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Research Article

Hypoglycemic Effects of Inactivated *Lactobacillus brevis* YM 1301 on T2DM Mice

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Lactobacillus brevis (*L. brevis*) is a widely used probiotic with health-promoting properties. Previous studies reported that *L. brevis* has beneficial impacts on T2DM mice. On the other hand, the differences in effects between live and inactivated *L. brevis* are still inconclusive. This study aims to evaluate the hypoglycemic effects of inactivated *L. brevis* YM1301 (YM1301) on T2DM mice induced by a high-fat diet (HFD) combined with streptozocin (STZ). T2DM mice were randomly stratified into four groups and administered either saline (model group), metformin (positive control group), live YM1301 (LB group), or inactivated YM1301 (ILB group). Results demonstrated that inactivated YM1301 reduced serum content of fasting blood glucose, insulin, and glycated hemoglobin, enhanced the level of glucose tolerance, and decreased insulin resistance in T2DM mice. Inactivated YM1301 also decreased fat accumulation in T2DM mice. In addition, inactivated YM1301 effectively promoted serum GLP-1 levels. These results showed that inactivated YM1301 can significantly improve symptoms of T2DM. This study provides theoretical feasibility for the development of low-cost, easy to store, safer, and more effective probiotic products related to *L.* brevis.

1. Introduction

The Food and Agriculture Organization and the World Health Organization (FAO and WHO) have defined probiotics as live bacteria which confer a health benefit on the host when administered in adequate amounts [1]. Probiotics' therapeutic benefits have been gradually identified in recent years. Probiotics can cure or relieve a variety of diseases through oral administration [2, 3]. By colonizing the human gut, probiotics directly or indirectly regulate the composition of the host's gut microbiota to bring health benefits [4]. The majority of probiotic preparations come in the form of live bacteria that can colonize the human intestine and compete with pathogenic bacteria to enhance the intestinal microecosystem and boost health. Research verified that *S. boulardii* has clear beneficial effects on children with acute diarrhea [5], and *Lactobacillus* GG is effective in treating acute gastroenteritis [6]. Probiotics could also prevent antibiotic-associated diarrhea by maintaining the gut barrier, restoring the gut microflora, and using other potential mechanisms [7].

Oral probiotics have a very poor chance of surviving once they enter the intestinal tract because of the strong acid environment of gastric juice and the presence of several digestive enzymes. It is also challenging to estimate the number of probiotics that successfully colonized the stomach and were still viable. According to studies, inactivated *A. muciniphila* has a better effect than live *A. muciniphila* at reducing body weight gain, glucose tolerance, and insulin resistance in obese mice fed a high-fat diet [8]. Therefore, in probiotic preparations, it is unclear whether live bacteria, bacterial metabolites, or both bring health benefits. Further investigation is still required for particular probiotic species. Substances released or

produced by microorganisms that directly or indirectly have a beneficial effect on the host are known as postbiotics [9]. Postbiotics could enhance intestinal epithelial function and modulate the immune or nervous systems through indirect modulation of the microbiota [10], and they also achieve similar effects on live bacteria in lowering blood glucose levels [11]. In addition, compared with probiotics, postbiotics have a better stability and safety profile, without the risk of inducing bacteraemia. Consequently, specific components of bacterial lysates, or inactivated bacteria, can be used as potential alternatives to live bacteria. Postbiotic preparation has better stability than probiotics, which can also be used as food ingredients. In addition, postbiotics are heat sterilised to allow high density concentration, keep contamination to minimum, and prolong their shelf life.

Intestinal flora is closely related to the occurrence and development of diabetes. Increased abundance of harmful bacteria can lead to the imbalance of intestinal flora and intestinal dysfunction, making diabetes susceptible [12]. Dysbiosis of intestinal flora can produce harmful metabolites and induce destruction of islet cells. An increase in Gram-negative bacteria increases the secretion of endotoxin, which is closely related to hyperglycemia and insulin resistance [13]. Lactic acid bacteria are the most common probiotics that could inhibit pathogenic bacteria and improve gastrointestinal function [13]. Related studies confirmed that lactic acid bacteria have a definite palliative effect on type II diabetes [14], and their mechanism is related to activating insulin signaling pathways, relieving insulin resistance, regulating intestinal flora, and reducing inflammation [15]. Therefore, this study focused on whether inactivated YM1301 (ILB) has a beneficial effect on type II diabetes symptoms.

2. Materials and Methods

2.1. Bacterial Cultures. YM1301 (LB) was provided by the Yunnan Institute of Microbiology, China. Both MRS broth medium and agar were purchased from Beijing Aobo Star Biotechnology Co., Ltd.

MRS solid medium was sterilised by autoclaving at 121°C for 25 min. After cooling down to room temperature on the inclined plane, LB was inserted and cultured at 37°C for 24 h in an incubator. The revitalisation process was repeated 3 times. Colonies on the inclined medium were selected and inoculated into MRS liquid medium. After 18 hours, LB cells were harvested by centrifugation. LB suspensions were obtained by diluting LB cells to 1×10^8 CFU/mL with normal saline. ILB suspensions were obtained by autoclaving. Live cells were counted by the colony-forming unit count using the spread plate technique.

2.2. Animals and Experimental Design. All Kunming mice were used according to the "Guidelines for the Care and Use of Laboratory Animals" of the National Institutes of Health and were approved by the Animal Care and Use Committee of Shaanxi Normal University (ECES-2019-0322).

Fifty male Kunming mice (6 weeks old, 18 ± 2 g) were purchased from the Experimental Animal Center of Xi'an Jiaotong University (Xi'an, China), animal production license No. SCXK (Shan) 2017-003. All mice were maintained in an environmentally controlled facility (23 ± 1°C room temperature and 50 ± 10 relative humidity) with a diurnal light cycle and were given free access to water and a standard rodent diet. Before the experiment, all animals were made to adapt to the laboratory environment for 7 days.

All mice were randomly divided into 2 groups, the normal control group (*N.* control, 10 rats) and the T2DM group (40 rats). The T2DM group mice were treated with a high-fat diet (HFD) for 5 weeks. At the 6th week, the mice were injected intraperitoneally with STZ (70 mg/kg, twice, 48 hours between injections, Sigma, USA). After 3 weeks, the mice were considered to be diabetic if their fasting blood glucose >11.1 mmol/L, which was detected by using a glucometer (Sinocare Biosensing Co., China). The T2DM model mice were randomly divided into 4 groups: (1) the model group, (2) the positive control group (*P.* control), (3) the YM1301 group (LB), and (4) the inactivated YM1301 group (ILB). At the 9th week, (1) *N.* control mice were given free access to normal diet and water and were orally gavaged with 0.2 normal saline. (2) Model mice were given free access to HFD and water and were orally gavaged with 0.2 normal saline. (3) *P.* control mice were given free access to HFD and water and were orally gavaged with 150 mg/kg metformin hydrochloride (Shandong Mingren FREDA Pharmaceutical Co., Ltd., China). (4) LB mice were given free access to HFD and water and were orally gavaged with LB solution (1×10^9 CFU/kg). (5) ILB mice were given free access to HFD and water and were orally gavaged with ILB (heat-inactivated LB) solution. The treatments with the abovementioned agents were performed daily for a 4-week study period.

2.3. Oral Glucose Tolerance Test and the Insulin Tolerance Test. The oral glucose tolerance test (OGTT) and the insulin tolerance test (ITT) were performed after a 4-week treatment. (1) In the OGTT, mice fasted for 12 h and blood glucose was determined (time = 0 min). Then, mice were orally administered glucose (2 g/kg), and blood glucose levels were measured at 30, 60, and 120 min. (2) In the ITT, mice fasted for 2 h and blood glucose was determined (time = 0 min). Then, mice were injected with insulin (Novo Nordisk, China) at a dose of 0.75 IU/kg, and blood glucose levels were measured at 30, 60, and 120 min. The glucose curve was plotted, and then, the area under the curve (AUC) was calculated using GraphPad Prism 7.04.

2.4. Blood and Tissue Sample Collection. At the end of the treatment (week 12), mice fasted for 12 h and were weighed; their fasting blood glucose (FBG) of tail venous blood was measured by using a glucometer (Sinocare Biosensing Co., China), and they were anesthetized with sevoflurane. Blood samples were collected from the orbital vein and centrifuged. Then, the serum was collected and stored at −80°C for

further assays. Liver, renal, appendix, muscle, and epididymal fat tissue samples were quickly removed, rinsed, weighed, and stored at −80°C.

2.5. Biochemical Analysis. Fasting insulin (FINS) was determined by using the insulin ELISA Kit (Novo Nordisk Pharmaceutical Co., China). Glycated hemoglobin (GHb) was determined by using the glycated hemoglobin ELISA Kit (Shanghai Enzyme Co., Ltd., China). Liver glycogen and muscle glycogen determination was determined by using the glycogen assay kit (Nanjing Jiancheng Bioengineering Institute, China). Urea nitrogen (BUN) and serum creatinine (SCR) determination followed the instructions of the BUN ELISA kit (Shanghai Enzyme Co., Ltd., China) and SCR ELISA kit (Shanghai Enzyme Co., Ltd., China). Glucagon-like peptide 1 (GLP-1) determination followed the instructions of the GLP-1 ELISA kit (Shanghai Enzyme Co., Ltd., China). HOMA-IR was calculated by the following formula: HOMA-IR = FBG (mmol/L) × FINS (mU/L)/22.5.

2.6. Statistical Analysis. All data were expressed as the mean ± standard deviation. The multisample analysis was performed through the one-way analysis of variance (ANOVA) using SPSS 16.0. Graphics were constructed using GraphPad Prism 6. Duncan's test was used to compute statistically significant differences at $p < 0.05$ and statistically significant differences at $p < 0.01$.

3. Results

3.1. Effects of Inactivated L. brevis YM1301 on Glucose Homeostasis and Insulin Sensitivity in T2DM Mice. As shown in Figure 1(a), the fasting blood glucose (FBG) level in T2DM mice after the 8-week induction by HFD and STZ was higher than that in normal mice (no animal mortality occurred at this induction dose) ($p < 0.01$). After the 4-week administration period, the fasting blood glucose level of the *P.* control, LB, and ILB groups was significantly decreased ($p < 0.01$) compared with that of the model group. T2DM mice also exhibited a significant increase in GHb. The treatment in the T2DM mice with all the abovementioned testing agents caused a significant decrease in GHb levels ($p < 0.01$) (Figure 1(b)). The OGTT results in Figure 1(c) show that the serum glucose level was higher in the model group than that in the *N.* control group and three treatment groups at each time point of measurements (0, 30, 60, and 120 min). The results in Figure 1(d) further reveal that the serum glucose AUC_{OGTT} of the *P.* control, LB, and ILB groups decreased significantly when compared to that of the model group ($p < 0.01$). In summary, YM1301 and inactivated YM1301 could both restore and maintain glucose homeostasis in the T2DM mice.

As shown in Figure 1(e), T2DM mice showed insulin resistance, since the model group retained high-glucose levels over the next 120 min after loading insulin. Oral treatment with LB and ILB produced a significant reduction in blood glucose at 120 min. The three treatment groups reduced the AUC_{ITT} values, respectively, compared with the model group, as shown in Figure 1(f) ($p < 0.01$). As shown in Figure 1(g), the fasting serum insulin (FINS) level of the model group was significantly higher than that of the *N.* control group ($p < 0.01$), which further confirmed the presence of insulin resistance in the model group. The serum insulin level and HOMA-IR of the *P.* control, LB, and ILB groups were significantly decreased compared with those of the model group after treatment, as shown in Figure 1(h) ($p < 0.01$). In conclusion, YM1301 and inactivated YM1301 both exhibited great efficacy in improving insulin sensitivity.

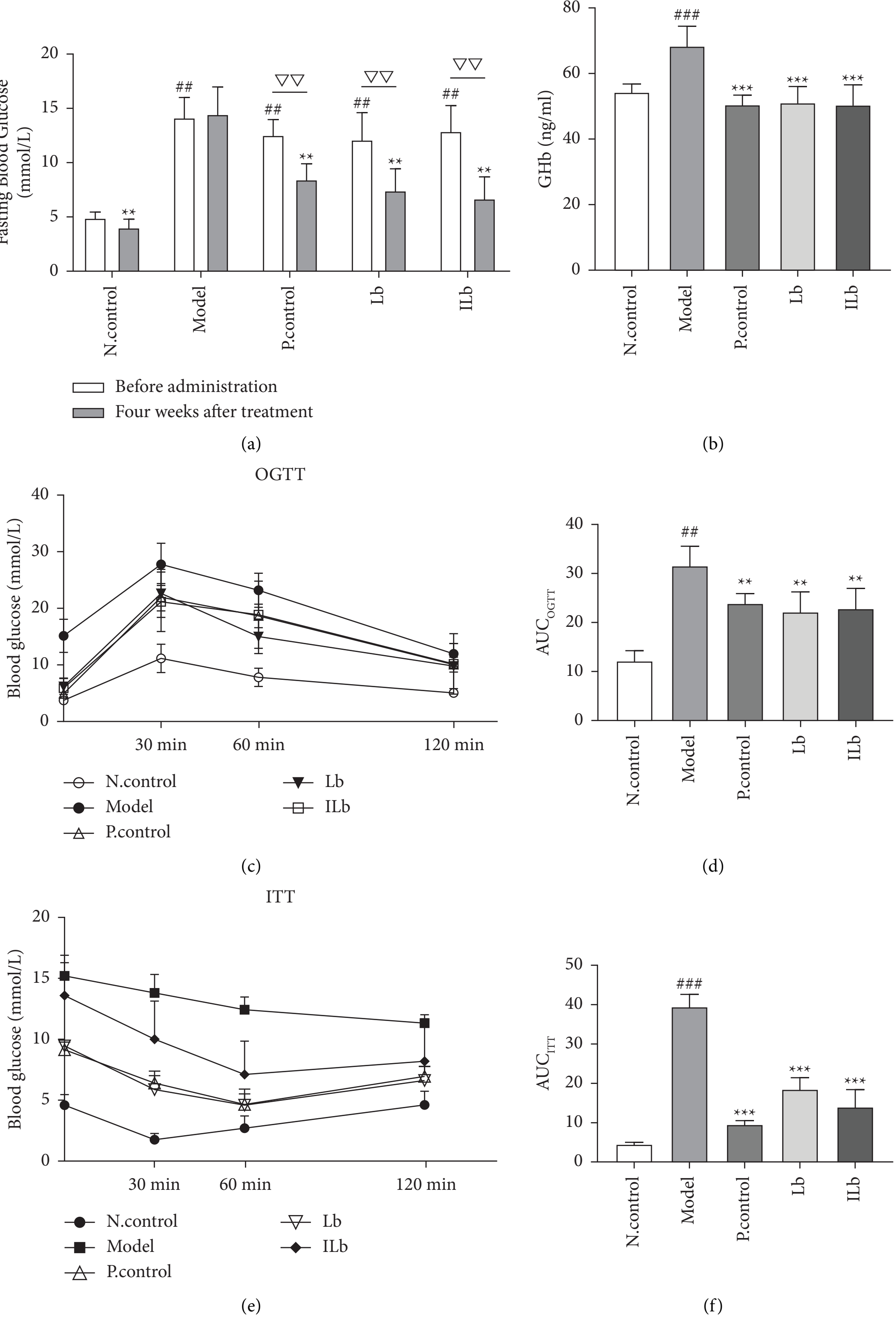
3.2. Effects of Inactivated L. brevis YM1301 on Glucolipid Metabolism-Related Indicators in T2DM Mice. As shown in Figure 2(a), the level of hepatic glycogen in the model group was significantly higher than that in the *N.* control group ($p < 0.01$). Administration of YM1301 and inactivated YM1301 significantly reduced the level of hepatic glycogen compared to the model group mice ($p < 0.05$). The myogenic glycogen content level was significantly lower in the *P.* control and LB groups than that in the model group (Figure 2(b)) ($p < 0.05$). In addition, myogenic glycogen content showed a decreasing trend in the ILB group compared to the model group, but there was no significant difference (Figure 2(b)) ($p > 0.05$).

Fat accumulation can exacerbate insulin resistance in T2DM. As shown in Table 1, the epididymal adipose tissue index (EATI) of the LB and ILB groups significantly reduced compared to that in the model group ($p < 0.05$). According to the result, administration of YM1301 and inactivated YM1301 can reduce fat accumulation in the T2DM mice.

Type II diabetes usually leads to abnormal lipid metabolism, which can cause inflammatory necrosis and fibrosis in the liver [16]. The results in Table 2 reveal that the liver index of mice was higher in the model group than that in the *N.* control group ($p < 0.05$). However, the liver index of mice was significantly reduced in the LB and ILB groups compared to that in the model group ($p < 0.05$). Moreover, the liver of mice in the model group showed a whitish color compared with the color of the liver in the other groups. In conclusion, administration of YM1301 and inactivated YM1301 could improve liver function in the T2DM mice.

A high-fat diet alters intestinal bacterial metabolism, thereby reducing cecum contents and cecum weight [17]. As shown in Table 3, the cecum index decreased significantly in the model group compared with the *N.* control group ($p < 0.05$), and the cecum index increased significantly in all the treatment groups compared with the model group ($p < 0.01$). The results suggest that administration of YM1301 and inactivated YM1301 have a restorative effect on dysbiosis of intestinal flora caused by type II diabetes.

3.3. Effects of Inactivated L. brevis YM1301 on Renal Function in T2DM Mice. Diabetic nephropathy (DN) is one of the complications of diabetes mellitus, which is the structural damage of glomeruli caused by the disorder of glucose metabolism. [18]. As shown in Table 4, there was no significant difference between the model group and the *N.*



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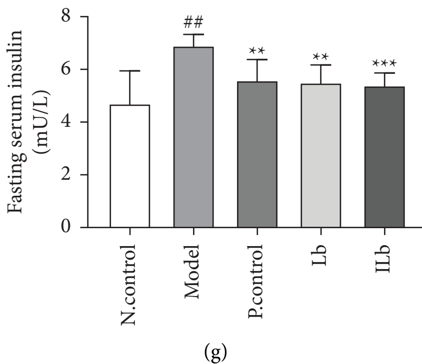

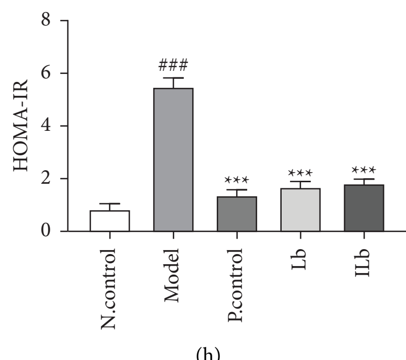

FIGURE 1: Effects of inactivated *L. brevis* YM1301 on glucose homeostasis and insulin sensitivity in the T2DM mice. (a) Inactivated *L. brevis* YM1301 reduced FBG in the T2DM mice. $^{\#\#}p < 0.01$ NC vs. other groups; $^{**}p < 0.01$ model vs. other groups; $^{\nabla\nabla}p < 0.01$ before administration vs. after a 4-week treatment ($n = 10$). (b) Inactivated *L. brevis* YM1301 reduced GHb in the T2DM mice. $^{\#\#}p < 0.01$ NC vs. model; $^{**}p < 0.01$ model vs. treatment groups ($n = 10$). (c) Inactivated *L. brevis* YM1301 improved glucose tolerance in the T2DM mice. (d) AUC_{OGTT}. $^{\#\#\#}p < 0.001$ NC vs. model; $^{**}p < 0.01$ model vs. treatment groups ($n = 10$). (e) Inactivated *L. brevis* YM1301 improved insulin tolerance in the T2DM mice. (f) AUC_{ITT}. $^{\#\#\#}p < 0.001$ NC vs. model; $^{***}p < 0.001$ model vs. treatment groups ($n = 10$). (g) Inactivated *L. brevis* YM1301 reduced FINS in the T2DM mice. $^{\#\#}p < 0.01$ NC vs. model; $^{**}p < 0.01$ model vs. treatment groups; $^{***}p < 0.001$ model vs. treatment groups ($n = 10$). (h) Inactivated *L. brevis* YM1301 reduced HOMA-IR in the T2DM mice. $^{\#\#\#}p < 0.001$ NC vs. model; $^{***}p < 0.001$ model vs. treatment groups ($n = 10$).

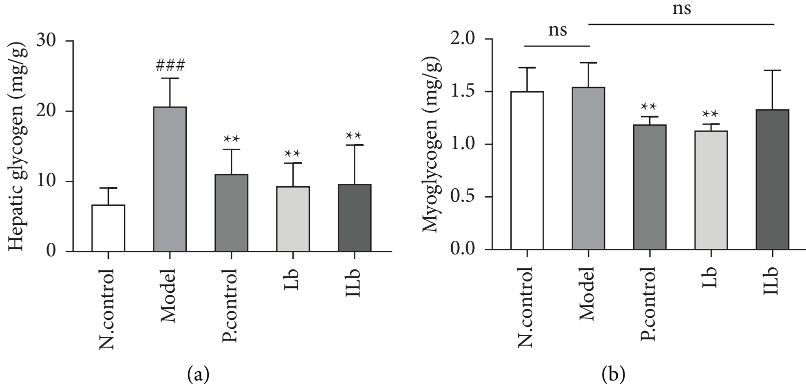

FIGURE 2: Effects of inactivated *L. brevis* YM1301 on biochemical parameters in the T2DM mice. (a) Inactivated *L. brevis* YM1301 reduced hepatic glycogen in the T2DM mice. $^{\#\#\#}p < 0.001$ NC vs. model; $^{**}p < 0.01$ model vs. treatment groups ($n = 10$). (b) Inactivated *L. brevis* YM1301 reduced myogenic glycogen in the T2DM mice but without any significant difference.

TABLE 1: Inactivated lactic acid bacteria reduced the epididymal adipose tissue index (EATI) in the T2DM mice.

Group	EATW (g)	EATI (%)
N. control	1.38 ± 0.10	2.80 ± 0.17
Model	$0.65 \pm 0.12^{\#}$	$1.39 \pm 0.22^{\#\#}$
P. control	$0.47 \pm 0.09^{*}$	1.07 ± 0.15
LB	$0.28 \pm 0.10^{**}$	$0.72 \pm 0.23^{**}$
ILB	$0.28 \pm 0.07^{**}$	$0.70 \pm 0.17^{**}$

$^{\#}p < 0.05$ NC vs. model; $^{\#\#}p < 0.01$ NC vs. model; $^{*}p < 0.05$ model vs. treatment groups; $^{**}p < 0.01$ model vs. treatment groups ($n = 10$).

TABLE 2: Inactivated lactic acid bacteria reduced the liver index in the T2DM mice.

Group	Liver weight (g)	Liver index (%)
N. control	1.57 ± 0.11	3.32 ± 0.18
Model	$2.43 \pm 0.11^{\#}$	$5.69 \pm 0.25^{\#\#}$
P. control	$2.10 \pm 0.12^{**}$	$5.07 \pm 0.35^{**}$
LB	$2.00 \pm 0.03^{**}$	$4.63 \pm 0.18^{**}$
ILB	$1.92 \pm 0.10^{**}$	$5.04 \pm 0.26^{**}$

$^{\#}p < 0.05$ NC vs. model; $^{\#\#}p < 0.01$ NC vs. model; $^{**}p < 0.01$ model vs. treatment groups ($n = 10$).

control group in the kidney weight and the kidney index of mice. Kidney weight of mice in the three treatment groups decreased compared with that in the model group ($p < 0.01$). However, the kidney index showed a decreasing trend in the LB and ILB groups compared to that in the model group, but there was no significant difference ($p > 0.05$).

As shown in Figure 3(a), the serum level of urea nitrogen (BUN) was significantly increased in the model group compared to that in the *N.* control group ($p < 0.01$), and the serum level of BUN in the three treatment groups was significantly decreased compared to that in the model group ($p < 0.01$). As shown in Figure 3(b), the level of serum creatinine (Scr) was significantly higher in the model group

Table 3: Inactivated lactic acid bacteria increased the cecum index in the T2DM mice.

Group	Cecum weight (g)	Cecum index (%)
N. control	0.63 ± 0.05	1.34 ± 0.16
Model	$0.37 \pm 0.03^{##}$	$0.83 \pm 0.11^{#}$
P. control	$0.57 \pm 0.04^{**}$	$1.35 \pm 0.11^{**}$
LB	$0.69 \pm 0.06^{**}$	$1.76 \pm 0.21^{**}$
ILB	$0.66 \pm 0.04^{**}$	$1.83 \pm 0.16^{**}$

$^{#}p < 0.05$ NC vs. model; $^{##}p < 0.01$ NC vs. model; $^{**}p < 0.01$ model vs. treatment groups ($n = 10$).

Table 4: Inactivated lactic acid bacteria reduced the kidney index in the T2DM mice.

Group	Kidney weight (g)	Kidney index (%)
N. control	0.62 ± 0.01	1.29 ± 0.03
Model	0.62 ± 0.02	1.34 ± 0.05
P. control	$0.50 \pm 0.02^{**}$	$1.19 \pm 0.05^{*}$
LB	$0.55 \pm 0.03^{**}$	1.28 ± 0.03
ILB	$0.48 \pm 0.03^{**}$	1.30 ± 0.03

$^{*}p < 0.05$ model vs. treatment groups; $^{**}p < 0.01$ model vs. treatment groups ($n = 10$).

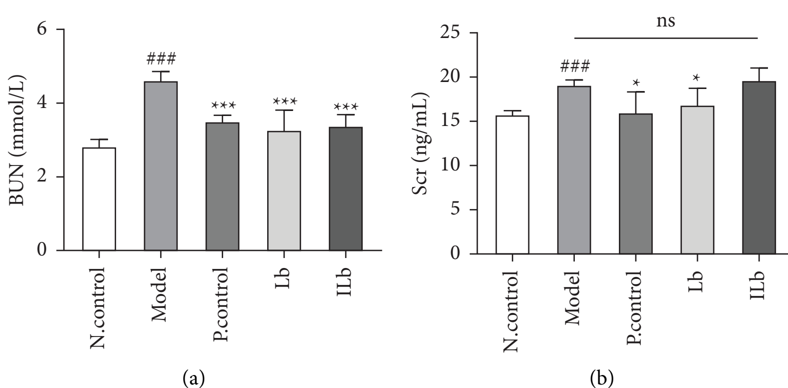

Figure 3: Effects of inactivated *L. brevis* YM1301 on renal function in the T2DM mice. (a) Inactivated *L. brevis* YM1301 reduced BUN in the T2DM mice. $^{###}p < 0.001$ NC vs. model; $^{***}p < 0.001$ model vs. treatment groups ($n = 10$). (b) Inactivated *L. brevis* YM1301 reduced SCr in the T2DM mice, but there was no significant difference ($P > 0.05$). $^{###}p < 0.001$ NC vs. model; $^{*}p < 0.05$ model vs. treatment groups.

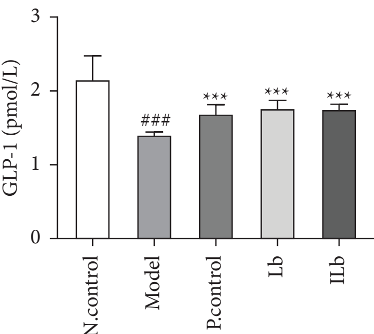

Figure 4: Inactivated *L. brevis* YM1301 increased expression of GLP-1 in the T2DM mice. $^{###}p < 0.001$ NC vs. model; $^{***}p < 0.001$ model vs. treatment groups ($n = 10$).

than that in the *N*. control group ($p < 0.01$). Compared with the model group, the Scr level in the Lb group decreased ($p < 0.01$), while the Scr level in the ILb group was not significantly different from the model group.

These results suggest that the effects of YM1301and inactivated YM1301 on renal function in diabetic mice still need further exploration.

3.4. Effects of Inactivated L. brevis YM1301 on Expression of GLP-1 in T2DM Mice. Glucagon-like peptide 1(GLP-1) is a gastrointestinal hormone secreted by ileal endocrine cells, which inhibits glucagon secretion by reducing gastric emptying and glucose dependence [19]. As shown in Figure 4, the GLP-1 level was significantly lower in the model group than that in the *N*. control group ($p < 0.01$), and it rose

significantly in the three treatment groups compared with that in the model group ($p < 0.01$).

4. Conclusions

This study confirmed that *L. brevis* YM1301 has a good antidiabetic effect. The antidiabetic effect of inactivated *L. brevis* YM1301 is similar to that of live bacteria.

5. Discussion

Our study demonstrated the antidiabetic effect of ILB on the T2DM mice induced by HFD/STZ. Results showed that ILB effectively reduced the fasting blood glucose level and improved glucose tolerance, insulin sensitivity, and insulin resistance in T2DM mice. ILB reduced fat accumulation in the T2DM mice. Moreover, the therapeutic effect of ILB was similar to that of LB.

Insulin stimulates glycogen synthesis and lowers blood sugar. However, the regulation of blood glucose is a very complicated process, which is closely related to the specific metabolic state of tissues. Liver glycogen is predominantly restored during the postprandial period in healthy humans, and conversion of glucose into glycogen is a major pathway for the removal of blood glucose by the liver during the postprandial state [20]. The previous literature showed that the sensitivity of glucose metabolism to insulin correlates inversely with glycogen content of the muscle [21]. Our results showed that, like LB, ILB could reduce muscle glycogen content in the T2DM mice and also showed a trend of decreasing liver glycogen content, but the data difference was not statistically significant, indicating that ILB may lower blood glucose by promoting the catabolism of glucose in tissues. These results provide clues for understanding the mechanism of anti-T2DM by ILB.

Current research on lactic acid bacteria against type II diabetes shows that *L. paracasei* NL41 can lower blood glucose by regulating the expression of genes related to glycogen synthesis and increasing hepatic glycogen reserves [22] and that *L. plantarum* Ln4 or *L. casei* CCFM419 can lower blood glucose by inhibiting intestinal α-glucosidase and delaying carbohydrate absorption [23]. Moreover, Lactobacilli also show potential in fat loss: LP-HFY01-fermented soybean milk strongly inhibits obesity induced by a high-fat diet and shows good potential for utilization [24]. On the other hand, when lipopolysaccharide-induced RAW 264.7 macrophages were treated with cell-free supernatants from *L. plantarum* IDCC 3501, the mRNA expression level of inflammatory markers (i.e., TNF-α, IL-1β, and IL-6) was significantly reduced [25], and some findings indicate that *L. reuteri* can protect the intestinal barrier and activate intestinal epithelial proliferation [26]. Existing studies cannot determine whether the antidiabetic effect of lactic acid bacteria requires colonization of viable bacteria on the intestine or merely the metabolites of lactic acid bacteria themselves can produce antidiabetic effects. This study confirmed that the hypoglycaemic effect of ILB was produced by metabolites of YM1301.

Studies have shown that various types of *Lactobacillus* may act through lactacystin, extracellular polysaccharides, short-chain fatty acid salts, or other components of the bacteria [27]. Lactic acid and acetic acid are the main end metabolites formed by *Lactobacillus* during fermentation, which have a broad spectrum of antimicrobial activity [28]. Bacteriocins include peptides, proteins, or more complex protein-lipid, carbohydrate complexes produced by lactic acid bacteria, which have a protective effect on the intestinal tract [29]. Due to the complexity of the metabolites of *Lactobacillus* and diabetes metabolism, the specific components of *Lactobacillus* which are responsible for the hypoglycaemic effect of ILB still need to be explored in subsequent studies.

On the one hand, the efficacy of current probiotic preparations lacks clear disease relevance, and existing products are often labelled as providing health benefits without a clear statement on specific diseases. The results of this trial confirmed that ILB preparations significantly reduced the symptoms of type II diabetes, allowing for a better definition of the population for probiotic preparations. In addition, postbiotic formulations could avoid some disadvantages of live probiotic preparations such as short shelf life, high production costs, and questionable safety. On the other hand, diabetes is a major worldwide disease in today's society with a huge number of patients. It is important to develop safe and effective adjunctive drugs for diabetes, especially dietary regimens based on nutritional supplements. This study provides the basis for the development of safe and stable postbiotic formulations for type II diabetes based on lactic acid bacteria.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

All the authors declare no conflicts of interest.

Authors' Contributions

F. Li and Q. Wei were involved in conception, design, writing, and revising the manuscript. N. Xue, J. Gao, Q. Wei, Y. Dang, R. Zhou, Y. Song, J. Sun, Y. Tian, and J. Wan were involved in collecting the data and editing the manuscript. All the authors read and approved the final manuscript.

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