Effects of soda water on blood lipid and metabolic profiling of urine in hyperlipidemia rats using UPLC/Triple-TOF MS

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ABSTRACT

The effects of a natural soda water (Shi Han Quan, SHQ) on hyperlipidemia and the changes of urine metabolic profiling by metabolomics techniques were investigate. Thirty six Wistar rats weighing 160–200 g were divided into control group, hyperlipidemia (HL) group, and hyperlipidemia + SHQ water (SHQ) group. The metabolites in urine were determined using ultra high performance liquid chromatography-triple-time of flight-mass spectrometry (UPLC/Triple-TOF MS). At the end of 1 month and 3 months, the total glyceride (TG) level was significantly lower in SHQ group compared to HL group. There was no significantly difference in total cholesterol (TC) levels in HL group compared with SHQ group. The results showed that dinking SHQ water can improve the TG, but with no effects on TC. After drinking SHQ water for 3 months, the rats in different groups could be classified into different clusters according to the metabolites in urine. Total 15 important metabolites were found and correlated with disturbance of amino acid, phospholipid, fatty acid and vitamin metabolism, which suggested the changes of metabolism in the body and possible mechanism by which SHQ improved the TG. These findings provide a new insight for the prevention and control of hyperlipidemia.

1. Introduction

World Health Organization (WHO) reported that the prevalence of obesity is on the rise every year due to unhealthy foods containing high fat and sugar and lack of physical activity, and there were more than 650 million obese adults and over 340 million overweight or obese children and adolescents globally in 2016 [1]. Obesity is usually accompanied by hyperlipidemia, and hyperlipidemia is considered to be a major risk factor for metabolic diseases such as dyslipidemia, atherosclerosis, and type 2 diabetes [2,3]. The clinical hypolipidemic drugs mainly include statins [4], niacin [5], acid sequestrants [6], microsomal triglyceride transfer protein (MTP) inhibitor [7], and peroxisome proliferator activated receptor α (PPAR α) agonist [8]. Many of these medications have significant adverse effects, such as rhabdomyolysis, hepatorenal toxicity, cognitive impairment, hepatic steatosis, increased transaminase, and gastrointestinal adverse reactions [4,7,9–11]. Hence, the discovery and investigation of a natural substance for reducing

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hyperlipidemia is particularly significant and important.

Studies reported that consumption of alkaline water had antioxidant effects that can preserve pancreatic beta cells with its anti-oxidant effects [12], prevent osteoporosis [13], and improves aging [14]. SHQ (Shi Han Quan), a natural soda water, discovered in China, has a pH range of 8.1–8.5. It is weakly alkaline and contains elements beneficial to human body (such as the boron and dissolved oxygen). Previous studies has suggested that SHQ may help prevent gouty inflammation through the regulation on the levels of intercellular adhesion molecule-1 (ICAM-1) and interleukin-6 in a cell experiment [15], and improve the blood glucose and insulin in mice [16]. Interleukin-6, ICAM-1, blood glucose and insulin were closely associated with blood lipid [17–19]. Therefore, the effects of SHQ on hyperlipidemia and the potential mechanisms need to be investigated.

Metabolomics refers to the systematic quantitative detection on the dynamic changes of metabolites of small molecule caused by physiological or pathological state or some intervention factors, and explore the metabolic changes of individual through the pathway analysis of metabolites [20,21]. Metabolomics has been for identifying the key metabolites of urine and explore the metabolic changes in obese men with hyperlipidemia [22]. Ultra-performance liquid chromatography coupled to a triple-Time of flight mass spectrometer (UPLC/Triple-TOF MS) has been extensively used in the analysis of metabolomics due to its broad dynamic range and ability to cover a wide range of chemical diversity [23–26]. Therefore, we evaluate the impact of SHQ soda water on hyperlipidemia and investigate the potential mechanisms of action with a metabolomics analysis based on UPLC/Triple-TOF MS and multivariate data analysis.

2. Materials and methods

2.1. Animals treatment

Thirty-six healthy male Wistar rats weighing 160–200 g were supplied by Changchun Changsheng Biotechnology Co., Ltd. All rats were housed in cages for acclimatizing the condition with a temperature ($20 \pm 2\,°C$) and a 12-h light-dark cycle for seven days before treatment. The rats were randomly divided into three groups according body weight including control group, high fat emulsion with distilled (hyperlipidemia, HL) group, and high fat emulsion with SHQ water (SHQ) group (n = 12 in each group). The control group was distilled water. SHQ water was provided by Heilongjiang Province Shihanquan Technology Development Co., Ltd. Water consumption of all rats was recorded. High fat emulsion contains 25 % lard, 5 % cholesterol, 10 % Tween-80, 10 % propylene glycol, 1 % sodium cholate, 0.5 % propylthiouracil, and distilled water. The high-fat emulsion was given by gavage to 1 % of the body weight of rats until the treatment ended. The rats were provided with a conventional diet (AIN-93G) in the study. Each group consisted of 12 rats, which were randomly divided into two subgroups (n = 6). After 1 and 3 months, the rats were sacrificed under chloral hydrate anesthesia, and abdominal aortic blood was collected, then centrifuged at $3000 \times g$ for 15 min, and stored at $-80\,°C$ for determinate total glyceride (TG) and total cholesterol (TC). At the end of the third month, urine were sampled and stored at $-80\,°C$ for the determination of metabolites. All experiments were performed in compliance with institutional guidelines and approved by the Animal Experimental Ethics Committee of Shanghai University of Medicine & Health Sciences.

2.2. Serum TG and TC determination

Serum TG and TC was determined with determination kit (Nanjing Jiancheng Bioengineering Research Institute Co., Ltd. Nanjing, China) using an automatic Microplate Reader (Multiskan mk3, Thermo Scientific, MA, USA).

2.3. Chemicals and reagents

LC/MS grade methanol, formic Acid, and acetonitrile were supplied by Fisher Chemical (Fisher Scientific International Inc., Pittsburgh, USA).

2.4. Metabolic profiling analysis by UPL/triple - TOF MS

2.4.1. Urine pretreatment and quality control of analysis
Metabolites in urine sample (100 μl) were determined with a 400 μl methanol: acetonitrile (1:1, v/v). After vortexing and ultrasonic extraction on ice for 10min, the sample was allowed to placed at $-20\,°C$ for 30min, and centrifuged at $3000 \times g$ at $4\,°C$ for 15 min. The supernatant was dried with nitrogen, then reconstituted with a mixture of 100 μl acetonitrile and water (1: 1). Finally, the reconstituted sample was transferred to sample vials for further analysis. Quality control samples (QC) were prepared by mixing all samples of equal volume for monitoring the stability of the analysis, and determined at regular intervals after every 6 samples. For avoiding sequential effects, different batches were injected in random crossover.

2.4.2. UPLC-MS/MS analysis
Metabolic profiling analysis was carried out using an UPLC system (ExionLC AD System) coupled to a triple-time of flight (Triple - TOF) Mass Spectrometer (ABSCIEX-Triple TOF 5600) with electrospray ionization in positive mode (AB SCIEX Corporation, Framingham, USA). To achieve separation of metabolites, a UPLC system was utilized, which was equipped with a BEH-C18 column. (2.1 $\times$ 100 mm $\times$ 1.7 μm, Waters, Milford, USA). The mobile phases consisted of solvent A and solvent B, which were composed of 0.1 % formic acid in water and 0.1 % formic acid in a mixture of acetonitrile and isopropanol (1:1, v/v), respectively. A gradient elution method was employed. The initial composition of solvent A was set to 95 % and then gradually decreased to 80 % within the first 3 min.

From 3 to 9 min, the composition of solvent A was further decreased to 5 %. The concentration of solvent A was maintained at 5 % from 9 to 13 min, followed by an increase to 95 % from 13 to 13.1 min. The system was then equilibrated by maintaining 95 % solvent A for 2.9 min (13.1–16 min). The flow rate (0.40 mL/min), injection volume (20 μL), and column temperature (40 °C) were all controlled during the experiment. MS analysis was conducted using specific settings for the source temperature (500 °C), ionspray voltage (5000 V), desolvation gas flow (600 L/h), and cone gas flow (50 L/h) in positive mode. The mass range (50–1000 m/z) for detection was also specified.

2.4.3. Data preprocessing

Progenesis QI 2.3 software was used to detect and align peaks in the raw data, which generated a data matrix with retention time, mass-to-charge ratio (m/z), and peak intensity. Metabolic features were detected in at least 80 % of any set of samples were retained for further analysis. Normalization was performed by sum to account for changes in urine concentration. Multivariate statistical analysis was then carried out with the R package (ropls, Version1.6.2, http://bioconductor.org/packages/release/bioc/html/ropls.html), which is available on the Bioconductor on Majorbio Cloud Platform (https://cloud.majorbio.com). Principle component analysis (PCA) was utilized for visualizing the metabolic data overview and assessing the data quality of the metabolomics platform, and global metabolic changes among groups was determine by the partial Least Squares Discriminant Analysis (PLS-DA). The R2 and Q2 parameters of PLS-DA model were used to evaluate model validity and the risk of over-fitting, and 200 permutation tests were performed to avoid over-fitting of model. Metabolites with variable importance in projection (VIP) values (>1) and p-values (<0.05) among groups were used as criteria for selecting potential biomarkers. The potential biomarkers were identified using the accurate mass, and MS/MS fragments spectra and isotope ratio difference via searching in reliable biochemical databases such as Metlin database (https://metlin.scripps.edu/) and Human metabolome database (HMDB) (http://www.hmdb.ca/). Specifically, the mass tolerance allowed for a margin of error (±10 ppm) between the measured and exact mass m/z values. MS/MS confirmation of metabolites were performed, only the metabolites with a high fragment score (>30) were considered confidently identified. Metabolic pathways analysis of important metabolites was performed with MetaboAnalyst 5.0 (http://www.metaboanalyst.ca/) [27]. Then, other pathways of important metabolites were interpreted by consulting references and databases.

2.5. Statistical analysis

Statistical analysis were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA), and data were expressed as mean ± standard deviation. The differences among groups were compared with one-way analysis of variance (ANOVA) followed by LSD or Dunnett T3 post-hoc test. A P value < 0.05 was set as statistically significant.

3. Results

3.1. Blood lipid levels of rats

At the end of 1 month, there was an increase trending for the TG level in HL group compared to control group (p = 0.074), and TG level was significantly lower at the end of 1 and 3 month in SHQ group compared with HL group. There was no significantly difference in TG levels between SHQ and control groups. At the end of 1 and 3months, the TC levels in both HL and SHQ groups were significantly higher compared to control group. There was no significantly difference in TC levels in HL group compared with SHQ group. The results showed that dinking SHQ water can improve the TG, but with no effects on TC (Table 1).

3.2. Urinary metabolomics profiling analysis of rats

A PCA on sample dataset including QC samples was performed for the initial quality overview of the analytical run, and QC samples were found to be closely clustered together in the scores plot (Fig. 1: red cross), which suggested excellent stability of the metabolomics platform. PLS-DA was performed to profile the metabolic alterations of rats in HL and SHQ groups, and find the important metabolites related to these changes response from high fat emulsion and drinking SHQ water. The rats in control, HL, and SHQ groups could be divided into distinctive clusters in PLS-DA scores plot for their metabolic differences among groups (Fig. 2A). The values of R2Y (0.992) and Q2 (0.952) for the PLS-DA model were all more than 0.5, which suggest the model was appropriate for the recognition analysis. Furthermore, the permutation test was applied for assessing the spurious risk of the PLS-DA model. The results indicated that all values of R2Y and Q2 on the left side were lower than the original points on the right side (Fig. 2B), which suggesting the valid of the

Table 1
The levels of blood lipid of rats in three groups.

	Control	HL	SHQ
TG at 1 moth (mmol/L)	0.36 ± 0.10	0.51 ± 0.21	0.30 ± 0.04[†]
TG at 3 moth (mmol/L)	0.38 ± 0.13	0.47 ± 0.08	0.29 ± 0.15[†]
TC at 1 moth (mmol/L)	1.39 ± 0.36	3.97 ± 0.69*	4.39 ± 0.33*
TC at 3 moth (mmol/L)	2.21 ± 0.46	5.73 ± 0.89*	5.40 ± 2.53*

*$P < 0.05$ compared with control group, and [†]$P < 0.05$ compared with HL group.
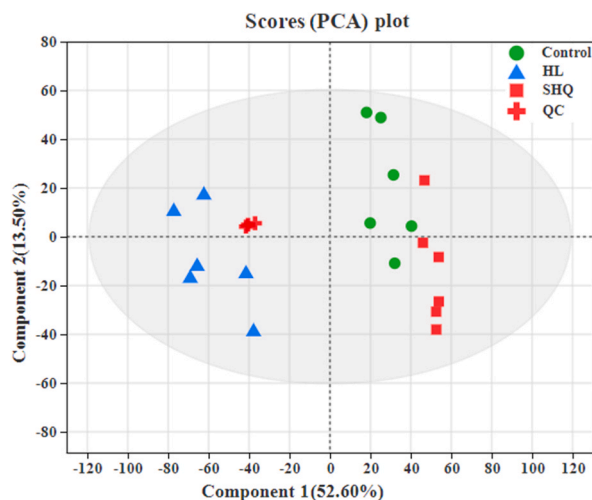
Fig. 1. Scores plots with PCA of urine metabolite in rats of Control, hyperlipidemia (HL), SHQ soda water + HL (SHQ), and quality control (QC) groups in the positive mode.
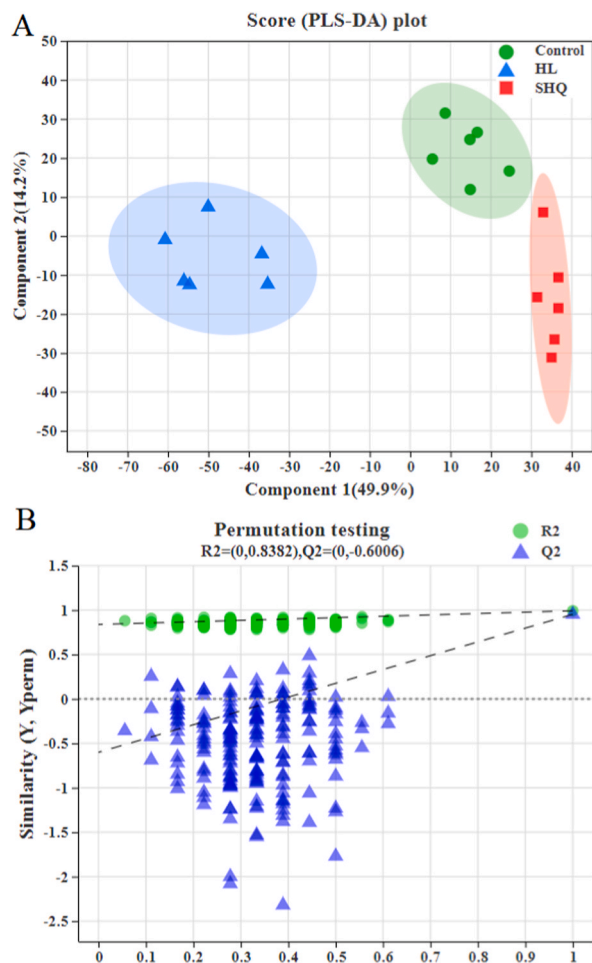

Fig. 2. PLS-DA analysis of urine metabolite in rats of Control, HL, and SHQ groups in positive ESI mode. A, score plot of PLS-DA analysis, one data point represents one rat; B, Permutation test of the PLS-DA model. The R2Y and Q2 values represent the goodness of fit and the predictability of the model, respectively.

PLS-DA model. As shown in Fig. 3, 60 and 43 important metabolites were identified in comparisons of HL vs. control and SHQ vs. HL groups, respectively. Among these metabolites, 15 metabolites were shared, which were significant lower in HL group compared to control group, and significant higher in SHQ group compared to HL group (Fig. 4, Fig. 5 and Table 2).

3.3. Metabolic pathways

Metabolic pathways analysis by references and databases showed changed metabolism involved in amino acid, phospholipid, fatty acid and vitamin metabolism (Table 2), which play vital roles in the TG improvement with drinking SHQ water. The metabolic pathway analysis using MetaboAnalyst 5.0 revealed that one vitamin metabolic pathway with an impact value ≥ 0.10, nicotinamide metabolism, was found to be the most important metabolic change (Fig. 6).

4. Discussion

In the current study, drinking SHQ water can improve the TG of rats with hypertriglyceridemia, and metabolomics was applied to find the important metabolites from thousands of small molecular endogenous metabolites, and characterize the metabolic changes of rats with high fat model and SHQ intervention. The results showed that 15 important metabolites were identified, and pathway analysis suggested the disturbance of amino acid, phospholipid, fatty acid and vitamin metabolism in the rats of HL group and metabolic improvements were observed in the rats of SHQ group, which were closely related TG.

Through the metabolic pathway analysis with MetaboAnalyst 5.0, one vitamin metabolic pathway from metabolite of trigonellinamide, nicotinamide metabolism was found to be the most important metabolic change. Nicotinamide is a vitamin B3 vitamer, which is a water-soluble nutritional elements participate in many important metabolic reactions and are essential to maintain the homeostasis and cellular metabolism. Nicotinamide can be converted from niacin after being absorbed by the human body, niacin and niacinamide are very important for all living cells. Vitamin B3 undergoes biosynthesis to produce nicotinamide adenine dinucleotide (NAD+) and nicotinamide adenine dinucleotide phosphate (NADP) [28], which play a crucial role in the electron transport chain and facilitate the oxidative phosphorylation of mitochondria [29], and involved in energy metabolism. Vitamin B3 (niacin form) can also reduce the blood levels of TG and low density lipoprotein [28]. Therefore, in the study, the changes of L-carnitine and trigonellinamide suggested the disturbed fatty acid and vitamin metabolism of rats in HL group, respectively, and the potential mechanism of SHQ improved the TC.

Metabolic pathways analysis using references and databases showed that most changed metabolic pathways affected by high fat model and SHQ intervention were amino acid metabolism, and related 11 metabolites accounts for 73 % of the total metabolites we found, which play important roles in the regulation of TG. These metabolites including betaine, 5-Hydroxyindoleacetylglycine, N-Acetyl-L-phenylalanine, hydroxyphenylacetylglycine, 2-Aminobenzoic acid, tyramine, 4-Guanidinobutanoic acid, 1-Methylhistamine, L-Arginine, spermidine, and spermine were found to be significantly lower in HL group compared to control group, and significantly higher in SHQ group compared to HL group. The changes of metabolites in HL group were inversed in SHQ group after drinking SHQ water.

Among these metabolites, the hydroxyphenylacetylglycine, 2-Aminobenzoic acid, and tyramine were involved in tyrosine metabolism. Tyrosine plays a important role for regulating the energy metabolism. Tyrosine metabolism was correlated with accumulation of triglyceride in oleic acid (OA)-treated HepG2 cells [26]. Supplementation with tyrosine could lead to the normalization of triglycerides and resist the increase of triglyceride in Rats with Diet-Induced Obesity. The production of proinflammatory cytokines was suppressed by amino acids in spleen cell lysates. Consumption of Tyr was observed to significantly alleviate signs of fatty degeneration in liver tissue morphology. Additionally, in splenocyte lysates, tyrosine inhibited the production of proinflammatory cytokines, which indicate an anti-inflammatory effect. Liver histomorphology analysis demonstrated that tyrosine intake significantly alleviated fatty
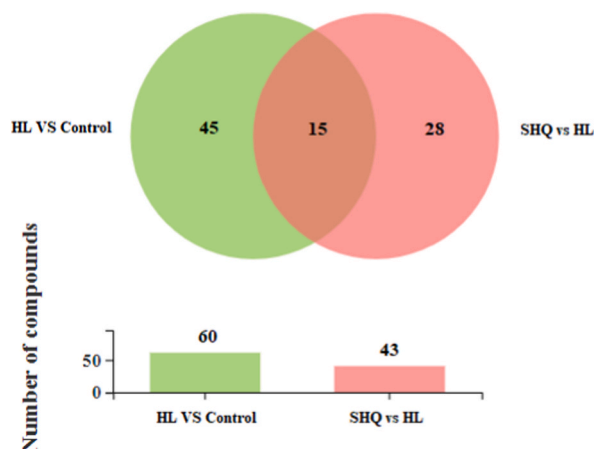

Fig. 3. Important metabolites in comparisons of HL vs. control and SHQ vs. HL groups.
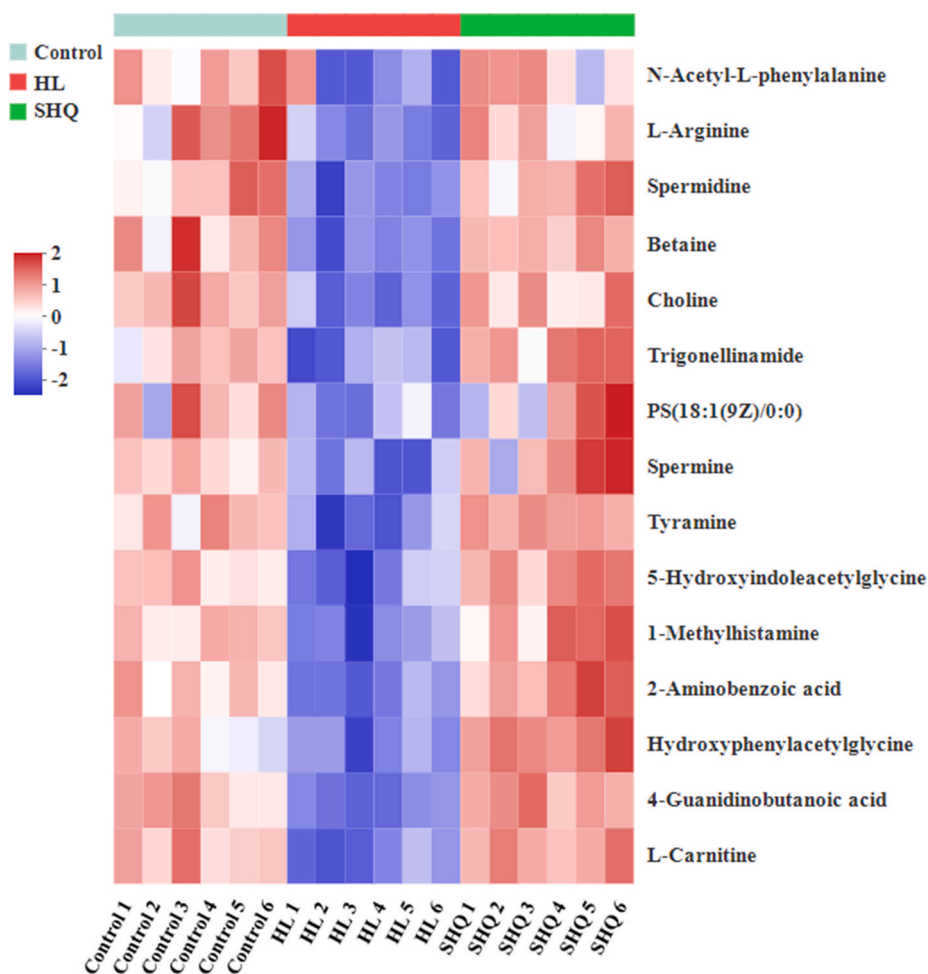
Fig. 4. Heat map visualization based on 15 biomarkers. Rows: samples; columns: metabolites. Light cyan: control group; red: HL group; Green: SHQ group. Color key shows the expression value of metabolite: dark blue: lowest; dark red: highest.

degeneration [30]. Changed metabolites of 4-Guanidinobutanoic acid and L-Arginine suggested disturbed arginine metabolism. A study was performed for evaluating the effects of L-arginine on antioxidant capacity, inflammation and lipid profiles in rats fed an atherogenic diet. The results showed that supplementation with L-Arginine could improve lipid profiles through lowering serum total cholesterol and triglycerides, and reduce oxidative stress, increase total antioxidant capacity by lowering C-reactive protein concentration and higher concentrations of superoxide dismutase and glutathione S-transferase [31]. Metabolites of spermidine and it's derivative, spermine involved in arginase metabolism. Arginase is the enzyme which synthesizes ornithine, a precursor from which spermidine and spermine are formed. Spermine could increase arginase activity, and increase the synthesis of ornithine [32]. In addition, they are basic compounds with key roles in physiological function as a chemical chaperone and glycation inhibitor on the lipid profile. Spermine can decrease the TC and LDL-c levels in STZ-induced diabetic rats [33], and diminish the increased triglycerides induced by carbon tetrachloride [32].

The other metabolites of betaine, 1-Methylhistamine, 5-Hydroxyindoleacetylglycine, and N-Acetyl-L-phenylalanine were involved in metabolism of glycine, histidine, tryptophan, and phenylalanine, respectively. In the process of metabolism of the organism, glycine participates in the biosynthesis of protein, nucleic acid and lipid [34,35], which can improve the inflammatory response of organism, enhance the antioxidant capacity and regulate the glucose and lipid metabolism of the organism [36–41]. Histidine can affect the biosynthesis of triglyceride [42], histidine metabolism disorder could aggravate lipid accumulation in the ox-LDL-treated bone marrow-derived macrophages [43]. A randomized controlled study in obese women with metabolic syndrome showed that supplementation with histidine can significant decrease the levels of cholesterol and triglycerides [44]. Low birth weight is closely correlated with glucose and lipid metabolism disorders in early life, supplementation with tryptophan reduced the hepatic gluconeogenesis and lipogenesis, but increased the glycolysis in LBW piglets [45]. Giannetto et al. [46] indicated that additional dietary tryptophan led to the hypotriglyceridaemic and influence the hepatic fatty acid synthesis in normal rats. Phenylalanine can improve the metabolism of energy (protein, lipid, and starch) through regulating the secretion or synthesis of lipase, trypsin and α-amylase by S6K1 and 4EBP1 (mRNA translation initiation factors) [47]. Therefore, the lower levels of these metabolites reflect the perturbation of amino
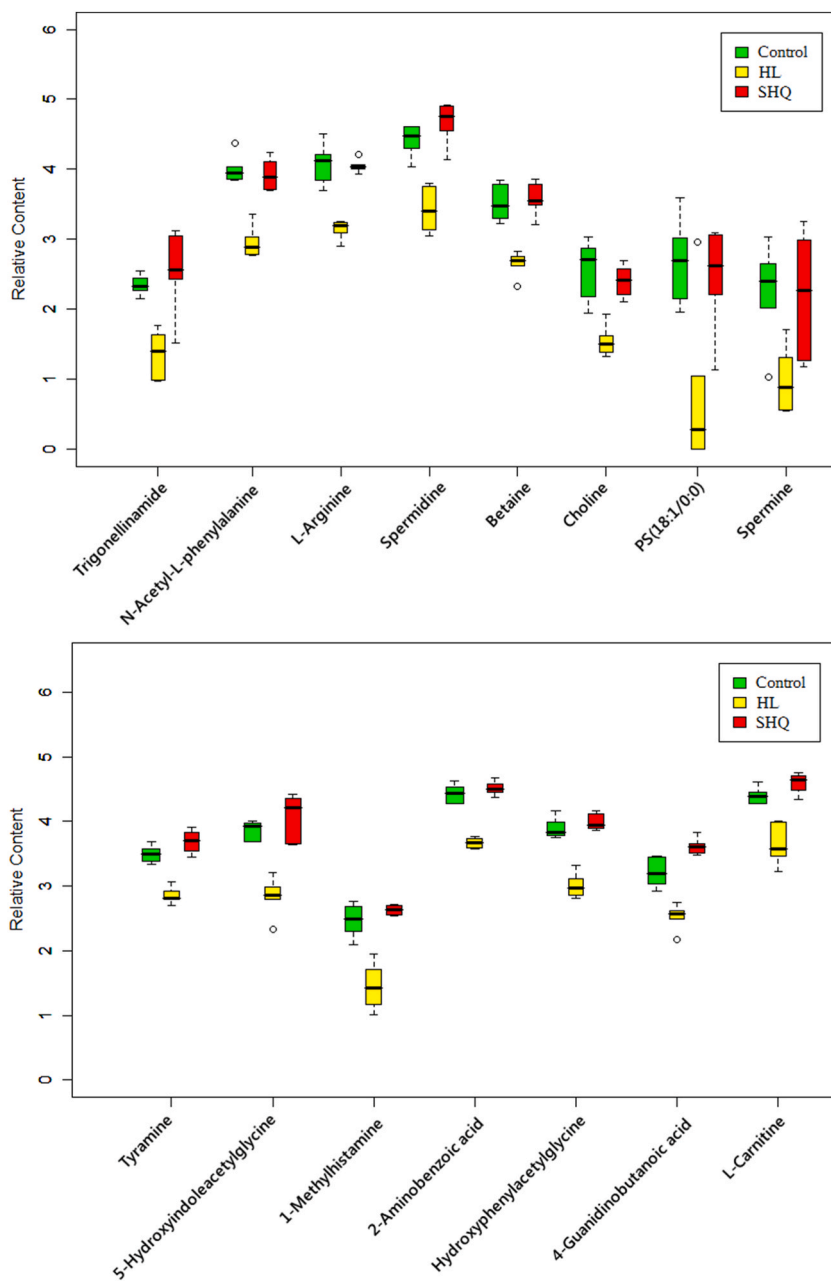
Fig. 5. Trending plot of 15 metabolites in positive mode.

metabolism, which maybe one of the reasons of higher TG in model group, and were correct in SHQ group.

The study also found abnormalities in phospholipid metabolism that were associated with choline and phosphatidylserine (PS). Disturbance of phospholipid metabolism related to choline and phosphatidylserine (PS) was also found. Choline deficiency can lead to abnormal phospholipid synthesis [48]. It is a water soluble nutrient, which plays an important role in the synthesis of the neurotransmitter acetylcholine [49]. Acetylcholine can promote Lipid droplet lipolysis and activate LD-mitochondria interactions, and affect the lipid metabolism and energy homeostasis [50]. Jack-Roberts et al. found that maternal choline supplementation in a mouse model of maternal obesity can significant alleviate the increase of hepatic triglyceride accumulation and reduce lipogenic gene expression in fetuses [51]. PS is a type of glycerophospholipid in which a phosphorylserine moiety is present at one of the glycerol substitution sites. Therefore, the changes of choline and PS indicated the metabolic disorder of phospholipid in response to the high fat intervention in HL group, and the improvement of metabolism with SHQ intake, which partly explain the changes of TC in HL and SHQ group.

L-carnitine is biosynthesized in human body with lysine and methionine as substrates, and is essential in the transportation of long-chain fatty acids to the mitochondria [52]. The decrease in carnitine contributes to an increase in fatty acyl coA, which can reduce the

Table 2

Identification of urine metabolites in UPLC Q-TOF MS positive ion mode.

RT (min)	*m/z* (Da)	Mass error (PPM)	Adducts	Formula	Identity	Pathway
0.79	137.0706	2.18	M + H	C7H8N2O	Trigonellinamide	Vitamins metabolism
2.44	208.0964	2.14	M + H	C11H13NO3	N-Acetyl-ʟ-phenylalanine	Amino acid metabolism
0.61	175.1184	3.12	M + H	C6H14N4O2	ʟ-Arginine	Amino acid metabolism
0.59	146.1648	2.45	M + H	C7H19N3	Spermidine	Amino acid metabolism
0.82	118.0861	1.63	M + H	C5H11NO2	Betaine	Amino acid metabolism
0.73	104.1072	2.04	M + H	C5H13NO	Choline	Phospholipid metabolism
8.55	524.2979	0.82	M + H	C24H46NO9P	PS(18:1/0:0)	Phospholipid metabolism
14.31	203.2225	2.56	M + H	C10H26N4	Spermine	Amino acid metabolism
1.12	138.0909	3.1	M + H	C8H11NO	Tyramine	Amino acid metabolism
3.77	231.0761	1.34	M + H–H2O	C12H12N2O4	5-Hydroxyindoleacetylglycine	Amino acid metabolism
0.77	126.1023	1.96	M + H	C6H11N3	1-Methylhistamine	Amino acid metabolism
2.32	120.0441	2.17	M + H–H2O	C7H7NO2	2-Aminobenzoic acid	Amino acid metabolism
2.41	210.0758	1.57	M + H	C10H11NO4	Hydroxyphenylacetylglycine	Amino acid metabolism
0.84	146.092	3.02	M + H	C5H11N3O2	4-Guanidinobutanoic acid	Amino acid metabolism
0.81	162.112	2.7	M + H	C7H15NO3	ʟ-Carnitine	Fatty acid metabolism

RT, Retention time; *m/z*, Measured mass to charge ratio; PS, phosphatidylserine.
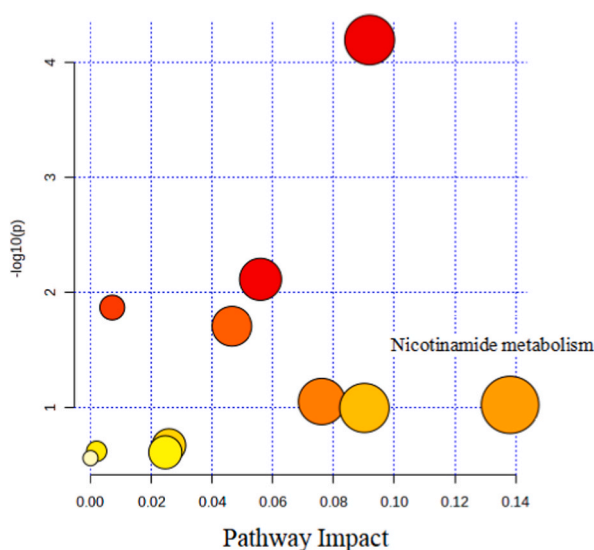

Fig. 6. Summary of pathway analysis.

efficiency of mitochondrial and promote oxidative stress and inflammation. The lack of mitochondrial carnitine availability may result in reduced fatty acid oxidation (marcovina et al., 2013; dinicolantoni et al., 2014) [53,54]. A randomized, double-blind study [55] evaluated the effects of ʟ-carnitine on body fat content and lipid metabolism in patients with diabetes. The results showed that the ʟ-carnitine could decrease the fat content of the body and triglyceride level. Therefore, the changes of ʟ-carnitine in the study suggested the disturbed fatty acid metabolism of rats in HL group, and the potential mechanism of drinking SHQ improved TC.

In the present study, it was found that SHQ water contains sodium bicarbonate, which gives it alkaline properties. Jin et al. [56] found that alkaline-reduced water made of magnesium and water (pH 10.0–10.5) can reduce the triglycerides and total cholesterol in blood. In addition, SHQ water contains Boron (about 1.0–2.0 mg/L), and Khaliq et al. [57] indicated that boron could decrease oxidative stress, affect lipid profile, and improve energy status in obese rabbits. Our study also has a few limitations. Firstly, urine was used for the metabolomis analysis, and omics analysis of multiple biological samples can determine more metabolites, and more metabolic changes of organism can be found; Secondly, C18 column was used to analyze metabolites in urine, which also reduces the number of determined metabolites compared with T3 column; Thirdly, the present study is performed in rats and not in human, further clinical study should be carried out for verifying our observation.

5. Conclusion

In summary, we evaluated the effect of drinking soda water on hyperlipidemia and explored the possible mechanism through determining urine metabolic profiling with a metabolomics platform based on UPLC/Triple-TOF MS/MS integrated with multivariate statistical analysis. Total 15 important metabolites were found, which were closed related to disturbance of amino acid, phospholipid,

fatty acid and vitamin metabolism, and improved by drinking SHQ water. The HCO_3^- and boron may be the important compounds of SHQ water improving the TG. These findings provide a new insight into the prevention and control of hyperlipidemia.

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Data availability statement

Data will be made available on request.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

Dan Han: Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Formal analysis, Investigation. **Litian Shi:** Data curation, Formal analysis. **Junjie Yu:** Data curation, Formal analysis. **Lixin Na:** Conceptualization, Methodology, Resources.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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