethnopharmacol., 117(2): 215-20.
26. Lee, S.I., J.S. Kim, S.H. Oh, K.Y. Park, H.G. Lee and S.D. Kim, 2008. Antihyperglycemic effect of *Fomitopsis pinicola* extracts in streptozotocin-induced diabetic rats. J. Med. Food, 11(3): 518-24.
27. Kota, N., V.R. Virendra Panpatil, B. Kaleb and V.K. Polasa, 2012. Dose dependent effect in the inhibition of oxidative stress and anticlastogenic potential of ginger in STZ induced diabetic rats, Food Chem., 135: 2954-2959.
28. Laxmi, V., K. Anirudh, K. Basant, K. Umesh and S. Rajesh, 2010. Antidiabetic activity of *Cassia occidentalis* (Linn) in normal and alloxan-induced diabetic rats. Indian J. Pharmacol., 42: 224-228.
29. Yaghmoor, S.S. and S.M. Khoja, 2010. Effect of cinnamon on plasma glucose concentration and the regulation of 6-phosphofructo-1-kinase activity from the liver and small intestine of streptozotocin induced diabetic rats. J. of Biolog. Sci., 10: 761-766.
30. Davis, S., 2006. Insulin, Oral Hypoglycemic Agents and the Pharmacology of Endocrine Pancreas, McGraw-Hill, Medical Publishing Division, pp: 1037-1058.

31. Al-Assaf, A.H., 2012. Antihyperglycemic and antioxidant effect of ginger extract on streptozotocin-diabetic rats. Paki. J. of Nutr., 11: 1107-1112.
32. Zhang, C.Y. and B.K. Tan, 2002. Antihyperglycemic and anti-oxidant properties of *Andrographis paniculata* in normal and diabetic rats, Clin. Exp., 27: 358-363.
33. Kavalali, G., H. Tuncel, S. Goksel and H.H. Hatemi, 2002. Hypoglycemic activity of *Urtica pilullifera* in streptozotocin-diabetic rats, J. Ethnopharm., 84: 241-245.
34. Bhutkar, M.A. and S.B. Bhise, 2011. Anti-Oxidative Effect of Tamarindus Indica in Alloxan Induced Diabetic Rats. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2(3): 33-39.
35. Ramudu, S.K., K. Mllikarjuna and S.R. Kesireddy, 2011. Efficacy of ethanolic extract of ginger on kidney lipid metabolic profiles in diabetic rats. Int. J. Diabet. Dev. Ctries., 31(2): 97-103.
36. Manley, S.E., I.M. Stratton, C.A. Cull, V. Frighi, E.A. Eeley, D.R. Matthews, R.R. Holman, R.C. Turner and H.A. Neil, 2000. Effects of three months diet after diagnosis of type 2 diabetes on plasma lipids and lipoproteins (UKPDS 45). UK Prospective Diabetes Study Group, Diabet. Med., 17: 518-523.
37. Holman, R., 2001. The UKPDS: implications for the dyslipidaemic patient. Acta Diabetol., 38: 9-14.
38. Sacks, F.M., A.M. Tonkin, T. Craven, M.A. Pfeffer and J. Shepherd, 2002. Coronary heart disease in patients with low LDL-cholesterol: benefit of pravastatin in diabetics and enhanced role for HDL cholesterol and triglyceride as risk factors, J. Am. Heart Associ., 105: 1424-1428.
39. Suryawanshi, N.P., A.K. Bhutey, A.N. Nagdeote, A.A. Jadhav and G.S. Manoorkar, 2006. Study of lipid peroxide and lipid profile in diabetes mellitus, Indian J. of Clin. Biochem., 21(1): 126-130.
40. Nurhanani Razali, Azlina Abdul Aziz, Chor Yin Lim and Sarni Mat Junit, 2015. Investigation into the effects of antioxidant-rich extract of Tamarindus indica leaf on antioxidant enzyme activities, oxidative stress and gene expression profiles in HepG2 cells. J. Med. Food, 11(4): 1216-1222.
41. Arkkila, P.E., P.J. Koskinen, I.M. Kantola and J.S. Viikari, 2001. Diabetic complications are associated with liver enzyme activities in people with type 1 diabetes. Diabetes Research and Clinical Practice, 52: 113-118.
42. Ana Angelica, H.F., L.B. Ethel, F.J. Ary and M.G. Cristiano, 2009. Effect of Naringerin on Biochemical parameters in the streptozotocin-induced diabetic rats. Brazilian Archives of Biology and Technology, 52: 51-59.
43. Hamden, K., S. Carreau, S. Lajmi, D. Aloulou, D. Kchaou and A. Elfeki, 2008. Protective effect of 17"-estradiol on hyperglycemia, stress oxidant, liver dysfunction and histological changes induced by alloxan in male rat pancreas and liver. Steroids, 94: 495-501.
44. Medina, J. and R. Moreno-Otero, 2005. Pathophysiological basis for antioxidant therapy in chronic liver disease. Drugs, 65: 2445-2461.
45. Verma, S.K. and A. Bordia, 1998. Antioxidant property of Saffron in man. Indian J. Med. Res., 52: 205- 207.
46. Uladimir, O.M., 2003. Coronary risk factor. J. Diabet. Assoc. India, 29: 3-8.
47. Jarald, E.E., S.B. Joshi and D.C. Jain, 2008. Antidiabetic activity of aqueous extract and non polysaccharide fraction of Cynodondactylon Pers. Indian Journal of Experimental Biology, 46: 660-667.
48. Shah, S.V., R. Baliga, M. Rajapurkar and V.A. Fonseca, 2007. Oxidants in chronic kidney disease. J. Am. Soc. Nephrol., 18: 16-28.
49. Shou-Chieh, W., L. Shiow-Fen, W. Chau-Jong, L. Chao-Hsin, L. Wen-Chin and Huei-L. Jane, 2009. Aqueous extract from *Hibiscus sabdariffa* Linnaeus ameliorate diabetic nephropathy via regulating oxidative status in an Experimental Animal Model. CAM, 4: 1-9.
50. Sudjaroen, Y., R. Haubner, G. Wutele, W.E. Hull, G. Erben, B. Spiegelhalder, S. Changbumrung, H. Bartch and R.W. Owen, 2005. Isolation and structure elucidation of phenolics antioxidants from Tamarind (*Tamarindus indica* L) seeds and pericarp. Food and Chem Toxicol., 43(11): 1673-1682.