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Lifeceramics-Treated Water Improves Serum Lipid Profile in Hyperlipidaemic Rats

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Abstract

Metabolic disorders such as hyperlipidaemia can be alleviated by drinking water. This study investigated whether lifeceramics (LC)-treated water (LC water) could improve hyperlipidaemia in rats. The LC water was prepared by mixing distilled water with LC particles composed of zeolite and oyster shells. Hyperlipidaemia was induced in rats via gavage with a high-calorie diet (HCD) rich in fat and sugar. The HCD-fed rats were classified into four groups: distilled water-drinking hyperlipidaemia group (hyper LP), low-dose LC water-drinking group (HCD + low LC), high-dose LC water-drinking group (HCD + high LC), and atorvastatin (ATS, a lipid-regulating drug) solution-drinking group (HCD + ATS). Control rats were fed a normal diet and distilled water. All rats were gavaged daily with diet and drinking water, and biochemical indices related to lipid metabolism, oxidative stress, and inflammation were measured after 20 weeks. Notably, higher serum lipid levels, including total cholesterol, triglycerides, and low-density lipoprotein cholesterol, were observed in the hyper-LP rats than in the control rats. However, the LC water-drinking rats exhibited lower serum lipid levels than the hyper-LP rats, as did the HCD + ATS rats. Serum catalase activity and glutathione levels increased and decreased, respectively, in the hyper-LP rats compared with those in the control rats but recovered to around the control levels in the HCD + high LC and HCD + ATS rats. Furthermore, serum tumour necrosis factor-α and adiponectin levels in the hyper-LP rats were increased and decreased, respectively, compared with those in the control rats, whereas their levels recovered to around the control levels following administration of the high or low dose of LC. Therefore, LC water can improve lipid metabolism dysfunction, antioxidant capacity, and inflammatory responses in hyperlipidaemic rats.

Keywords

Lifeceramics, Hyperlipidaemia, Serum Lipid Profile, Anti-Oxidant Capacity, Inflammatory Response

1. Introduction

Hyperlipidaemia is a lipid metabolism disorder that can lead to atherosclerosis, which is the underlying cause of heart attack, stroke, and peripheral vascular disease [1]-[3]. Hyperlipidaemia can disrupt oxidation-reduction balance and induce an imbalance in inflammatory factors or disorders in various organs [3]-[10].

Various agents, such as statins, can be used to treat hyperlipidaemia by lowering lipid levels. However, these drugs may cause side effects, including myopathy and organ injury [5] [11]-[14], and research on non-statin lipid-lowering therapies has recently advanced [15]. Consequently, the establishment of new anti-hyperlipidaemic strategies, including the identification of substances from natural resources, especially those that can improve blood lipid levels without side effects, is required. Thus, natural resources with anti-hyperlipidaemic activities have been reported [16] [17].

Adequate water intake is essential for maintaining overall health and preventing disease. Recently, we reported a reduction in serum uric acid levels following the administration of lifeceramics (LC)-treated water (LC water) in hyperuricaemic rats [18]. LC is composed of zeolite and oyster shells under high temperature and pressure conditions [18]. We also reported the protective effects of LC water against oxidative stress in cultured human cells [19] [20]. In addition, in the livers of alcoholic rats, LC administration decreased and increased malondialdehyde (MDA) and glutathione (GSH) levels, respectively, suggesting an anti-oxidative effect of LC on alcoholic hepatic injury [21].

In contrast, increased intake of a high-calorie diet (HCD) rich in fat and sugar may cause hyperlipidaemia [22]-[24]. This study aimed to investigate the effects of LC water consumption on hyperlipidaemia in rats by estimating serum lipid levels, antioxidant indices, and inflammatory factors.

2. Materials and Methods

2.1. Reagents

LC particle powder was obtained from Wedge Co., Ltd. (Fuji, Japan). Kits for the measurement of levels of total cholesterol (TC) (cat. no. 20190610), triglycerides (TG) (cat. no. 20190608), low-density lipoprotein cholesterol (LDL-C) (cat. no. 20190615), high-density lipoprotein cholesterol (HDL-C) (cat. no. 20190612), MDA (cat. no. 20190328), catalase (CAT) activity (cat. no. 2018053), GSH (cat. no. 20190513), and superoxide dismutase (SOD) activity (cat. no. 20190330) were purchased from Jian Cheng Biotechnology Co., Ltd. (Nanjing, China). ELISA kits to measure tumour necrosis factor-α (TNF-α) (cat. no. 20190513) and adiponectin

(ADPN) (cat. no. 20190514) levels were purchased from Jian Cheng Biotechnology Co., Ltd. All other reagents were obtained from Beijing BD Biotechnology Co., Ltd. (Beijing, China).

2.2. Animals and Treatment

LC water was prepared by mixing distilled water with LC particles, and the solution was allowed to stand for 18 h at 22˚C ± 1˚C to precipitate the large particles of LC [18]. Sixty male Sprague-Dawley rats (6 weeks old, weighing 190 - 210 g) were purchased from Beijing Vital River Laboratory Animal Technology Co., Ltd. (Beijing, China; licence number SCXK2016-0006). This study was approved by the Animal Ethics Committee of the Chengde Medical University (Chengde, China) (Applied No. 201601128; IACUC Issue No. CDMULAC-20160116-003). All animals were treated according to protocols for animal care approved by the Committee and housed in plastic cages and maintained under standard laboratory conditions (12-h light/dark cycle at 22˚C ± 1˚C and 50% ± 5% humidity), as described previously [18] [25].

The rats were allowed to adapt to the feed for 3 days and then randomly divided into five independent groups (n = 12 each) based on the treatment (**Table 1**). Control rats were gavaged with a normal diet and distilled water as drinking water, whereas the other rats were gavaged with HCD rich in fat and sugar to induce hyperlipidaemia [26]. The HCD-gavaged rats were divided into four groups: hyperlipidaemia (hyper LP), HCD + low LC, HCD + high LC, and HCD + atorvastatin (ATS). Different types of drinking water were administered to the HCD-gavaged rats as follows: distilled water in the hyper-LP, low-dose LC water in the HCD + low LC, high-dose LC water in the HCD + high LC, and ATS solution in the HCD + ATS groups (**Table 1**). All the rats were gavaged daily for 20 weeks. The LC dose administered to rats in the present study was deduced from the dose usually administered to humans (9 - 90 mg/kg/day). The dosage of ATS was decided based on a previous report in which the drug was administered to improve symptoms in dyslipidaemic rats [27]; a slightly lower dose was administered to rats for a longer period in our study than in the previous report. The ATS dose used in our study was 2 - 3 times higher than that generally administered to humans. ATS

Table 1. Treatment groups (*).

Diet and addition in drinking water	Control[1)]	Hyper LP[2)]	HCD + low LC	HCD + high LC	HCD + ATS
HCD	–	+	+	+	+
LC[a)]	–	–	50	100	–
ATS[a)]	–	–	–	–	2

*n = 12 per group. HCD: high-calorie diet, LC: lifeceramics, ATS: atorvastatin. [a)]mg/kg/day. [1)]Control rats were gavaged with normal diet and distilled water. [2)]Hyper LP rats were gavaged with distilled water.

was dissolved in distilled water. The LC water and ATS solution were administered daily as drinking water. The daily consumption of drinking water was recorded and the drinking water was replaced with freshly prepared water. The mean amount of drinking water consumed per rat per day was 20 ml regardless of the type of water provided.

2.3. Blood and Tissue Sample Collection and Visceral Index Calculation

Body weights of the rats were measured at the beginning and the end of the experiment. Blood was collected from the abdominal aorta at the end of the 20-week treatment period. The serum was separated from the blood and cryopreserved until use. At the end of the experimental period, the epididymal fat and liver were rapidly dissected and weighed to determine the epididymal fat index (relative weight of the fat to the body weight [%]) and liver index (relative weight of the liver to the body weight [%]).

2.4. Biochemical Assays

In each of the separated serum samples, blood lipid content (TC, TG, LDL-C, and HDL-C levels) and anti-oxidant capacity (CAT activity, GSH concentration, SOD activity, and MDA concentration) were determined using commercial kits, according to the manufacturer's instructions. Levels of the serum inflammatory factors, TNF-α and ADPN, were measured using the manufacturer-provided standards according to the manufacturer protocols.

2.5. Statistical Analysis

Data are presented as mean ± standard deviation (SD). Differences among groups were assessed by one-way analysis of variance (ANOVA) using SPSS software (version 17.0). Statistical significance was set at $P < 0.05$.

3. Results

3.1. Body Weight, Epididymal Fat Index, and Liver Index

Body weight in the hyper-LP rats increased to approximately 1.3-fold compared to that in the control rats after the 20-week experimental period (**Figure 1(A)**). However, the weight after 20 weeks in the HCD + high LC rats was significantly lower than that in the hyper-LP rats, even if it seemed to be slightly higher than that in the control rats. This result indicated that administration of the high-dose LC water resulted in a decrease in the weight of the hyper-LP rats (**Figure 1(A)**). The body weights of the other two groups (HCD + low LC and HCD + ATS) were slightly lower than that in the hyper-LP rats, with no significant difference. The epididymal fat and liver indices in the hyper-LP rats were approximately 1.3-fold and 1.7-fold higher, respectively than those in the control rats (**Figure 1(B)** and **Figure 1(C)**). Both indices in the hyper-LP rats also decreased in the HCD + low LC and HCD + high LC rats, whereas neither index differed significantly between

the hyper-LP and HCD + ATS rats; the epididymal fat index of the rats gavaged with the high dose of LC decreased to around the control level (Figure 1(B) and Figure 1(C)).

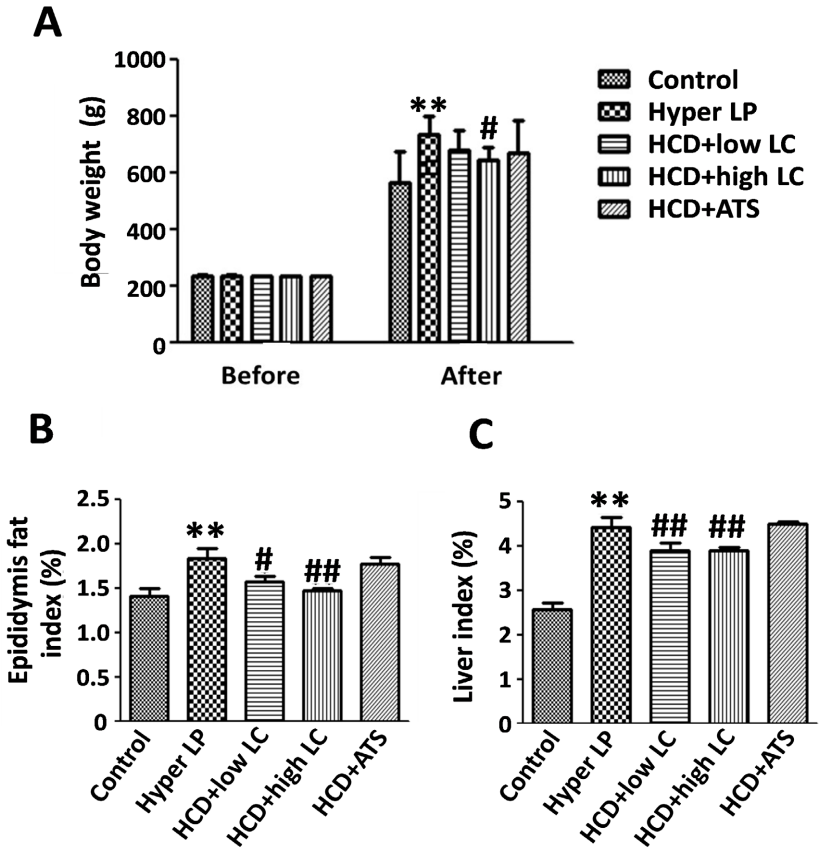

Figure 1. Body weight and epididymal fat and liver indices in the hyperlipidaemic rats following various treatments. The body weights of the rats in each group were measured before and after the 20-week experimental period (A). At the end of the experimental period, the epididymal fat and liver were weighed, and the epididymal fat index (relative weight of the fat to the body weight [%]) (B) and liver index (relative weight of the liver to the body weight [%]) (C) were determined. n = 12 per group. Data are presented as mean ± standard deviation (SD). $^{**}P < 0.01$ vs. control; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$ compared with hyper LP. Hyper LP: hyperlipidaemia; HCD: high-calorie diet; LC: lifeceramics; ATS: atorvastatin.

3.2. Serum Lipid Profile

TC, TG, and LDL-C levels in the hyper-LP rats were approximately 1.4-fold, 1.8-fold, and 1.8-fold higher, respectively than those in the control rats with significant differences (Figures 2(A)-(C)). In contrast, their levels were reduced in the HCD + low LC, HCD + high LC, and HCD + ATS rats; TC and TG levels recovered to around the control levels in the HCD + high LC rats (Figures 2(A)-(C)). HDL-C levels did not differ significantly among the five groups (Figure 2(D)).

3.3. Serum Anti-Oxidant Indices

Serum CAT activity was approximately 1.5-fold higher in the hyper-LP rats than

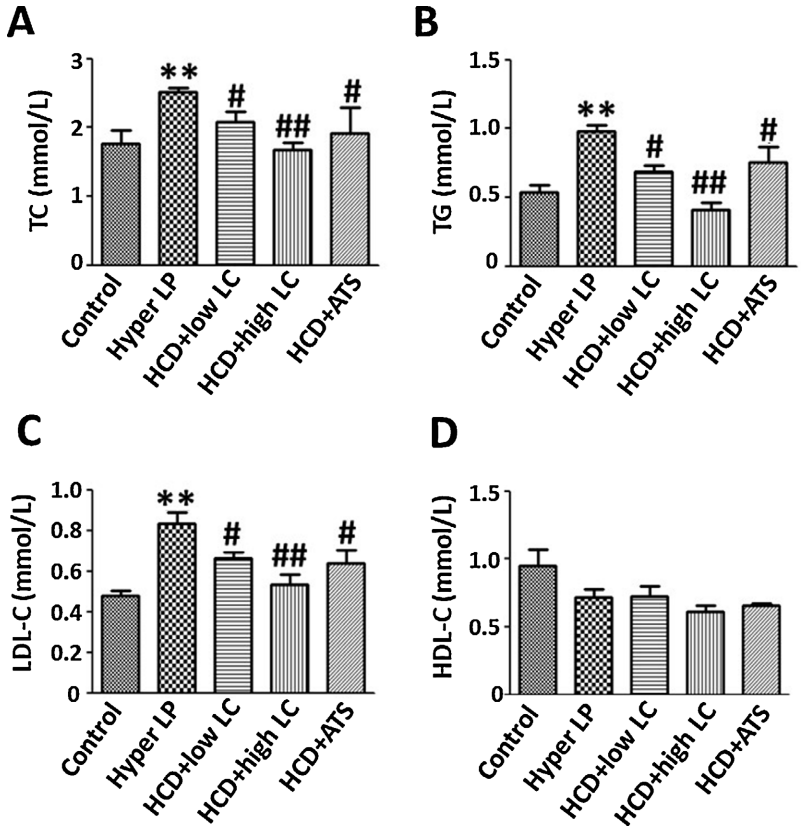

Figure 2. Serum lipid profile of hyperlipidaemic rats following various treatments. At the end of the 20-week experimental period, total cholesterol (A), triglycerides (B), low-density lipoprotein cholesterol (C) and high-density lipoprotein cholesterol (D) levels were analysed in rats in each group. n = 12 per group. Data are expressed as mean ± SD. $^{**}P < 0.01$ vs. control; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$ compared with hyper LP. Hyper LP: hyperlipidaemia; HCD: high-calorie diet; LC: lifeceramics; ATS: atorvastatin; TC: total cholesterol; TG: triglycerides; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol.

in the control rats (Figure 3(A)). However, this activity decreased in the HCD + low LC, HCD + high LC, and HCD + ATS rats compared to that in the hyper-LP rats, and the decreased level was lower than or around the control level (Figure 3(A)). GSH levels in the hyper-LP rats decreased by approximately 50% of those observed in the control rats, whereas the levels did not decrease and were similar to the control levels in the HCD + high LC and HCD + ATS rats (Figure 3(B)). Serum SOD activity was slightly lower in the hyper-LP rats than in the control rats; the difference was not statistically significant. However, it increased significantly in the rats treated with both low and high doses of LC compared with that in the hyper-LP rats. The activity in the rats treated with the low LC dose seemed to increase even when compared with that in the control rats (Figure 3(C)). The MDA concentration was 2-fold higher in the hyper-LP rats than in the control rats (Figure 3(D)). In contrast, the levels in hyper-LP rats recovered to around the control levels following low- and high-dose LC administration, as well as following ATS administration (Figure 3(D)).

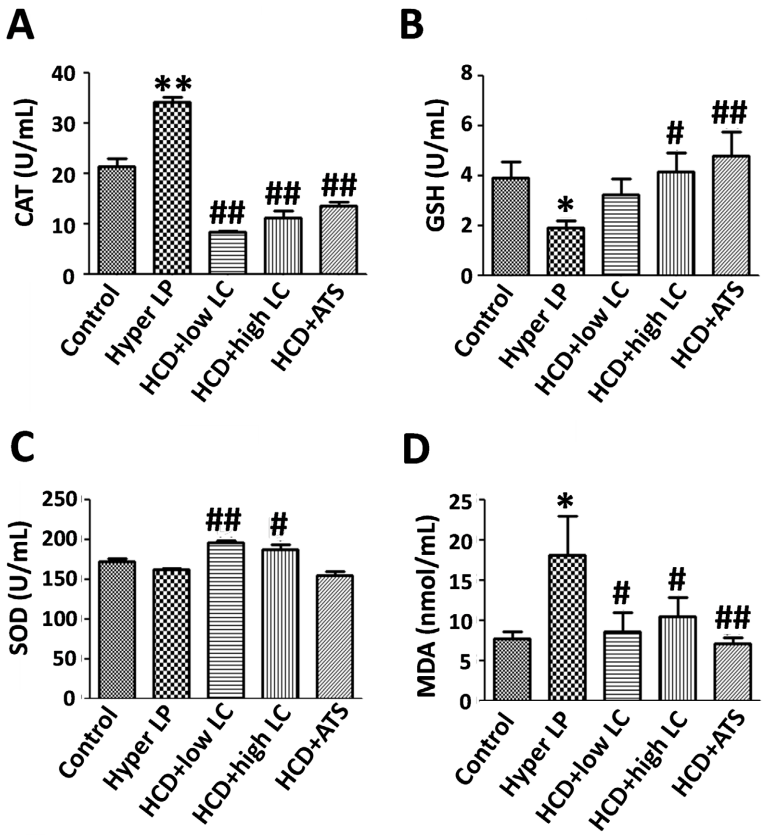

Figure 3. Anti-oxidant index of serum in the hyperlipidaemic rats following various treatments. At the end of the 20-week experimental period, catalase activity (A), glutathione concentration (B), superoxide dismutase activity (C), and malondialdehyde concentration (D) were analysed in rats of each group. n = 12 per group. Data are expressed as mean ± SD. $^{*}P < 0.05$, $^{**}P < 0.01$ vs. control; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$ compared with hyper LP. Hyper LP: hyperlipidaemia; HCD: high-calorie diet; LC: lifeceramics; ATS: atorvastatin; CAT: catalase; GSH: glutathione; SOD: superoxide dismutase; MAD: malondialdehyde.

3.4. Serum TNF-α and ADNP Levels

TNF-α levels were approximately 1.3-fold higher in the hyper-LP rats than in the control rats with a significant difference (Figure 4(A)). However, the increased levels were reduced to approximately control levels in the HCD + high LC rats and decreased slightly without a significant difference in the HCD + low LC and HCD + ATS rats (Figure 4(A)). The ADPN concentration in the hyper-LP rats decreased to approximately 76% compared with that in the control rats, but significantly increased in the HCD + low LC rats compared to that in the hyper-LP rats; the concentration in the rats with the low LC dose seemed to increase even when compared with that in the control rats (Figure 4(B)). The ADNP levels increased slightly, without a significant difference, in the HCD + high LC and HCD + ATS rats compared to those in the hyper-LP rats (Figure 4(B)).

4. Discussion

Identifying and developing new substances, particularly those from natural

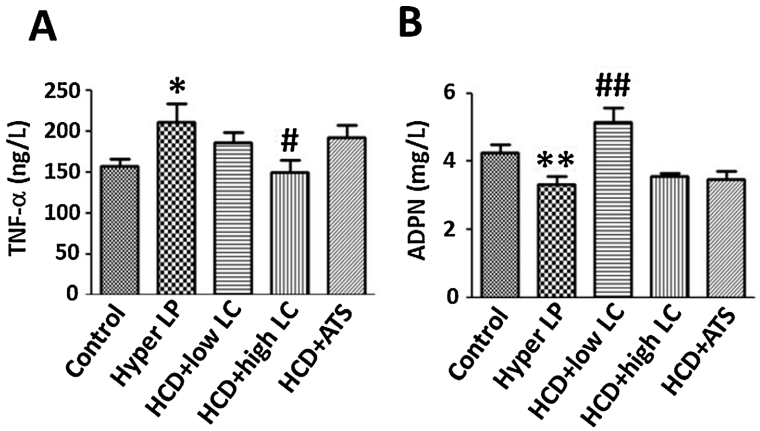

Figure 4. Serum tumour necrosis factor-*a* and adiponectin levels in the hyperlipidaemic rats following various treatments. At the end of the 20-week experimental period, tumour necrosis factor-*a* (A) and adiponectin (B) levels were analysed in rats in each group. n = 12 per group. Data are expressed as mean ± SD. $^{*}P < 0.05$, $^{**}P < 0.01$ vs. control; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$ compared with hyper LP. Hyper LP: hyperlipidaemia; HCD: high-calorie diet; LC: lifeceramics; ATS: atorvastatin; TNF-*a*: tumour necrosis factor-*a*; ADPN: adiponectin.

resources that can improve blood lipid profiles without side effects, are crucial. Interestingly, the intake of a natural zeolite-containing diet suppressed the increase in body weight, liver weight, and epididymal fat weight and decreased plasma lipid levels, such as those of TC, TG, and HDL-C, in mice with high-fat diet-induced obesity and type 2 diabetes mellitus [28]. In the future, zeolite is expected to be applied to functional foods aimed at preventing high blood sugar, hyperlipidaemia, and obesity associated with a high-fat diet. On the other hand, oyster shells are used for various products, such as fertilizers, interiors, and accessories, in groundbreaking ways that take advantage of their characteristics and main ingredients. However, most oyster shells were discarded. Therefore, LC was developed by using zeolite and oyster shells together for ceramicization to increase the zeolite efficacy. In particular, LC was manufactured with the idea of changing the size of the zeolite pores and increasing the mineral content [29]. In this study, we examined the effects of zeolite- and oyster shell-derived LC on hyperlipidaemia in rats. Notably, no changes in the physical condition of the rats were observed when they were fed only normal diet and LC water, as reported previously [18] [30]. However, the hyper-LP rats gavaged with the HCD rich in fat and sugar exhibited an increase in body weight and the liver and epididymal fat indices (**Figure 1**), along with the serum lipid levels of TC, TG, and LDL-C (**Figure 2**), indicating the induction of hyperlipidaemia, as previously reported [26]. However, the weight gain exhibited a decreasing trend in the HCD-gavaged rats following LC water administration (**Figure 1**). Furthermore, the increased TC, TG, and LDL-C levels were reduced by LC water (**Figures 2(A)-(C)**). Therefore, LC water effectively inhibited the worsening of the blood lipid profile in rats with hyperlipidaemia, although the HDL-C levels did not differ significantly between the groups (**Figure 2(D)**).

Dyslipidaemia, including hyperlipidaemia, is characterised by the dysregulation

of multiple systems, such as the oxidant/anti-oxidant balance [31]. CAT is an anti-oxidant enzyme that scavenges hydrogen peroxide (H_2O_2) and protects against the peroxidation of cell wall lipids and lipoproteins. In this study, serum CAT activity increased in the hyperlipidaemic rats (**Figure 3(A)**). In contrast, the increased CAT activity was reduced in the rats administered LC water as well as those administered ATS (**Figure 3(A)**). CAT activity has been reported to decrease in patients with hyperlipidaemia [32], whereas another study reported no significant interaction between hyperlipidaemia and the activity of anti-oxidative enzymes, including CAT [33]. Further studies are warranted to clarify the causal relationship between hyperlipidaemia and CAT activity and its subsequent effect [33].

GSH and SOD also exert anti-oxidant effects, and both GSH levels and enzymatic SOD activity decrease in hyperlipidaemia [34] [35]. Consistently, a decrease in the GSH levels was observed in the hyperlipidaemic rats in this study (**Figure 3(B)**). However, the decreased GSH levels that accompanied hyperlipidaemia were recovered to the control levels in the rats administered LC water and ATS (**Figure 3(B)**). SOD activity also seemed to decrease in the hyper-LP rats, but increased in the rats administered LC water (**Figure 3(C)**). In addition, estimation of oxidative stress-induced products is critical for elucidating the causal relationship between hyperlipidaemia and the antioxidant enzyme activity. An increase in serum MDA levels due to lipid peroxidation may occur because of hyperlipidaemia-associated changes in oxidative status [31]. Notably, the hyperlipidaemic rats exhibited an increase in the serum MDA levels; however, these levels recovered to the control levels following LC water and ATS administration (**Figure 3(D)**). Therefore, hyperlipidaemia in the rats in this study appears to be associated with the oxidative status, and drinking LC water may effectively improve it.

We also measured the levels of other remarkable factors, such as TNF-α and ADNP, which contribute to hyperlipidaemia. The levels of TNF-α and ADNP increased and decreased, respectively, in the hyperlipidaemic rats compared with the control levels, and both of these recovered to around the control levels following LC water and ATS administration (**Figure 4**). TNF-α is a pleiotropic pro-inflammatory cytokine and is proposed to contribute to metabolic diseases [36]. Lower ADNP levels have been suggested to be linked to dyslipidaemia and high TG levels in humans [37] [38]. Therefore, fluctuations in their levels in this study may be associated with fluctuations in the blood lipid profile.

We found the anti-hyperuricaemic [18] [25] and anti-liver damage effects [21] in addition to the anti-hyperlipidaemic effect of LC water in rats, suggesting that LC water promotes human health. In addition, we reported that LC water mitigated stress conditions and suppressed renal function deterioration in human [39]. Recently, we started a metabolome analysis [40] to analyse the effect of LC water consumption in humans using low molecular weight metabolites in the blood. Thus, drinking LC water may be applicable for protecting human health against unhealthy conditions, although a more detailed dose-response analysis, such as testing a wider range of LC water concentrations and including pharmacokinetic data, could enable

the establishment of a clear dose-response relationship and determine the optimal dosage for the maximal efficacy of LC water drinking.

5. Conclusion

We suggest that LC water has a multifaceted efficacy in the anti-hyperlipidaemic action reported here, including previously reported anti-oxidative [19] [20], anti-inflammatory [21], and anti-hyperuricemic [18] actions, although the mechanisms underlying its efficacy remain unclear. Our findings underscoring the beneficial effects of LC water in hyperlipidaemic rats may serve as a foundation for improving human health conditions.

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Authors' Contributions

During the research and preparation of the manuscript, Jingyao Yu (JY), Xiaobo Tong (XT), and Kuihua Li (KL) performed the experiments, and JY and XT prepared and analysed the experimental data. XT and Nobuo Suzuki designed the study and prepared the manuscript as corresponding authors, respectively. Atsushi Suzuki and Kazuko Kita (KK) revised, and KK submitted the manuscript. All the authors have read and agreed to publish this manuscript.

Ethical Approval and Consent to Participate

All experiments on rats were approved by Beijing Vital River Laboratory Animal Technology Co., Ltd. (Beijing, China) and were conducted in accordance with the institutional and ethical guidelines of the Animal Ethics Committee of Chengde Medical University.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Gami, A.S., Witt, B.J., Howard, D.E., Erwin, P.J., Gami, L.A., Somers, V.K., *et al.* (2007) Metabolic Syndrome and Risk of Incident Cardiovascular Events and Death. *Journal of the American College of Cardiology*, **49**, 403-414. https://doi.org/10.1016/j.jacc.2006.09.032

[2] Catapano, A.L., Maggi, F.M. and Tragni, E. (2000) Low Density Lipoprotein Oxida-

tion, Antioxidants, and Atherosclerosis. *Current Opinion in Cardiology*, **15**, 355-363. https://doi.org/10.1097/00001573-200009000-00008

[3] Maury, E. and Brichard, S.M. (2010) Adipokine Dysregulation, Adipose Tissue Inflammation and Metabolic Syndrome. *Molecular and Cellular Endocrinology*, **314**, 1-16. https://doi.org/10.1016/j.mce.2009.07.031

[4] Kanoski, S.E. and Davidson, T.L. (2011) Western Diet Consumption and Cognitive Impairment: Links to Hippocampal Dysfunction and Obesity. *Physiology & Behavior*, **103**, 59-68. https://doi.org/10.1016/j.physbeh.2010.12.003

[5] Jiang, C.J. and Yuan, Q. (2016) Side Effects and Clinical Observation of Statins. *Chinese Journal of Practical Medicine*, **11**, 193-194.

[6] Lahera, V., Goicoechea, M., Garcia de Vinuesa, S., Miana, M., de las Heras, N., Cachofeiro, V., *et al.* (2007) Endothelial Dysfunction, Oxidative Stress and Inflammation in Atherosclerosis: Beneficial Effects of Statins. *Current Medicinal Chemistry*, **14**, 243-248. https://doi.org/10.2174/092986707779313381

[7] Karalis, K.P., Giannogonas, P., Kodela, E., Koutmani, Y., Zoumakis, M. and Teli, T. (2009) Mechanisms of Obesity and Related Pathology: Linking Immune Responses to Metabolic Stress. *The FEBS Journal*, **276**, 5747-5754. https://doi.org/10.1111/j.1742-4658.2009.07304.x

[8] Pirola, L. and Ferraz, J.C. (2017) Role of Pro- and Anti-Inflammatory Phenomena in the Physiopathology of Type 2 Diabetes and Obesity. *World Journal of Biological Chemistry*, **8**, 120-128. https://doi.org/10.4331/wjbc.v8.i2.120

[9] Brestoff, J.R. and Artis, D. (2015) Immune Regulation of Metabolic Homeostasis in Health and Disease. *Cell*, **161**, 146-160. https://doi.org/10.1016/j.cell.2015.02.022

[10] Lumeng, C.N. and Saltiel, A.R. (2011) Inflammatory Links between Obesity and Metabolic Disease. *Journal of Clinical Investigation*, **121**, 2111-2117. https://doi.org/10.1172/jci57132

[11] Thompson, P.D., Panza, G., Zaleski, A. and Taylor, B. (2016) Statin-Associated side Effects. *Journal of the American College of Cardiology*, **67**, 2395-2410. https://doi.org/10.1016/j.jacc.2016.02.071

[12] Vinci, P., Panizon, E., Tosoni, L.M., Cerrato, C., Pellicori, F., Mearelli, F., *et al.* (2021) Statin-Associated Myopathy: Emphasis on Mechanisms and Targeted Therapy. *International Journal of Molecular Sciences*, **22**, Article 11687. https://doi.org/10.3390/ijms222111687

[13] Cheon, D.Y. and Jo, S. (2022) Adverse Effects of Statin Therapy and Their Treatment. *Cardiovascular Prevention and Pharmacotherapy*, **4**, 1-6. https://doi.org/10.36011/cpp.2022.4.e4

[14] Ruscica, M., Ferri, N., Banach, M., Sirtori, C.R. and Corsini, A. (2022) Side Effects of Statins: From Pathophysiology and Epidemiology to Diagnostic and Therapeutic Implications. *Cardiovascular Research*, **118**, 3288-3304. https://doi.org/10.1093/cvr/cvac020

[15] Abdul-Rahman, T., Bukhari, S.M.A., Herrera, E.C., Awuah, W.A., Lawrence, J., de Andrade, H., *et al.* (2022) Lipid Lowering Therapy: An Era beyond Statins. *Current Problems in Cardiology*, **47**, Article ID: 101342. https://doi.org/10.1016/j.cpcardiol.2022.101342

[16] Elseweidy, M.M., Elawady, A.S., Sobh, M.S. and Elnagar, G.M. (2022) Lycopene Ameliorates Hyperlipidemia via Potentiation of Amp-Activated Protein Kinase and Inhibition of Atp-Citrate Lyase in Diabetic Hyperlipidemic Rat Model. *Life Sciences*, **308**, Article ID: 120934. https://doi.org/10.1016/j.lfs.2022.120934

[17] Dongmo, F., Djantou, E.B., Mahamat, A.H., Dongmo, S.S. and Yanou, N.N. (2024) Effect of Aqueous Extract of *Boscia senegalensis* on Hyperglycemia, Hyperlipidemia and Oxidative Stress Induced in Rats. *Journal of Diabetes Mellitus*, **14**, 49-68. https://doi.org/10.4236/jdm.2024.141006

[18] Li, K., Tong, X., Yu, J., Gao, X., Gao, F., Liu, X., *et al.* (2020) Lifeceramics-Treated Water Reduces Serum Uric Acid Levels and Improves Hemorheological Activity in Hyperuricemic Rats. *Biomedical Reports*, **13**, Article No. 22. https://doi.org/10.3892/br.2020.1329

[19] Kita, K., Sugaya, S., Tanaka, T., Dong, M., Sato, C. and Suzuki, N. (2013) Effects of Lifeceramics-Treated Water on Resistance to Oxidative Stress in Human Cells. *Food & Function*, **11**, 14-19.

[20] Kita, K., Fukuyo, M., Kaneda, A. and Suzuki, N. (2021) Antioxidative Effects of Lifeceramics-Treated Water in Cultured Human Cells: Suppression of H_2O_2-Induced Cell Death, Accumulation of Reactive Oxygen Species, and Changes in Gene Expression. *Food & Function*, **17**, 14-21.

[21] Liu, X., Guo, S.H., Ma, X., Dong, M. and Suzuki, N. (2018) Protective Effect and Mechanism of Lifeceramics on Chronic Alcoholic Liver Injury in Rats. *Chinese Journal of Clinical Rational Drug Use*, **11**, 40-42.

[22] I, K., N, M., Y-J, Y. and J-Y, L. (2018) Induce Hyperlipidemia in Rats Using High Fat Diet Investigating Blood Lipid and Histopathology. *Journal of Hematology and Blood Disorders*, **4**, Article 104. https://doi.org/10.15744/2455-7641.4.104

[23] Rodríguez-Correa, E., González-Pérez, I., Clavel-Pérez, P.I., Contreras-Vargas, Y. and Carvajal, K. (2020) Biochemical and Nutritional Overview of Diet-Induced Metabolic Syndrome Models in Rats: What Is the Best Choice? *Nutrition & Diabetes*, **10**, Article No. 24. https://doi.org/10.1038/s41387-020-0127-4

[24] Udomkasemsab, A. and Prangthip, P. (2019) High Fat Diet for Induced Dyslipidemia and Cardiac Pathological Alterations in Wistar Rats Compared to Sprague Dawley Rats. *Clínica e Investigación en Arteriosclerosis*, **31**, 56-62. https://doi.org/10.1016/j.arteri.2018.09.004

[25] Li, K., Tong, X., Yao, W., Wang, X., Suzuki, A. and Suzuki, N. (2017) Study on Hemorheological Properties of Erythrocytes in Asymptomatic Hyperuricemia Rat Model. *International Journal of Medical Research and Health Sciences*, **6**, 1-7.

[26] Wang, Y., Peng, D., Liu, X., Xie, R. and Li, X. (2017) Validation Research and Regulation Exploration of High Fat-Introduced Hyperlipidemia Model in Rats. *Chinese Journal of Comparative Medicine*, **6**, 5-10.

[27] Zheng, D., Liang, Q., Zeng, F., Mai, Z., Cai, A., Qiu, R., *et al.* (2015) Atorvastatin Protects Endothelium by Decreasing Asymmetric Dimethylarginine in Dyslipidemia Rats. *Lipids in Health and Disease*, **14**, Article No. 41. https://doi.org/10.1186/s12944-015-0041-2

[28] Kubo, K. and Kawai, Y. (2021) Zeolite Improves High-Fat Diet-Induced Hyperglycemia, Hyperlipidemia and Obesity in Mice. *Journal of Nutritional Science and Vitaminology*, **67**, 283-291. https://doi.org/10.3177/jnsv.67.283

[29] Sato, K. (2002) Do you Drink the Water of Life? Jiyu Kobo Press.

[30] Tong, X., Dong, M., Kita, K., Zhu, T., Ma, X., Suzuki, A. and Suzuki, N. (2018) Search for Food Materials That Support Healthy Conditions, Based on The Human SOS Response Theory. *Chiba Medical Journal*, **94**, 15-22.

[31] Fentoğlu, Ö., Kırzıoğlu, F.Y., Bulut, M.T., Kumbul Doğuç, D., Kulaç, E., Önder, C., *et al.* (2015) Evaluation of Lipid Peroxidation and Oxidative DNA Damage in Patients

with Periodontitis and Hyperlipidemia. *Journal of Periodontology*, **86**, 682-688. https://doi.org/10.1902/jop.2015.140561

[32] Kaviarasan, K., Arjunan, M.M. and Pugalendi, K.V. (2005) Lipid Profile, Oxidant-Antioxidant Status and Glycoprotein Components in Hyperlipidemic Patients with/without Diabetes. *Clinica Chimica Acta*, **362**, 49-56. https://doi.org/10.1016/j.cccn.2005.05.010

[33] Rivera-Mancía, S., Jiménez-Osorio, A.S., Medina-Campos, O.N., Colín-Ramírez, E., Vallejo, M., Alcántara-Gaspar, A., *et al.* (2018) Activity of Antioxidant Enzymes and Their Association with Lipid Profile in Mexican People without Cardiovascular Disease: An Analysis of Interactions. *International Journal of Environmental Research and Public Health*, **15**, Article 2687. https://doi.org/10.3390/ijerph15122687

[34] Yang, R., Shi, Y., Hao, G., Li, W. and Le, G. (2008) Increasing Oxidative Stress with Progressive Hyperlipidemia in Human: Relation between Malondialdehyde and Atherogenic Index. *Journal of Clinical Biochemistry and Nutrition*, **43**, 154-158. https://doi.org/10.3164/jcbn.2008044

[35] Minhajuddin, M., Beg, Z.H. and Iqbal, J. (2005) Hypolipidemic and Antioxidant Properties of Tocotrienol Rich Fraction Isolated from Rice Bran Oil in Experimentally Induced Hyperlipidemic Rats. *Food and Chemical Toxicology*, **43**, 747-753. https://doi.org/10.1016/j.fct.2005.01.015

[36] Sethi, J.K. and Hotamisligil, G.S. (2021) Metabolic Messengers: Tumour Necrosis Factor. *Nature Metabolism*, **3**, 1302-1312. https://doi.org/10.1038/s42255-021-00470-z

[37] Matsubara, M., Maruoka, S. and Katayose, S. (2002) Decreased Plasma Adiponectin Concentrations in Women with Dyslipidemia. *The Journal of Clinical Endocrinology & Metabolism*, **87**, 2764-2769. https://doi.org/10.1210/jcem.87.6.8550

[38] von Eynatten, M., Hamann, A., Twardella, D., Nawroth, P.P., Brenner, H. and Rothenbacher, D. (2006) Relationship of Adiponectin with Markers of Systemic Inflammation, Atherogenic Dyslipidemia, and Heart Failure in Patients with Coronary Heart Disease. *Clinical Chemistry*, **52**, 853-859. https://doi.org/10.1373/clinchem.2005.060509

[39] Suzuki, N., Kita, K., Sugaya, S., Tanaka, T., Dong, M. and Tong, X.B. (2015) Health Care Promotion by Lifeceramics. Chiba Researchers Network for Health Care Promotion.

[40] Suzuki, A., Shiga, T., Sato, K., Shoda, M. and Yamaguchi, J. (2025) Metabolome Analysis in Patients with Heart Failure and Implantable Cardioverter Defibrillators. *Heart and Vessels*, **40**, 86-90. https://doi.org/10.1007/s00380-024-02452-z