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Original Article

Nutrition Section

Effects of *Lactobacillus acidophilus* on Biochemical Indices and Liver Histology in Streptozotocin-induced Diabetic Rats

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ABSTRACT

Introduction: Type 2 Diabetes Mellitus (T2DM) is a chronic disease reportedly caused by insulin resistance and characterised by hyperglycaemia and altered lipid profile. Administration of probiotics may improve the prognosis of diabetes as well as alleviate associated complications and metabolic disorders. *Lactobacillus acidophilus* supplementation has been reported to have hypoglycaemic effect, maintain blood insulin level and inhibit lipid peroxidation.

Aim: To study the effects of *L. acidophilus* ATTCC4356 on plasma glucose, lipid profile, markers of liver function and hepatic histology in streptozotocin-induced diabetic rats.

Materials and Methods: Thirty-six adult albino rats were divided into six groups. Group 1 served as controls (given placebo as graded doses of distilled water), Group 2 as diabetic untreated, Groups 3, 4 and 5 received 0.05 mL, 0.1 mL and 0.2 mL (1.5×10^8 CFU) *L. acidophilus* respectively while Group 6 was treated with glibenclamide at 10 mg/kg body weight orally for four weeks. Blood glucose, lipid profile, liver enzymes, albumin and total protein were measured, microbiological profiling of faecal sample was done and hepatic tissue examined histologically. Data were analysed statistically using SPSS Version 18.0. Differences in value of biochemical parameters among the treated groups and controls were analysed using ANOVA and p-values <0.05 were considered significant.

Results: Significant decrease in glucose levels ($p<0.05$) were observed in control and treated groups compared with diabetic untreated rats with the lowest value (75.83 mg/dL) recorded in the group administered 0.2 mL *L. acidophilus* after 2 weeks. Alkaline Phosphatase (ALP) and Aspartate Aminotransferase (AST) activities were moderately decreased by probiotics treatment. There were non-significant reductions in triglyceride, total cholesterol and low density lipoprotein cholesterol ($p>0.05$) in treatment groups. Histological changes include mild haemorrhage and fibrosis across the hepatic cyto-architecture of treated and untreated rats but not controls.

Conclusion: Administration of 0.05 mL, 0.1 mL and 0.2 mL graded doses of *L. acidophilus* probiotics had weight-reducing, hypoglycaemic effects, improves dyslipidemia and hepatic enzymes activity in diabetic rats compared to controls. This showed the desirable characteristics of probiotics in ameliorating biochemical abnormalities associated with T2DM even at lower dosage. However, *L. acidophilus* did not bring about observable preservation of hepatic cytoarchitecture nor reversal of histopathological alterations associated with T2DM in diabetic-induced rats.

Keywords: Diabetes, Glucose, Lipid, Probiotics

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic health problem characterised by hyperglycaemia as a consequence of insulin resistance or from defects in beta cell insulin production [1]. Globally, approximately 366 million people are living with diabetes with about 5 million in Nigeria reflecting a prevalence rate of 8-10% in the developing country [2]. Chronic hyperglycaemia if uncontrolled can lead to the risk of microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular damage including ischaemic heart disease, stroke and peripheral vascular disease [3]. Dietary interventions, lifestyle changes and exercise are factors that may decrease the risk of developing diabetes [4,5]. With the increase in the incidence of diabetes and its associated macro and micro-vascular end-organ damage, there is a requirement for a natural and safe approach to control and delay such complications.

Effect of insulin loss on the liver leads to glycogenolysis and an increase of hepatic glucose production. Mild chronic elevations of transaminases often reflect underlying insulin resistance [6]. Studies have reported some biochemical abnormalities including concomitant increase in liver enzymes activity with insulin resistance, elevated Low Density Lipoprotein-Cholesterol (LDL-C), hypercholesterolemia, hypertriglyceridemia and reduced High Density Lipoprotein-Cholesterol (HDL-C) in diabetics [7,8]. The drugs widely used in clinical management of diabetes are insulin, sulfonylureas, biguanide, glycosidase inhibitors, aldose reductase inhibitor, thiazolidinediones, carbamoylmethylbenzoicacid, however, existing treatments have limitations such as weight gain, dizziness, bloating and hepatic toxicity [9,10]. Consequently, increasing demand for alternative therapies particularly dietary based interventions is advocated. One of the novel approaches currently is through the intervention of probiotics. Probiotics are live microbial food supplements which when administered in adequate amount confer a health benefit on the host; examples of probiotics are *Lactobacillus rhamnosus* GG, *Lactobacillus acidophilus*, and *Bifidobacterium bifidum* [11].

Several health benefits have been accredited to probiotics, including effects on gastrointestinal tract function and diseases, immune function, hyperlipidemia, hypertension and allergic conditions [12]. The use of probiotic as dietary supplements significantly delayed the onset of glucose intolerance, hyperglycaemia, hyperinsulinemia, dyslipidemia and oxidative stress in high fructose-induced diabetic rats, demonstrating a lower risk of diabetes and its complications [10]. It has also been demonstrated that probiotics can decrease the blood glucose through improvement in inflammation and prevention of β-cell destruction in animal models. Several new mechanisms by which probiotics exert their beneficial effects have been identified and it is now well established that significant differences exist between different probiotic bacterial species and strains and the benefits accrued are highly strain specific [12]. Thus, in order to harness the therapeutic potentials of probiotics for the wellbeing and health management of diabetic population in the country, it

would be appropriate to investigate their anti-diabetic effects in a rat model.

Single and double blinded controlled trials revealed that *Lactobacillus* strains including *L. acidophilus, L. bifidum, L. bulgaris* and *L.Casei* supplementation brought about improved plasma glucose levels, non-significant reductions in triglycerides and significant increase in HDL-C in type 2 diabetes [7,13]. However, a study of effect on probiotics on blood lipid levels by Sun J and Buys N, did not find any significant relationship between triglyceride, HDL-C levels and probiotics use [14]. Similarly, Yao K et al., recorded no significant improvement in lipid metabolism upon probiotics administration in T2DM patients [15].

Notably, significant reductions in AST, alanine aminotransferase and gamma glutamyl transferase activities after treatment with probiotics in patients with liver disease compared with the use of standard therapy alone substantiates the ability of probiotics to prevent altered intestinal microbiota that may induce liver damage [16-18].

There are discrepancies in reports of previous studies on effects of probiotics supplementation on plasma lipid profile in diabetes [7,13-15]. Moreover, information on the composite effects of probiotics on lipid profile, markers of liver function and modifications in hepatic cytoarchitectrein diabetes mellitus is scanty [19] therefore; the present study investigates the effect of *Lactobacillus acidophilus* administration on the body weight, plasma lipid profile, liver enzyme activities as well as liver histology in streptozotocin-induced diabetic Wistar rats.

MATERIALS AND METHODS

This is an interventional case-control study. This study was conducted at the research laboratory of the College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria. The present study was conducted from May 2018 to June 2018.

Laboratory Animal Model

A total of 36 adult male Albino rats weighing between 80-110 gm were acquired from the animal house unit of Department of Biomedical Laboratory Sciences, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria. They were kept in clean cages under standard laboratory conditions of 12 hour light and 12 hour dark cycle with temperature of 65-75°F (~18-23°C) and 40-60% humidity throughout the experimental period.

The animals were induced with Streptozotocin (STZ) before investigating the effects of the novel *Lactobacillus acidophilus* ATTCC 4356. A proposal for this study was submitted to the College Research and Ethics Committee of Ladoke Akintola University of Technology, Osogbo, Nigeria that regulate experiments involving human and animal model. Approval was sought for and obtained from the College Research and Ethics Committee (Ref. no: LAU/CHS/CS/CRE/003) before commencement of the study.

Streptozotocin Model

The animals were fed on antibiotics free ration and given water *ad libitum* for one week. They were then grouped into 6: Group 1 served as the control, Group 2 as diabetic untreated, Groups 3, 4 and 5 received 0.05 mL, 0.1 mL and 0.2 mL of *L. acidophilus* ATTCC4356 (1.5×10^8 CFU/mL) respectively with turbidity level of 0.5 Mac Farland Standard while Group 6 received glibenclamide at 10 mg/kg body weight orally by gavage in drinking water daily for four weeks. The control group was given distilled water. Glibenclamide (Daonil) was used as standard drug.

The animals were fasted for 6 hours before intravenous injection with streptozotocin at the dose of 50 mg/kg body weight except for the control and standard drug groups. Streptozotocin induces diabetes within three days by destroying the beta cells of pancreatic islets of langerhans resulting in decreased endogenous insulin release [20].

Blood glucose levels were monitored every day until diabetic glucose levels of 350 mg/dL was attained and then the animals were subsequently enrolled in the study.

Bacterial Culture

Stock cultures of *L. acidophilus* was obtained from Federal Institute of Industrial Research, Oshodi, Lagos, Nigeria and resuscitated on de Man, Rogosa and Sharpe (MRS) broth, plated on MRS agar and confirmed by standard microbiological procedure. Inoculum were prepared with sterile MRS broth and standardised to obtain 0.05 and 0.1 mL and 0.2 mL of L acidophilus in groups 3-5, respectively. To determine faecal shedding of the organism in the stool samples of the oral inoculated rats, faecal samples were collected and stored in a sterile sample bottle until transported to the laboratory for microbiological processing. Approximately, 1 gm of faecal sample was obtained from all rats and serially diluted 10-fold (from 10^{-1} to 10^{-7}) with sterile physiological saline solution (0.9% NaCl) and subsequently homogenised for 3 minutes by hand rocking. Dilutions were then plated onto selective agar medium (de Man–Rogosa–Sharpe agar Oxoid Ltd., Hampshire UK) for enumeration of Lactobacilli. *Lactobacillus* plates were incubated anaerobically at 37°C for 48 hour. Bacteria were enumerated by visual counting of colonies using the best replicate set from dilutions that resulted in 30 to 300 colonies per plate. The microbial enumerations were expressed as base-10 logarithm colony-forming units per gram of one gram of rat faecal sample.

Blood Sample Collection and Biochemical Measurements

The control and diabetic rats were anaesthetised with ether (2 minutes contact), 5 mL peripheral venous blood was collected from the tail vein and appropriate volumes dispensed into fluoride oxalate bottle (for glucose analysis) and pyrogen-free plain sample containers. Serum was separated from blood by centrifugation at 2500×g for 10 minute and kept frozen until analysis.

Fasting blood glucose level was measured weekly by the glucose-oxidase-peroxidase method as previously described [21]. After week 4 of experiment, Triglyceride (TG), Total Cholesterol (TC) and HDL-C were quantified using commercially available enzymatic kits (Boehringer Mannheim, Germany). Low density lipoprotein-cholesterol was calculated using Friedewald formula: (LDL-C=TC-TG/5–HDL-C).

Plasma albumin was estimated based on the bromocresol green method (AgappeDiagnostics, Switzerland). Total protein, ALT, AST were analysed using marketed reagent (Randox laboratory limited, County Antrim, UK) and ALP by direct colourimetric endpoint method (Teco diagnostics, Anaheim, CA).

Histological Investigations

The experimental animals were anaesthetised by chloroform, sacrificed and histological examination was performed after the fourth week of experiment. Liver tissue samples from all animals were excised and immediately fixed in 10% formalin overnight, embedded in paraffin, cut into 5 µm sections, placed on slides and stained with Haematoxylin and Eosin (H&E). Photomicrographs were taken at 40x and 100x magnifications for each group and compared with the control.

STATISTICAL ANALYSIS

Data were analysed using SPSS Version 18.0 and were expressed as mean±Standard Error of Mean (SEM). Group comparisons for body weight, blood glucose and other biochemical parameters were carried out using one way analysis of variance. Where the results were significant ($p<0.05$), multiple comparisons post-test were done using Tukey's test.

RESULTS

The effects of *L.acidophilus* on the body weight of the experimental animals and the control group are shown in [Table/Fig-1]. There were no significant differences in body weight of probiotics treatment group compared to controls (p>0.05). However, at week 4, the body weight of rats in the treated groups were decreased than that of controls (p<0.05).

From [Table/Fig-2], significant decrease (p<0.001) in blood glucose level was observed in the treated animals than glibenclamide treated rats and controls after Day 1. The increase in glucose concentration (p<0.001) recorded in the intervention Groups 2, 3 and 4 were reversed after one week of *L.acidophilus* administration with the lowest value recorded in the group treated with 0.2 mL probiotics.

Results of lipid profile analysis showed modest non-significant increases in triglyceride and total cholesterol levels (p>0.05) in STZ-induced diabetic than probiotics treated animals with least values recorded in 0.1 mL and 0.2 mL of *L. acidophilus* respectively while the highest value was recorded in Group 6. A similar pattern was observed for blood LDL-C but Group 3 (0.05 mL) had the lowest value. Glibenclamide-treated rats showed a non-significant increase in HDL-C compared to the other groups [Table/Fig-3].

The effect of probiotics on markers of liver function was depicted in [Table/Fig-4]. Serum AST was increased in diabetic rats than controls (p<0.01) and probiotics treatment groups (p<0.05). ALT level was decreased by 0.1 mL in treated group as compared to other groups (p<0.01) while ALP was significantly decreased in standard drug than controls.

Histopathological Findings

The [Table/Fig-5a-f] represents the light photomicrographs of rat hepatic histomorphological presentation showing panoramic views of adult male rat liver histology (100x magnification). The Portal Triad system (PT) composed of the Hepatic vein (Hv), Hepatic artery (Ha), Bile duct (Bd), Hepatocytes (H) as well as the hepatic duct system and other vessels are well demonstrated but not conspicuously across the micrographs.

In control animals, the section showed a liver tissue with well-preserved architecture. The portal triads are in good order. There are no areas of fibrosis, inflammation or necrosis. There is mild dilatation of the sinusoids.

Comparative observation across the other experimental groups showed a well outlined array of hepatic cells and vessels with no observable cytoarchitectural distortion except for mild haemorrhage localised within the walls of the hepatic blood vessels in the diabetic untreated group while that of the 0.2 mL LA treated animals are characterised by mild to severe haemorrhage and fibrosis across the hepatic cytoarchitecture represented by the yellow arrow at 100x magnification.

DISCUSSION

Diabetes mellitus is a disease that results from altered insulin secretion bringing about changes in blood glucose dynamics. Increase in blood glucose level may result from a decrease in production of insulin thereby inhibiting glucose entry into cells. The same effect will be seen if insulin is secreted from the pancreas but is not properly utilised by target cells [14]. Control of blood sugar, dyslipidemia

BW	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	p-value
Initial	88.67±2.19	106.83±1.96	104.67±2.16	105.80±2.42	105.0±1.37	105.33±2.53	<0.01*
Week 1	100.83±4.92	98.20±3.79	77.83±15.96	95.83±2.52	83.17±5.35	94.17±2.29	0.22
Week 2	127.67±6.51	123.80±10.43	100.33±20.71	118.50±7.46	107.0±7.88	116.83±5.90	0.51
Week 3	127.50±7.58	131.80±12.31	110.67±22.83	108.83±3.99	105.50±1.96	124.33±7.92	0.74
Week 4	134.00±7.14	125.33±22.10	105.67±21.64	103.17±23.55	103.0±21.65	116.25±10.22	<0.01*

[Table/Fig-1]: Changes in body weight (g) of animals studied (mean±SEM).
*significant@p<0.05, BW: Body weight

Variables	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	p-value
Initial	82.83±2.87	80.50±3.11	80.17±2.77	67.67±13.90	78.83±2.24	79.50±2.43	0.69
Week 1	85.33±3.85	345.00±20.32	156.00±31.49	182.00±2.59	159.00±2.92	251.33±13.46	0.01*
Week 2	87.83±2.44	338.40±17.49	115.33±24.17	121.00±5.22	103.17±4.42	109.17±3.90	<0.01*
Week 3	85.33±3.31	359.20±24.24	85.00±17.32	81.00±16.41	73.67±14.99	97.17±2.98	<0.01*
Week 4	89.75±1.49	398.67±64.97	89.33±18.20	85.83±18.55	75.83±15.5	105.25±5.22	<0.01*

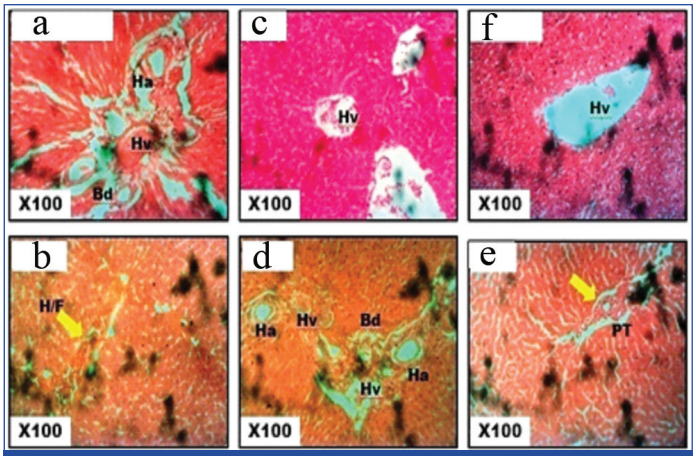
[Table/Fig-2]: Blood glucose level (mg/dL) per week in treated and control animals (mean±SEM).
*significant@p<0.05

Parameters/Groups	1	2	3	4	5	6	p-value
TG (mg/dL)	113.28±10.2	146.03±22.1	106.20±6.05	84.96±11.4	112.28±18.0	97.35±20.8	0.26
TC (mg/dL)	150.81±5.04	176.28±9.31	146.95±15.5	155.45±3.33	139.99±6.16	156.92±11.9	0.05
LDL-C (mg/dL)	54.14±2.45	58.01±7.23	38.67±1.00	50.27±5.19	47.23±3.94	44.14±3.87	0.05
HDL-C (mg/dL)	20.11±1.45	23.20±3.87	20.62±3.41	23.98±4.13	29.39±3.59	31.90±5.55	0.20

[Table/Fig-3]: Serum lipid profile of animals studied (mean±SEM).
TG: Triglyceride; TC: Total cholesterol; LDL-C: Low density lipoprotein; HDL-C: High density lipoprotein

Parameters/Groups	1	2	3	4	5	6	p-value
AST (U/L)	37.52±1.80	59.34±4.08	35.45±4.95	39.08±3.55	36.66±1.82	26.45±3.62	0.01*
ALT (U/L)	31.55±2.33	39.36±1.43	18.90±1.80	33.22±2.59	34.06±3.91	33.48±2.75	0.02*
ALP (U/L)	53.02±10.47	38.10±1.90	39.80±2.61	33.66±2.13	36.84±1.82	29.65±2.87	0.03*
ALB (g/L)	31.17±2.33	26.20±2.63	32.60±1.89	34.60±2.64	33.50±4.50	27.75±0.85	0.21
TP (g/L)	56.83±1.76	55.75±2.32	59.60±2.50	66.40±3.31	62.80±2.03	60±1.50	0.05

[Table/Fig-4]: Effect of *L.Acidophilus* on liver function markers (mean±SEM).
*significant@p<0.05; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase, ALB: Albumin; TP: Total protein



[Table/Fig-5]: Light photomicrographs of rat hepatic histomorphological presentation (x100).
H: Hepatocytes; Hv: Hepatic vein; PT: Portal triad system; Ha: Hepatic artery; Bd: Bile duct; H/F-Fibrosis **a)** represents hepatic histology of control rats showing hepatic tissue with well preserved architecture with no fibrosis but mild dilatation of the sinusoids; **b)** represents hepatic histology of diabetic untreated rats showing mild haemorrhage localised within the walls of hepatic blood vessels with fibrosis (yellow arrow); **c)** crepresents hepatic histology of rats treated with 0.05 mL *L.acidophilus*. This showed no observable cytoarchitectural distortion except for haemorrhage; **d)** represents hepatic histology of rats treated with 0.1 mL *L.acidophilus* showing hepatic inflammation and necrosis; **e)** represents hepatic histology of rats treated with 0.2 mL *L.acidophilus*. showing severe haemorrhage and fibrosis (yellow arrow); **f)** represents hepatic histology of rats administered glibenclamide (standard drug). This showed haemorrhage within the walls of hepatic vein

and other risk indices are essential in the management of diabetes. Probiotics are reported to play a beneficial role in alleviating the deleterious effects of metabolic factors associated with diabetes [22-24]. This study was therefore designed to determine the effects of probiotics treatment on blood glucose level, lipid profile and histological alterations in diabetes-induced Wistar rats.

In this study a significant decrease was observed in the concentration of blood glucose in the rat groups treated with probiotics and glibenclamide. This observation may be due to adequate release of insulin which helps to regulate blood glucose level [22] by promoting the storage of glucose in the liver or it may be as a result of increase in utilisation of glucose in the body or as a result of administration of probiotics which might have repaired the damaging beta cells and in turn trigger endogenous insulin production [25]. This is in agreement with the findings of the work by Yadav H et al., on effect of probiotics supplementation on diabetes-induced rats that showed the ability of *L. gasseri* and *L. acidophilus* in delaying progression of diabetes and thus reducing hyperglycaemia in their experimental animals [26]. They attributed their observations to the ability of probiotics supplemented dahi in inhibiting the depletion of insulin thereby facilitating entry of glucose into cells for utilisation.

Triglycerides are fats that are stored and used up as energy. Cholesterol is the precursor of steroid hormones and bile acids and it is important as storage and transport form of energy [27]. Probiotics including *L.acidophilus* have been reported to have hypocholesterolemic effect and bring about decrease in blood triglyceride and low density lipoprotein cholesterol in T2DM patients according to some studies [7,8]. Lipid profile results from this study showed non-significant increases in triglyceride and total Cholesterol levels in the diabetic untreated group but decreased levels in the probiotic treated groups compared to controls. This observation is in agreement with reports of 2 controlled trial studies by Mazloom Z et al., [7] and Sun J and Buys N, [14] that reported the effectiveness of probiotics on lowering lipids in cardiovascular disease and Type 2 diabetes. However, at variance with another by Yao K et al., that found no significant relationships between probiotics intake and improved lipid metabolism in diabetics [15]. Probiotics organism exerts its TG-lowering effect in hypertriglyceridemic rats probably by promoting the lipolytic action of lipoprotein lipase enzyme in degradation of TG-rich lipoproteins into fatty acids and glycerol in the adipose tissue [28]. This corroborates the reversal of the weight gain that was observed in the diabetic group after treatment with *Lactobacillus acidophilus*. Probiotics are also reported to be involved in upregulating mRNA expression of Apolipoprotein A-V and bile acid receptor (FXR) both essential in fatty acid metabolism [28].

Results from the present study showed an increase in serum HDL-C and a non-significant decrease in LDL-C level in probiotic treated groups when compared to the control group. This suggested a positive effect of the *L. acidophilus* administered to the Wistar rats. This observation is in line with a previous research carried out by Mehdi GJ et al., on effect of probiotics on blood parameters that showed increased HDL, decreased total and LDL cholesterol in their experimental animals upon consumption of yoghurt containing *Lactobacillus acidophilus* and *Bifidobacteria* probiotics [8]. LDL-C is small particles that could penetrate arterial intima, build-up and accumulate in the blood vessels predisposing to development of atherosclerosis and thus referred to as 'bad' cholesterol. HDL on the other hand plays a beneficial role of helping in reverse transport of excess cholesterol from peripheral tissues to the liver for excretion [7]. A proposed mechanism for cholesterol-lowering effect of probiotics is through its action of deconjugation of bile salt thus preventing its recycling and thereby inhibiting reabsorption and subsequent excretion of bile salts [29].

ALT and AST are intracellular hepatic enzymes that are leaked into the circulation when there is injury to the hepatic cells resulting in increased activity in blood. Elevated concentrations of alkaline phosphatase and bilirubin are reflections of impaired biliary function and cholestasis while plasma albumin level is a marker of synthetic ability of the liver [6]. ALP and AST activities were decreased in the probiotics and standard drug treated group than the controls while albumin and total protein were not significantly different in rats administered 0.05 and 0.1 mL *L. acidophillus*. This observation was similar to reports from other studies on the role of probiotics on liver enzymes' activity [16-18]. This could be regarded as a beneficial effect of administering *Lactobacillus acidophilus* which is effective in maintaining the integrity and activity of the epithelial cells lining the biliary duct indicating a direct effect of probiotics in improving liver function [30].

Results of the histopathological analysis from the present study did not reveal any appreciable effects of probiotics on hepatic architecture in diabetic-induced rats. This is similar to reports from a study that showed no significant improvement in liver parameters in hepatic encephalopathy upon treatment with *L. acidophilus* preparation [31] and at variance with another [19] that observed an improvement in liver morphology after probiotics treatment. There may be other underlying factors responsible for the mild morphological distortions observed in the hepatocytes in the present study. A previous study on liver disease and diabetes mellitus also reported an association between hyperglycaemia and damage to hepatocytes. It was suggested that the mild fibrosis recorded in liver cells in diabetes is due to accumulation of fat (steatosis) in vesicles thereby displacing hepatic cytoplasm [32].

LIMITATION

The small sample size of the experimental rats may reduce the statistical power of evaluating the analysed parameters. The short duration of the study could hinder a concise conclusion on effects of probiotics intervention. A further study is expected to explain the underlying mechanisms of beneficial effects of *L.acidophillus* administration on diabetes related biochemical parameters and histological abnormalities.

CONCLUSION

This study demonstrated that administration of *Lactobacillus acidophilus* had a hypoglycaemic effect, improved dyslipidemia and hepatic enzymes activities but had no effect on the hepatocyte haemorrhage and fibrosis associated with diabetes in the studied

animals compared to controls. Administration of probiotics at higher doses and for a longer period of time could bring about the desired effects of ameliorating the distortions in hepatic cyto-architecture as observed in this study.

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