Cholesterol-lowering effect of Lactobacillus plantarum NCU116 in a hyperlipidaemic rat model

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ABSTRACT

The cholesterol-lowering effect of Lactobacillus plantarum (L. plantarum) NCU116 on lipid metabolism of rats fed on a high fat diet was investigated. Sprague-Dawley rats were randomly divided into normal diet (ND) group, a high fat diet (HFD) group, HFD plus L. plantarum NCU116 groups with two different doses (NCU116-L, 10^8 colony forming units (CFU)/mL; NCU116-H, 10^9 CFU/mL). After treatment for 5 weeks, L. plantarum NCU116 had the potential ability to regulate lipid metabolism levels, morphology of liver and adipose tissues. In addition, the bacterium significantly improved gene expression of low-density lipoprotein (LDL) receptor and cholesterol 7α-hydroxylase (CYP7A1). These results suggest that L. plantarum NCU116 was able to alter lipid metabolism and reduce the cholesterol level, in particular, in the rats on a high fat diet through regulating gene expression of key factors relating to LDL receptor and CYP7A1.

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1. Introduction

Hyperlipidaemia is a significant risk factor for developing cardiovascular diseases (CVDs) that is a leading cause of death in many countries. Hyperlipidaemia is characterized by very high levels of cholesterol in the blood (Chen, Jiao, & Ma, 2008; Scicchitano et al., 2014). It has been reported that even a 1% decrease in serum cholesterol levels is estimated to result in 2–3% reduction in the risk of coronary artery disease (Hu, Wang, Li, Jin, & Wang, 2013; Law, Wald, Wu, Hackshaw, & Bailey, 1994). The World Health Organization (WHO) has predicted that by 2030, approximately 23.3 million people will die from CVDs, and CVDs are projected to remain the single leading cause of death (WHO, 2013). However, due to the high prices and side effects of the commonly used drugs, it is urgent to develop new effective strategies and technologies to reduce serum cholesterol for preventing CVDs (Nguyen, Kang, & Lee, 2007).

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Abbreviations: CVDs, cardiovascular diseases; CYP7A1, cholesterol 7α-hydroxylase; HDL-C, high-density lipoprotein cholesterol; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; LDL-C, low-density lipoprotein cholesterol; SREBP-2, sterol regulatory element-binding protein-2; TC, total cholesterol; TG, triacylglycerols

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Recent studies have shown that the composition of intestinal microbiota may play a key role in maintaining gut homeostasis (Omar, Chan, Jones, Prakash, & Jones, 2013; Ranadheera, Evans, Adams, & Baines, 2014; Young, 2012). It has been shown that some species of intestinal microbiota, such as lactobacilli could reduce the serum cholesterol level through bacterial assimilation in the intestine (Gilliland, Nelson, & Maxwell, 1985), and deconjugation of bile salts by Lactobacillus species that produce the enzyme bile salt hydrolase (De Smet, De Boever, & Verstraete, 1998; Pereira, McCartney, & Gibson, 2003). Some previous report showed that lactobacilli have the property of cholesterol lowering, but the mechanism has not been fully understood yet.

*L. plantarum* NCU116 was recently isolated from pickled vegetables (Xiong et al., 2013). We have previously shown that this bacterium is characterized with good performance in high-density cultivation, high tolerance in artificial gastric and intestinal fluids, bile salt and high salt environment in vitro, and with a strong antibacterial activity (Xiong, Guan, Song, Hao, & Xie, 2012; Xiong et al., 2011). However, it is unclear the character in vivo of the probiotic. The present study was to investigate the effects of *L. plantarum* NCU116 on high fat diet induced hyperlipidaemia in a rat model.

### 2. Materials and methods

#### 2.1. Experimental animals and bacterial strain

Forty male Sprague-Dawley (SD) rats with the body weight of 120–150 g were obtained from Vital River Lab Animal Technology Co., Ltd (Beijing, China, Certificate number: SCXK (jing) 2012-0001). Animals were acclimatized to the laboratory conditions for 1 week before commencement of the animal experiment. They were housed at an ambient temperature of 23 ± 1 °C, 12/12 h of light–dark cycle with ad libitum food and water. All animals used in this study were cared for in accordance with the Guidelines for the Care and Use of Laboratory Animals published by the U.S. National Institutes of Health (NIH Publication 85-23, 1996), and all experimental procedures were approved by the Nanchang University Medical College Animal Care Review Committee. Freeze-dried *L. plantarum* NCU116 powder were suspended in sterile saline solution and diluted to the desired doses. In the pre-experiment, for assessment of the approximate concentrations of viable bacteria, suitable dilutions of the culture were plated onto Man-Rogosa-Sharpe Agar (Land Bridge Technology, Beijing, China) and colony forming units (CFU) were counted after being incubated at 37 °C for 48 h.

#### 2.2. Experimental design

After acclimation, rats were randomly divided into four groups as follows: (1) ND: rats on the normal diet; (2) HFD: rats on the high fat (and high cholesterol) diet; (3) NCU116-L: rats on the high fat diet plus 10^8 CFU/mL *L. plantarum* NCU116 and with 10 mL per kilogram body weight by oral administration; (4) NCU116-H: rats on the high fat diet plus 10^9 CFU/mL *L. plantarum* NCU116 and with 10 mL per kilogram body weight by oral administration. Rats of ND and HFD groups received the same volume of vehicle instead of NCU116 suspension per day during the same period. The dietary treatments continued for the remaining days of the trial. The normal diet and high fat diet consists were performed on the basis of a previous report (Xing, Zhang, Hu, Wu, & Xu, 2009).

#### 2.3. Analyses of serum lipids

Blood samples were obtained from the retro-orbital sinus into prechilled tubes at the end of every week following food deprivation for 12 h. The blood samples were then immediately centrifuged at 1000 × g for 10 min and the serum was recovered for further analyses. Levels of serum lipids including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triacylglycerols (TG) were determined using assay kits (Beihua-Kangtai Clinical Reagent Company, Beijing, China) according to the manufacturer’s instructions.

#### 2.4. Oral glucose tolerance test and histopathologic examination

The measurement of oral glucose tolerance test and histopathologic examination were performed as described in a previous report (Zhu et al., 2013).

#### 2.5. Quantification of serum insulin, leptin and adiponectin

The concentrations of serum insulin, leptin and adiponectin were determined using radioimmunoassay kits (Sino-UK Institute, Beijing, China) and an Automatic Radioimmunoassay Counter (R-911, University of Science and Technology of China, Hefei, China).

#### 2.6. RT-qPCR analyses of gene expression

Total RNA was extracted from the liver with TRIZol reagent (Life Technologies, Carlsbad, CA, USA). cDNA was obtained by reverse transcription using the RevertAid™ First Strand cDNA Synthesis Kit (Thermo Scientific Fermentas, Vilnius, Lithuania) according to the manufacturer’s instructions. The mRNA expression of genes were measured by 7900HT Fast Real-Time PCR System (Applied Biosystems, Foster City, CA, USA) using SYBR® Premix Ex Taq™ (Takara, Kusatsu, Japan). Data analysis was carried out using the 2−ΔΔCt method. We used the housekeeping gene for β-actin for normalization. The sequences of the primers used for RT-qPCR were as follows (Invitrogen China Limited, Beijing, China): low density lipoprotein (LDL) receptor (F5′ CAGCTCTGTGTGAACCTCAGA -3′, R 5′ TTCTTCAGGTTCGGGATCAG -3′) (Parolini et al., 2013); 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase (F5′ CCGAGCCTAACAAGCTGGAAA -3′, R 5′ CCATGGGACCTGTTACTCT -3′) (Rigamonti et al., 2010); cholesterol 7α-hydroxylase (CYP7A1), (F5′ CACCATTCGCAACCTTTT -3′, R 5′ GTACCCGAGGTACCTGAT -3′) (Mandimika et al., 2012); sterol regulatory element-binding protein-2 (SREBP-2) (F5′ AGACTTGTCATGGGGAG -3′, R 5′ GGGAGACATGAAAGGAGA -3′) (Rigamonti et al., 2010); β-actin (F5′ TTGTGTCCGTGTTGCTCT -3′, R 5′ TAATGTCAGCCACAGTTC -3′) (Aziz et al., 2008).
and water consumption of all the rats were recorded. As shown in Table 1, with the similar amount of food intake and water consumption, the body weight of ND group increased from 227.58 to 336.38 g, and HFD group increased from 246.89 to 407.57 g during the experiment, while NCU116-L and NCU116-H groups demonstrated a significant decrease of body weight at the end of the experiment (P < 0.05).

### Table 1 – Body weight, food intake and water consumption in the four groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>First week</th>
<th>Second week</th>
<th>Third week</th>
<th>Fourth week</th>
<th>Fifth week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td>ND</td>
<td>227.58 ± 2.91a</td>
<td>263.77 ± 3.88a</td>
<td>292.62 ± 5.68a</td>
<td>317.43 ± 6.86a</td>
<td>336.38 ± 6.92a</td>
</tr>
<tr>
<td></td>
<td>HFD</td>
<td>246.89 ± 2.64a</td>
<td>300.61 ± 2.14a</td>
<td>340.93 ± 3.19a</td>
<td>378.50 ± 4.41c</td>
<td>407.57 ± 4.90b</td>
</tr>
<tr>
<td></td>
<td>NCU116-L</td>
<td>244.72 ± 2.82b</td>
<td>289.70 ± 3.24b</td>
<td>327.52 ± 4.20b,c</td>
<td>361.55 ± 5.02b</td>
<td>387.11 ± 5.6b</td>
</tr>
<tr>
<td></td>
<td>NCU116-H</td>
<td>241.83 ± 4.05b</td>
<td>285.29 ± 5.29b,c</td>
<td>321.17 ± 6.03b</td>
<td>354.74 ± 6.27b</td>
<td>380.22 ± 6.76b</td>
</tr>
<tr>
<td>Food intake (g/d)</td>
<td>ND</td>
<td>25.58 ± 0.74</td>
<td>26.83 ± 1.27</td>
<td>25.71 ± 1.12</td>
<td>25.87 ± 0.51b</td>
<td>25.80 ± 0.79b</td>
</tr>
<tr>
<td></td>
<td>HFD</td>
<td>26.51 ± 0.66</td>
<td>27.20 ± 1.48</td>
<td>25.60 ± 1.01</td>
<td>24.39 ± 0.56b,b</td>
<td>25.49 ± 0.49b,b</td>
</tr>
<tr>
<td></td>
<td>NCU116-L</td>
<td>25.79 ± 0.48</td>
<td>24.31 ± 0.80</td>
<td>23.61 ± 1.00</td>
<td>23.77 ± 0.59a</td>
<td>23.72 ± 0.81a,b</td>
</tr>
<tr>
<td></td>
<td>NCU116-H</td>
<td>24.70 ± 0.56</td>
<td>24.93 ± 1.16</td>
<td>24.28 ± 0.90</td>
<td>23.75 ± 0.56a</td>
<td>23.48 ± 0.59a</td>
</tr>
<tr>
<td>Water consumption (mL/d)</td>
<td>ND</td>
<td>34.23 ± 0.65</td>
<td>33.87 ± 2.33</td>
<td>35.37 ± 0.97</td>
<td>35.53 ± 1.33</td>
<td>34.83 ± 1.28</td>
</tr>
<tr>
<td></td>
<td>HFD</td>
<td>34.50 ± 1.28</td>
<td>34.17 ± 3.80</td>
<td>35.08 ± 2.02</td>
<td>34.42 ± 2.22</td>
<td>38.38 ± 2.68</td>
</tr>
<tr>
<td></td>
<td>NCU116-L</td>
<td>33.17 ± 0.65</td>
<td>31.57 ± 1.85</td>
<td>31.17 ± 0.75</td>
<td>31.07 ± 0.92</td>
<td>33.67 ± 0.99</td>
</tr>
<tr>
<td></td>
<td>NCU116-H</td>
<td>33.83 ± 1.56</td>
<td>30.73 ± 2.20</td>
<td>31.23 ± 1.27</td>
<td>31.57 ± 1.50</td>
<td>33.23 ± 1.19</td>
</tr>
</tbody>
</table>

ND: rats on the normal diet; HFD: rats on the high fat diet; NCU116-L: rats on the high fat diet + 10⁸ CFU/mL L. plantarum NCU116; NCU116-H: rats on the high fat diet + 10⁹ CFU/mL L. plantarum NCU116. Results are expressed as the means ± SEM (n = 10). Values within a column with different superscripts are significantly different (P < 0.05).

### 2.7. Statistics

Results were expressed as mean ± standard error of mean (SEM), and the data were analyzed by SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). One-way analysis of variance (ANOVA) with Duncan’s multiple range test was used to compare the differences among various groups. A value of P < 0.05 was considered to be statistically significant.

### 3. Results

#### 3.1. Body weight, food intake and water consumption

During the 5 weeks of the experiment, body weight, food intake and water consumption of all the rats were recorded. As shown in Table 1, with the similar amount of food intake and water consumption, the body weight of ND group increased from

### Table 2 – Effect of L. plantarum NCU116 treatment on serum lipids (mmol/L).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>First week</th>
<th>Second week</th>
<th>Third week</th>
<th>Fourth week</th>
<th>Fifth week</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>ND</td>
<td>1.07 ± 0.13a</td>
<td>1.17 ± 0.08</td>
<td>1.14 ± 0.16a</td>
<td>1.07 ± 0.11a</td>
<td>1.15 ± 0.10a</td>
</tr>
<tr>
<td></td>
<td>HFD</td>
<td>1.40 ± 0.12b</td>
<td>1.65 ± 0.16</td>
<td>2.13 ± 0.25b</td>
<td>2.30 ± 0.10c</td>
<td>2.51 ± 0.08c</td>
</tr>
<tr>
<td></td>
<td>NCU116-L</td>
<td>1.34 ± 0.10b</td>
<td>1.61 ± 0.16</td>
<td>1.66 ± 0.14b</td>
<td>1.92 ± 0.05c,b</td>
<td>2.16 ± 0.24c,b</td>
</tr>
<tr>
<td></td>
<td>NCU116-H</td>
<td>1.26 ± 0.04b</td>
<td>1.45 ± 0.29</td>
<td>1.56 ± 0.16a</td>
<td>1.78 ± 0.21b</td>
<td>1.84 ± 0.15b</td>
</tr>
<tr>
<td>TG</td>
<td>ND</td>
<td>0.32 ± 0.03a</td>
<td>0.41 ± 0.03a</td>
<td>0.34 ± 0.07</td>
<td>0.48 ± 0.04a</td>
<td>0.49 ± 0.05a</td>
</tr>
<tr>
<td></td>
<td>HFD</td>
<td>0.53 ± 0.07a</td>
<td>0.62 ± 0.09b</td>
<td>0.58 ± 0.10</td>
<td>0.77 ± 0.07b</td>
<td>0.81 ± 0.06b</td>
</tr>
<tr>
<td></td>
<td>NCU116-L</td>
<td>0.36 ± 0.03a</td>
<td>0.48 ± 0.06b</td>
<td>0.45 ± 0.07</td>
<td>0.63 ± 0.07b,b</td>
<td>0.62 ± 0.03a</td>
</tr>
<tr>
<td></td>
<td>NCU116-H</td>
<td>0.39 ± 0.03a</td>
<td>0.43 ± 0.06b,b</td>
<td>0.45 ± 0.06</td>
<td>0.55 ± 0.07a,a</td>
<td>0.58 ± 0.07a,a</td>
</tr>
<tr>
<td>HDL-C</td>
<td>ND</td>
<td>0.73 ± 0.04a</td>
<td>0.76 ± 0.02b</td>
<td>0.75 ± 0.03c</td>
<td>0.74 ± 0.02b</td>
<td>0.75 ± 0.05b</td>
</tr>
<tr>
<td></td>
<td>HFD</td>
<td>0.64 ± 0.03a</td>
<td>0.56 ± 0.03a</td>
<td>0.54 ± 0.05a</td>
<td>0.54 ± 0.04a</td>
<td>0.52 ± 0.04a</td>
</tr>
<tr>
<td></td>
<td>NCU116-L</td>
<td>0.73 ± 0.03a</td>
<td>0.63 ± 0.03a</td>
<td>0.63 ± 0.02b,b</td>
<td>0.60 ± 0.03a</td>
<td>0.59 ± 0.05b,b</td>
</tr>
<tr>
<td></td>
<td>NCU116-H</td>
<td>0.68 ± 0.04a</td>
<td>0.64 ± 0.02a</td>
<td>0.68 ± 0.04c,b</td>
<td>0.64 ± 0.07b,b</td>
<td>0.68 ± 0.06b,b</td>
</tr>
<tr>
<td>LDL-C</td>
<td>ND</td>
<td>0.23 ± 0.02a</td>
<td>0.26 ± 0.06a</td>
<td>0.25 ± 0.03a</td>
<td>0.25 ± 0.04a</td>
<td>0.23 ± 0.04a</td>
</tr>
<tr>
<td></td>
<td>HFD</td>
<td>0.45 ± 0.04a</td>
<td>0.73 ± 0.04b</td>
<td>1.33 ± 0.14b</td>
<td>1.41 ± 0.09c</td>
<td>1.52 ± 0.06d</td>
</tr>
<tr>
<td></td>
<td>NCU116-L</td>
<td>0.36 ± 0.03a</td>
<td>0.67 ± 0.03b</td>
<td>0.80 ± 0.03b</td>
<td>0.93 ± 0.04b</td>
<td>1.01 ± 0.10b</td>
</tr>
<tr>
<td></td>
<td>NCU116-H</td>
<td>0.40 ± 0.03a</td>
<td>0.61 ± 0.06b</td>
<td>0.64 ± 0.05b</td>
<td>0.85 ± 0.03b</td>
<td>0.90 ± 0.05b</td>
</tr>
</tbody>
</table>

ND: rats on the normal diet; HFD: rats on the high fat diet; NCU116-L: rats on the high fat diet + 10⁸ CFU/mL L. plantarum NCU116; NCU116-H: rats on the high fat diet + 10⁹ CFU/mL L. plantarum NCU116. Results are expressed as the means ± SEM (n = 10). Values within a column with different superscripts are significantly different (P < 0.05).
to the HFD group, but there were no significant differences (P > 0.05).

3.3. Effect of *L. plantarum NCU116* on serum glucose

Glucose intolerance of the rats was determined by the oral glucose tolerance test that was performed at the end of the 5 weeks. For the same amount of glucose given orally, the peak of serum glucose in the four groups appeared at 30 min, and gradually reduced at the next 90 min (Fig. 1). During the test, HFD group exhibited significant improvement of glucose tolerance compared to the ND group (P < 0.05). However, *L. plantarum NCU116* decreased glucose compared to the HFD group during the same time, but there were no significant differences (P > 0.05).

3.4. Regulation of insulin, leptin and adiponectin

Fasting insulin and leptin levels of HFD group were significantly higher than those of the ND group (P < 0.05) and the high dose of NCU116 reduced the level of insulin near to the level of ND group (Fig. 2). Adiponectin level of HFD group was significantly lower than that of ND group (P < 0.05). Supplementation of *L. plantarum NCU116* increased the level of adiponectin. The high dose of group (NCU116-H), in particular, attained the level close to the ND group, which was significantly different from the HFD group (P < 0.05).

3.5. Histopathology of liver and adipose tissues

Figure 3 illustrates the effects of *L. plantarum NCU116* on histopathology of liver and adipose tissues. Hematoxylin and eosin staining showed the differences in liver tissue structures and lipids accumulation of rats with four different dietary treatments (Fig. 3A). The liver of ND group rats had a well-organized structure, while significant morphological changes were observed in the HFD group. The structures of livers displayed a large degree of damages in the rats from HFD group and hepatocytes showed signs of necrosis and lipid vacuolization. Hepatocyte steatosis and lipid accumulation were obviously alleviated by the supplement of *L. plantarum NCU116* compared with HFD group. The rats in HFD group demonstrated increased adipocyte size in comparison with ND group (Fig. 3B). This was confirmed by the changes in adiposity indices and adipocyte number per spot. The adipocyte size was partly restored by *L. plantarum NCU116*.

3.6. mRNA expression levels of liver associated with cholesterol metabolism

Hepatic mRNA expression for cholesterol metabolism-related genes, LDL receptor, CYP7A1, HMG-CoA reductase, and SREBP-2 resulted in different levels (Fig. 4). The inclusion of high fat dietary resulted in a significant downregulation of LDL receptor, HMG-CoA reductase,SREBP-2 mRNA expression in HFD group (P < 0.05) compared with ND group, whereas oral supplementation of *L. plantarum NCU116* upregulated the respective mRNA expressions compared with the HFD group. mRNA of CYP7A1 expression levels in HFD, NCU116-L and NCU116-H groups were higher than control group respectively, and the NCU116-H group had the highest level.

4. Discussion

Hyperlipidaemia (usually elevated serum levels of TC, TG and LDL-C, accompanied by a reduced HDL-C level) is strongly
associated with CVDs (Ross, 1993). In this study, the rat model with hyperlipidaemia was induced by feeding a high fat diet. We demonstrated that the oral administration of _L. plantarum_ NCU116 strain benefited lipid metabolism, including cholesterol-lowering and mRNA expression effects.

The results showed that _L. plantarum_ NCU116 significantly decreased the serum TC, TG, and LDL-C and enhanced the serum HDL-C during the 5 week experimental period. It was well known that high fat diet could increase TC, TG and LDL-C levels in the blood, resulting in an increased risk for the
development of atherosclerosis (Guo et al., 2011), while high level of HDL-C can decrease the risk of cardiovascular events (Bao et al., 2012). In addition, LDL-C was found to be the most dangerous factor among serum lipids owing to increasing penetration of oxidized LDL-C into arterial walls and forming atherosclerotic plaque lesions (Goto & Brinton, 2004; Guo et al., 2011; Ross, 1993). Decreasing serum TC and LDL-C levels is effective for reducing the risk of atherosclerosis (Bao et al., 2012; Pischon et al., 2005).

The rats on HFD exhibited increasing glucose tolerance when compared with ND group. In addition, glucose induced insulin secretion, body weight gain and visceral and subcutaneous adipose weight were significantly increased in HFD fed rats compared with other three groups of rats on different diets (Cani et al., 2008). Furthermore, hormones such as insulin, leptin and adiponectin play an important role in lipid metabolism. A previous research has indicated that leptin secretion is affected by insulin (Lee & Fried, 2006). Report showed that rats with obesity exhibit high plasma levels of leptin (Hansen, Jelsing, & Vrang, 2012). Adiponectin is secreted from adipocytes and plays an important role in glucose and lipid metabolism, insulin resistance (Kadowaki et al., 2006). The observations reported in this study suggest that the decrease in leptin level and increase in adiponectin level may have resulted from the improvement of insulin sensitivity by the oral administration of L. plantarum NCU116.

 Elevated markers of inflammation, increased visceral adiposity fat accumulation in the liver are accompanied frequently by elevated serum lipid levels, and have been linked to insulin resistance, dyslipidemias and cardiovascular risk (Satapathy et al., 2011). Histologic analyses in the present study showed that rats on L. plantarum NCU116 displayed a significant reduction in hepatic lipid deposition. Moreover, excess fat accumulation in the liver may lead to hepatic oxidative stress and liver damage (Bao et al., 2012). The reduction in liver and adipose tissue mass of L. plantarum NCU116 treated rats suggests that the administration of the bacterium can alleviate HFD induced hepatic steatosis and obesity.

The cholesterol level in blood is regulated by three distinct pathways, namely absorption, synthesis, and excretion (Kumar et al., 2013). In the present study, we explored the possible mechanism of cholesterol-lowering effect of L. plantarum NCU116 by examining the expression and activity of LDL receptor, HMG-CoA reductase, CYP7A1 and SREBP-2 in the liver. LDL receptor is located on the hepatocyte surface that mediates endocytosis of LDL-C and is regulated by a transcriptional control mechanism (Goldstein & Brown, 2009). In the HFD group, the mRNA expression level of LDL receptor was significantly decreased, and resulted in increase of serum LDL-C level. The L. plantarum NCU116 decreased the level of LDL-C may be involved in this process. As the process cholesterol and TG are used by liver and excreted in fecal, a dense molecule known as LDL is left. LDL still maintains a large amount of cholesterol. The protein layer allows liver to use this cholesterol, LDL receptors on these tissues that make this interaction possible (Kumar et al., 2012). Bile acids and cholesterol inhibited HMG-CoA reductase expression (Brown & Goldstein, 1986), and this study demonstrated that supplementation with L. plantarum NCU116 augmented the hepatic HMG-CoA reductase mRNA expression compared with the HFD group. The gene expression of SREBP-2 was inhibited by the high fat diet induced hyperlipidaemic rats, and SREBP-2 is well known for its regulatory role in cholesterol uptake and cholesterol synthesis (Wong, Quinn, & Brown, 2006). The results showed that L. plantarum NCU116 improved expression of the genes. Therefore, the reduction of serum cholesterol levels by L. plantarum NCU116 may be partly through promoting SREBP-2 expression levels. In addition, the high fat diet led to an increase in CYP7A1 mRNA level. A previous study found that over expression of CYP7A1 effectively decreased the TC and LDL-C levels in blood of hamsters fed on a high fat diet (Spady, Cuthbert, Willard, & Meidell, 1995). CYP7A1 is a microsomal cytochrome p450 enzyme that catalyzes the first and rate-limiting step in the classic bile acid biosynthetic pathway, so it regulates the overall rate of bile acid synthesis (Li & Chiang, 2013). The present study showed that oral administration of L. plantarum NCU116 with the high fat diet increased gene expression of CYP7A1 in the liver of hyperlipidaemic rats. This may be the mechanism by which L. plantarum NCU116 reduced serum TC and LDL-C, and is beneficial to prevent coronary artery disease and atherosclerosis.

In summary, this study demonstrated that L. plantarum NCU116 may have a potential for the treatment of hyperlipidaemic rats induced by high fat diet. The results indicated that L. plantarum NCU116 had the potential abilities to regulate lipid metabolism (TC, TG, LDL-C, HDL-C), and morphology of liver and adipose. The bacterium also improved gene expression of LDL receptor and CYP7A1 and this may be the possible mechanism of L. plantarum NCU116 affecting lipid metabolism and have cholesterol-lowering effects in rats fed on a high fat diet. Thus, these results indicated that L. plantarum NCU116 may have a potential for the treatment of hyperlipidaemia.

Conflict of interest

The authors declare no competing financial interest.

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Appendix: Supplementary material

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