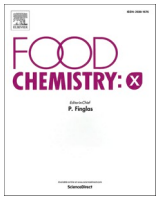
Food Chemistry: X 20 (2023) 101025

Contents lists available at ScienceDirect

Food Chemistry: X

journal homepage: www.sciencedirect.com/journal/food-chemistry-x



Lactiplantibacillus plantarum fermentation enhanced the protective effect of kiwifruit on intestinal injury in rats: Based on mitochondrial morphology and function

Yun Ma, Xiao Chen, Ruiyu Xu, Hongyan Niu, Qun Huang, Yan Zhou *

The Key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education, Guizhou Provincial Engineering Research Center of Ecological Food Innovation, School of Public Health, Guizhou Medical University, Guiyang 550025, China

ARTICLE INFO

Keywords:
Lactic acid bacteria
Fermented kiwifruit
Intestinal injury
Mitochondria
Intestinal barrier function

ABSTRACT

Fermented foods have protective effects on body health. In our previously study, we found *Lactiplantibacillus plantarum* fermentation enhanced antioxidant activity of kiwifruit *in vitro* digestion. Then, in this work we explored the protective effect of fermented kiwi on intestinal injury induced by acute lipopolysaccharide (LPS) stress. Compared to non-fermented kiwi pulp (KP), *Lactiplantibacillus plantarum* fermented kiwi pulp (FKP-LP) contained more peptides, hormones and vitamins contents, lesser nucleic acid and carbohydrate contents. FKP-LP could relieve the intestinal injury by improving morphological of tight junction and upregulating tight junction proteins mRNA expression. Fermented kiwi maintained the mitochondrial morphology, mitochondrial respiratory function, and mitochondrial homeostasis, and relieved the LPS induced injury by regulating the contents of energy substances, and the respiratory chain complex enzyme activity through the pathway of AMPK and its downstream factors including PGC-1α, NRF1, NRF2, TFAM, and ULK2.

1. Introduction

Intestinal mucosa is the largest interface between the body and the external environment (Turner, 2009). Intestinal mucosal mechanical barrier can hinder the invasion of pathogenic microorganisms and toxins, maintaining the stability of the intestinal environment, which plays a key role in the body health (Chen et al., 2021; Turner, 2009). The mechanical barrier damage will lead to the increase of intestinal permeability, facilitate translocation of harmful substances and pathogens to the bloodstream, and induce some diseases, such as infections with intestinal pathogens, inflammatory bowel disease, irritable bowel syndrome, even systemic diseases such as obesity and diabetes (Gleeson, 2017; König et al., 2016). Therefore, improving the damage of intestinal mucosal epithelial barrier function is crucial to maintain the health and prevent the diseases (Feng et al., 2017).

The growing number of scientific research has revealed the positive impact of fermented foods on human health. The most widespread fermented products are dairy products like yogurt. However, other food matrixes such as fruits, and vegetables have also been widely studied and showed many beneficial effects on health. Fruits are excellent matrices for lactic acid fermentation, based on their high content of carbohydrates, polyphenols, vitamins, minerals, and dietary fibers (Septembre-Malaterre, Remize, & Poucheret, 2018; Szutowska, 2020). According to the latest taxonomy, 12 genera of lactic acid bacteria are commercially used in the processing of various functional food products. Among these, *Lactiplantibacillus* is the most commonly used genus for the fermentation of fruits and vegetables (Carr, Chill, & Maida, 2002). Numerous studies have researched the changes of the components during juice fermentation processes, such as antioxidant activity, total phenolic, flavonoid and anthocyanin content (Szutowska, 2020). Fermentation of mulberry juice (Morus nigra) by different *Lactiplantibacillus* strains contributed to a significant increase of total phenolics, anthocyanin, and flavonoid content, and to an improvement of antioxidant activity (Kwaw et al., 2018). Fermentation of cherry juice by a *Lactiplantibacillus plantarum* strain contributed to the bioconversion of protocatechuic acid into catechol and caffeic acid into dihydrocaffeic acid, both of which are characterized by a high bioavailability for humans (Filannino, Bai, Di Cagno, Gobbetti, & Gänzle, 2015).

Lactiplantibacillus plantarum fermented pomegranate juice could be a potential treatment of some chronic inflammatory diseases, based on its inhibitory activity towards pro-inflammatory mediators (IL-4, IL-6, IL-17a, and TNFα) (Filannino et al., 2013). Administration of fermented

* Corresponding author at: Key Laboratory of Environmental Pollution Monitoring and Disease Control, Guizhou Medical University, Guiyang China.
E-mail address: zhouyan6125@126.com (Y. Zhou).

https://doi.org/10.1016/j.fochx.2023.101025
Received 4 September 2023; Received in revised form 18 November 2023; Accepted 21 November 2023
Available online 5 December 2023

cactus pear juice by *Lactiplantibacillus plantarum* to obese mice caused a significant decrease in the body weight gain and ameliorated the insulin resistance, hyperglycemia, and hyperlipemia that characterize obesity (Verón et al., 2019). Carrot juice fermented by *Lactiplantibacillus plantarum* regulated the levels of blood glucose and related hormones including insulin and glucagon in type-2- diabetic rats, which might have the potential for the treatment of diabetes (Li et al., 2014). The fermented tomato juice by *Lactiplantibacillus plantarum* was characterized by the largest improvement to intestinal barrier integrity (Valero-Cases, Roy, Frutos, & Anderson, 2017).

Kiwifruit is a kind of nutritious fruit, containing high vitamin C, and dietary fiber, vitamin E and folate, as well as various bioactive components, including a wide range of antioxidants, phytonutrients and enzymes, which benefits to digestive, immune and metabolic health (Richardson, Ansell, & Drummond, 2018). In our previously study, we found that compared to other, Lactiplantibacillus (such as *Lactiplantibacillus acidophilus and Lactiplantibacillus casei*), kiwi fermented by *Lactiplantibacillus plantarum* had higher antioxidant and living bacteria *in vitro* digestion (Chen, Yuan, Wang, Zhou, & Sun, 2021). Mitochondria, a sensitive site for free radical action, was easily to oxidative damage. Recent years, maintaining mitochondrial function had been recognized as the key to alleviating intestinal damage and promoting intestinal health. Polyphenol may promote mitochondrial biogenesis to ensure gut healthy. Whether kiwifruit fermented by *L. plantarum* can alleviate intestinal mitochondrial oxidative damage is not clear.

In the present study, the constitution between fermented and unfermented kiwi were determined by non-targeted metabolomics. Later, fermented and non-fermented kiwi were supplemented to Sprague-Dawley rats to explore the preventive effect on intestinal injury induced by acute LPS (lipopolysaccharide) stress.

2. Materials and methods

2.1. Chemicals and reagents.

Kiwifruit were from Guizhou SanJin ShengGuo Green Food Co., Ltd, Guiyang, China. *Lactiplantibacillus plantarum* were from Yaxin Biological Co., Ltd, Taiwan, China. Folin-Ciocalteu reagent, ethylene diamine tetraacetic acid, 2,2′-azo-bis-3-ethyl benzothiazoline-6-sulfonic acid, and sodium citrate were from Tianjin Fengchuan Chemical Reagent Co., Ltd.

Hydroxyl radical detection kit, superoxide anion detection kit, Diamine oxidase (DAO) were purchased from Nanjing Jiancheng Biological Co., Ltd. RNA extraction kit (Trizol) were from Beyotime Biotechnology Co., Ltd. Genomic reverse transcription kit (Prime Script RT reagent Kit with g DNA Eraser, RT), PCR reaction kit (TB Green TM Premix Ex Taq TM II), Hematoxylin and Eosin Staining Kit (H&E), Catalase (CAT) kit, malondialdehyde (MDA) kit, total superoxide dismutase (*T*-SOD) kit, glutathione peroxidase (GSH-px), and the respiratory chain complex enzyme activity (MRCC I, MRCC III, MRCC IV, and MRCC V) were from Shanghai Solarbio Bioscience & Technology Co., LTD. Chloroform, isopropyl alcohol, and absolute ethanol (analytically pure) were from Tianjin Kemiou Chemical Reagent Co., Ltd.

2.2. Preparation of fermented kiwifruit pulp

The ripe kiwi fruit were peeled, pulped, adjusted pH to 5.0 with sodium citrate, added 10 % sucrose, then putted in a water bath at 70 °C for 30 min, cooled to room temperature, divided it into jars (100 g fruit pulp in each jar). After that, the *Lactiplantibacillus* powder (commercial products, 10^{12} CFU/g, colony-forming unit, CFU) was determined the number of viable bacteria and then diluted in sterile water at a concentration of 10^6/mL, 0.1 mL of the solution was added to 100 g kiwi fruit pulp (10^5 CFU/100 g). Lactic acid bacteria were inoculated at 10^5 CFU/100 g and fermented at 37 °C for 72 h.

2.3. Determination of the change of the antioxidant capacity between fermented and nonfermented kiwi pulp

The *Lactiplantibacillus plantarum* fermented kiwi pulp (FKP) and kiwi pulps (KP) samples (10 mL) was added 80 % methanol (30 mL), heated at 60 °C and 450 W for 20 min by ultrasound (KQ-500DE, Kunshan Ultrasonic Instruments Co., Ltd., Kunshan, China), and the supernatant was filtered for the subsequent determination.

The total phenolic acid and the total flavone content were determined basically according to previous report (Singh, Kunwar, Srinivasan, Nanjan, & Priyadarsini, 2009; Zhang et al., 2013). Briefly, for total phenolic acids, 0.5 mL of water and 0.05 mL of the sample as described as above were added to a test tube. Folin-Ciocalteu reagent and of sodium carbonate (7 %) solution were added, and the absorbance of the solution was measured at 760 nm after 90 min. The measurements were compared with a standard calibration curve plotted for gallic acid solution and the total phenolic content was expressed as gallic acid equivalents in mg/100 g of extract.

For total phenolic acids, 1 mL of the sample, 1.5 mL of water, and 0.75 mL of 5 % $NaNO_2$, 0.75 mL of 10 % $Al(NO_3)_3$,10 mL of 4 % NaOH were added. Rutin was used as the standard and the total flavonoid content of the sample was expressed as rutin equivalent in mg/100 g at the absorbance of 510 nm. Determination of lactic acid bacteria content was performed according to GB 4789.35-2016.

Determination of antioxidant capacity of DPPH (2,2-diphenyl-1-picrylhydrazyl) and ABTS (2,2′-azinobis-(3-ethyl- benzothiazoline-6-sulfonic acid)) were performed according to previously reports by LUO and RE (Luo, Zhao, Yang, Shen, & Rao, 2009; Re et al., 1999). Hydroxyl radical and superoxide anion radical scavenging ability were determined using an assay kit.

2.4. Analysis of the effect of Lactiplantibacillus plantarum fermentation on the composition of kiwi fruit by untargeted metabolomics

The composition of FKP-LP and KP was analyzed by non-targeted metabonomics technology, and the changes of differential metabolites of kiwifruit before and after *Lactiplantibacillus plantarum* fermentation were determined by multivariate statistical analysis method. For the pretreatment of UPLC, the sample mixed with same mass of water (100 μL) was added 400 μL of 80 % methanal, mixed and stood in ice bath for 5 min, then centrifured (D3024R, SCILOGEX, America) at 15000 × g for 20 min at 4 °C. The supernatant was collected and for the consequent experiments. The Blank sample was 53 % methanal which was treated with the same pretreatment method of the sample. The UPLC-MS (Q Exactive™ HF, ThermoFisher, USA) system was performed with Agilent UPLC C18 column (2.1 × 100 mm), mobile phase (A: 0.1 % methanoic acid, B: 5 mM ammonium acetate) and 0.2 mL/min of flow rate at 40 °C of column temperature. Both positive and negative ion modes are used for detection with at a spray voltage of 3.2 kV, sheath gas velocity of 40 arb, auxiliary air velocity of 10 arb, capillary voltage of 320 °C.

2.5. Animal experiment of LPS-damaged intestine of rats

Male SD (Sprague–Dawley) rats weighing 200 ± 20 g were provided by the Guizhou Medical University Animal Center. The study was approved by the Ethics Committees of Guizhou Medical University. The rats were housed in cages under normal conditions at 20–25 °C under 55 %-58 % humidity and under a 12-hr light/dark cycle. After 1 week of adaption, SD rats were randomly divided into 4 groups (n = 8, there were 8 rats in each group), the control group (Control), lipopolysaccharide group (LPS), kiwifruit pulp with *Lactiplantibacillus plantarum* powder group (KP + LP, 10^{10} CFU/g *Lactiplantibacillus plantarum* were added to kiwi pulp, which the content of *Lactiplantibacillus plantarum* were similar with that in FKP, 10 g/kg/day), and kiwifruit pulp fermented by *Lactiplantibacillus plantarum* fermented group (FKP-LP, 10 g/kg/day). All animals were free access to diet (Standard feed provided by

the Guizhou Medical University Animal Center) and water.

Animals were administrated as once a day for 4 weeks as described above, among which, control and LPS groups were administrated the same volume of distilled water. During the period, the body weight and food intake were recorded. On day 26th of the experiment, LPS (3 mg/kg) were intraperitoneal injected in the rats of LPS, KP + LP, and FKP-LP groups for intestinal injury. On day 28th, after fasting 12 h, animals were anesthetized, and the plasma and the colon were collected. The plasma was centrifuged at 3000 r/min for 10 min at 4 °C. The colon was washed with saline, weighed, and portion of the colon were frozen and reserved at −80 °C for consequent analysis. The other portion of colon was immersed in 10 % neutral paraformaldehyde solution and electron microscopy fixation solution, then reserved at 4 °C for consequent analysis.

2.6. Analysis of effects of FKP-LP on DAO content and morphology of LPS-damaged intestine

The activity of DAO in plasma and intestine was detected by spectrophotometry using DAO kit according to the instruction. Morphological changes of colon of different groups were observed by pathological sections, and tight junctions of intestinal epithelial cells were observed by transmission electron microscopy to determine the effect of fermented and unfermented kiwifruit pulp on LPS-damaged intestine of rats.

Real-time PCR was used to detect tight junction protein gene expression (Claudin, Occludin and ZO-1) in the intestinal mucosa to further clarify the preventive effect of kiwifruit pulp on the damage of intestinal mucosal mechanical barrier in fermented and unfermented kiwifruit pulp. The primers for Claudin, Occludin and ZO-1 were shown in supplementary Table 1.

For analysis of H&E staining, the intestine taken from rats were fixed in 10 % formaldehyde for 24 h. After the gradient dehydration with ethanol, xylene transparent, embedded in paraffin, the intestine tissue was precooled and sectioned (4–5 μm), and then stained with hematoxylin and eosin (H&E) and mounted with mounting medium. Images were captured with Ti2R optical inverted microscope (Nikon, Tokyo, Japan) at 100× magnification.

For the observation with transmission electron microscope, the intestine taken from rats were fixed in 2.5 % glutaraldehyde for 24 h, stained with osmic acid, dehydrated by ethanol and acetone gradient, and added with epoxypropane for 20 min. The tissues were immersed with a mixture of epoxypropane and embedding medium (1:1) for 1 h, and then immersed by embedding medium for 3 h. The immersed tissues were fully polymerized at 35 °C, 45 °C and 60 °C for 12 h, 12 h and 24 h, respectively, and sliced. The sections were stained for 10 min with uranyl acetate, washed by distilled water, stained by lead citrate for 10 min, and washed again with distilled water. The images were captured under transmission electron microscope.

2.7. Analysis of effects of FKP-LP on mitochondrial activity of LPS-damaged intestine

The activities of MDA, SOD, GSH and CAT in intestinal mitochondria were detected by spectrophotometry to clarify the damage mitigation effect of kiwifruit pulp on intestinal mucosal mechanical barrier before and after fermentation using *T*-SOD, MDA, CAT and GSH-px kit according to the instructions.

HPLC system was adapted to determine the content of ATP, ADP, and AMP. The tissue sample of 0.2 g was added 0.4 mol/L perchloric acid for 2 min ultrasound, then stood in ice bath for 10 min, and centrifuged (3500r/min) for 10 min and filtered. The HPLC was employed with column of Agilent C18 (4.6 × 250 mm), flow rate of 1 mL/min, mobile phase (A: methanol, B: 50 mmol/L of KH_2PO_4) and detected at 254 nm and 30 °C of column temperature.

The respiratory chain complex enzyme activity (MRCC I, MRCC III, MRCC IV, and MRCC V) was detected using commercial kit.

2.8. Analysis of effects of FKP-LP on RNA expression of LPS-damaged intestine

Total RNA was isolated from the frozen intestine samples with of Trizol according to the manufacturer's instructions. The cDNA was prepared using the Genomic reverse transcription kit. The real time-PCR was performed on a fluorescence quantitative PCR instrument ((ABI-viiA7, Applied Biosystems, Carlsbad, CA, USA) using the TB Green TM Premix Ex Taq TMII to determine the content of specific mRNAs. The values were normalized to β-actin mRNA compared to those of the control group. The primers used were as shown in supplementary Table 1.

2.9. Statistical analysis

The metabonomic analysis includes composition analysis of non-fermented and fermented kiwi by heatmap, principal components analysis (PCA), partial least squares-discriminant analysis (PLS-DA), the most important 25 metabolism between non-fermented and fermented kiwi were shown in box diagram, random forest analysis and metabolic pathway. To definition the typical differential metabolism between raw kiwi and fermented kiwi, T test was used, and the most important 25 metabolites were selected by P-values from small to large. For random forest analysis, "Mean Decrease Accuracy" and "Mean Decrease Gini" were used to measure the importance of a metabolite in discriminating groups in the random forest. For enrichment analysis of metabolic pathway, significant differences between groups (T Test, $p < 0.05$) were selected, and which metabolic pathways these metabolites occur in was analyzed. By calculating the ORA (Over Representation Analysis) p values of these pathways, whether the metabolites of concern (metabolites with significant differences) significantly enriched in these metabolic pathways was analyzed.

SPSS17.0 software was used. When the measurement data were normally distributed, they were described by mean ± standard deviation, and when the data were in line with normal distribution and homogeneity of variance. One-way analysis of variance was used to compare the mean of multiple groups, SNK method was used when the variances were homogeneous, Games-Howell test was used when the variances were not homogeneous. $P < 0.05$ indicates statistical significance.

3. Result

3.1. Effects of Lactiplantibacillus plantarum fermentation on composition of kiwi fruit pulp

In order to explore the different effect of raw kiwi and fermented kiwi on intestinal barrier function, firstly, we analyzed the composition changes in kiwi pulp after *Lactiplantibacillus plantarum* fermentation. In this section, antioxidant ability and small molecule metabolites between non-fermented and fermented kiwi were determined. Compared to raw kiwi pulp, fermented kiwi pulp showed higher antioxidant ability. After fermentation, the content of total phenolic acid and total flavonoid were increased from 116.49 mg/100 g, 19.94 mg/100 g to 157.00 mg/100 g, and 60.71 mg/100 g, respectively ($P < 0.05$). The scavenging activities of DPPH, ABTS, hydroxyl and superoxide anion radical were increased by 240.77 %, 20.83 %, 7.24 %, and 15.41 % in FKP-LP samples compared to KP (shown in supplementary Table 2).

Changes in small molecule metabolites were detected by non-targeted metabonomics. The percentage accumulation of top 20 metabolites under positive and negative ion modes were shown in Fig. 1A and B. In positive modes, the contents of D-*threo*-Isocitric acid, Indole-3-acrylic acid, DL-Tryptophan, 2-hydroxylpentanoic acid, 2-Hydroxyphenylalanine were increased in FKP-LP when compared to KP, and the

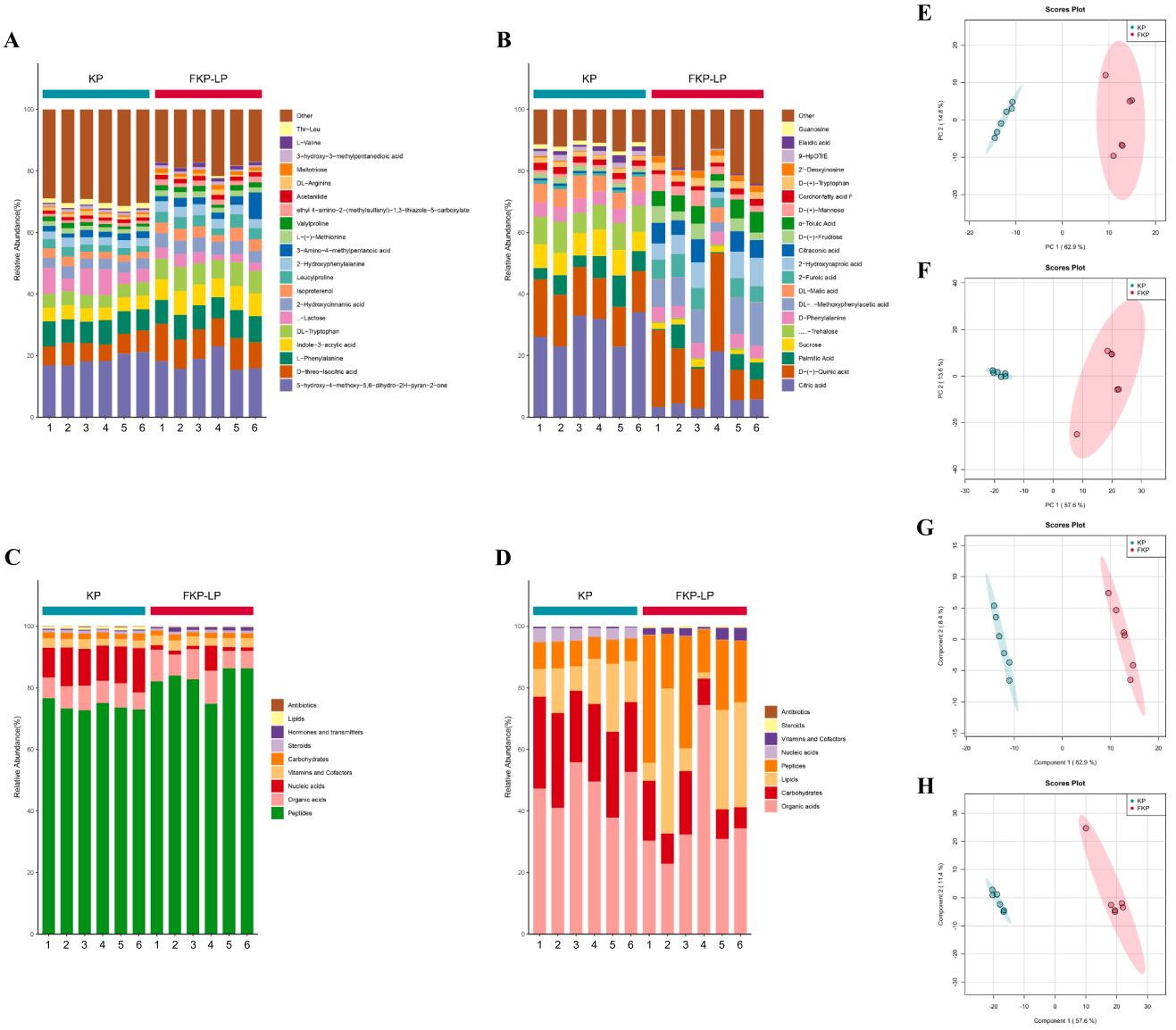


Fig 1. Contents of the components of kiwifruit pulp (KP) and fermented kiwifruit pulp by *Lactiplantibacillus plantarum* (FKP-LP). (A) Histogram of percentage accumulation of top 20 metabolites under positive ion mode. (B) Histogram of percentage accumulation of top 20 metabolites under negative ion mode. (C) Histogram of percentage accumulation of metabolites which playing biological roles under positive ion mode. (D) Histogram of percentage accumulation of metabolites which playing biological roles under negative ion mode. (E) Principal components analysis (PCA) scores plot of component under positive ion mode. (F) PCA scores plot of component under negative ion mode. (G) PLS-DA (Partial least squares-discriminant analysis) scores plot of component under positive ion mode. (H) PLS-DA scores plot of component under negative ion mode.

contents of α-lactose, DL-arginine, Thr-Leu were decreased (Fig. 1A). These top 20 metabolites were contributed to 9 classes, as shown in Fig. 1C, compared to KP, the contents of peptides, organic acid, vitamins and cofactors, steroids, and hormones and transmitters in FKP-LP were increased, while the contents of nucleic acid, and lipids were decreased.

In negative modes, compared to raw kiwi pulp, *Lactiplantibacillus plantarum* fermented kiwi pulp, the contents of citic acid, palmitic acid, surose, α,α-trehalose, DL-malic acid, guanosine, elaidic acid were decreased, and the contents of D-(-)-quninc acid, DL-α-methoxyphenylacetic acid, 2-furoic acid, 2-hydroycaproic acid, citraconic acid were increased (Fig. 1B). These 20 compounds were divided into 8 classes, by fermentation, the contes of lipids, peptides, vitamins and cofactors were increased, while organic acids, carbohydrates, nucleic acids were decreased (Fig. 1D).

PCA (principal components analysis) and PLS-DA (partial least squares discriminant analysis) were used to analyze the differences between the two groups to establish a metabolomics model of kiwifruit pulp. From PCA score and PLS-DA score under positive (Fig. 1E and F) and negative (Fig. 1G and H) ion modes, the two groups in the figure are obviously distributed in different areas, it indicated that the metabolite composition and structure of the FKP-LP group and KP group were quite different.

Later, in order to demonstrate the key metabolites influenced by fermentation, unidimensional statistical analysis was used, 25 metabolites were selected by P-values. Under positive ion mode, 19 compounds were increased after fermentation, include artemisinin, 10-hydroxydecanoic acid, pyridoxamine, tras-zeatin etc., while 6 metabolites were decreased, such as dextromethorphan hydrobromide, tanespimycin, 16-heptyne-1,2,4-triol etc. (Fig. 2A). In negative model, 18 metabolites were increased in FKP-LP, there were methoxyestredol,

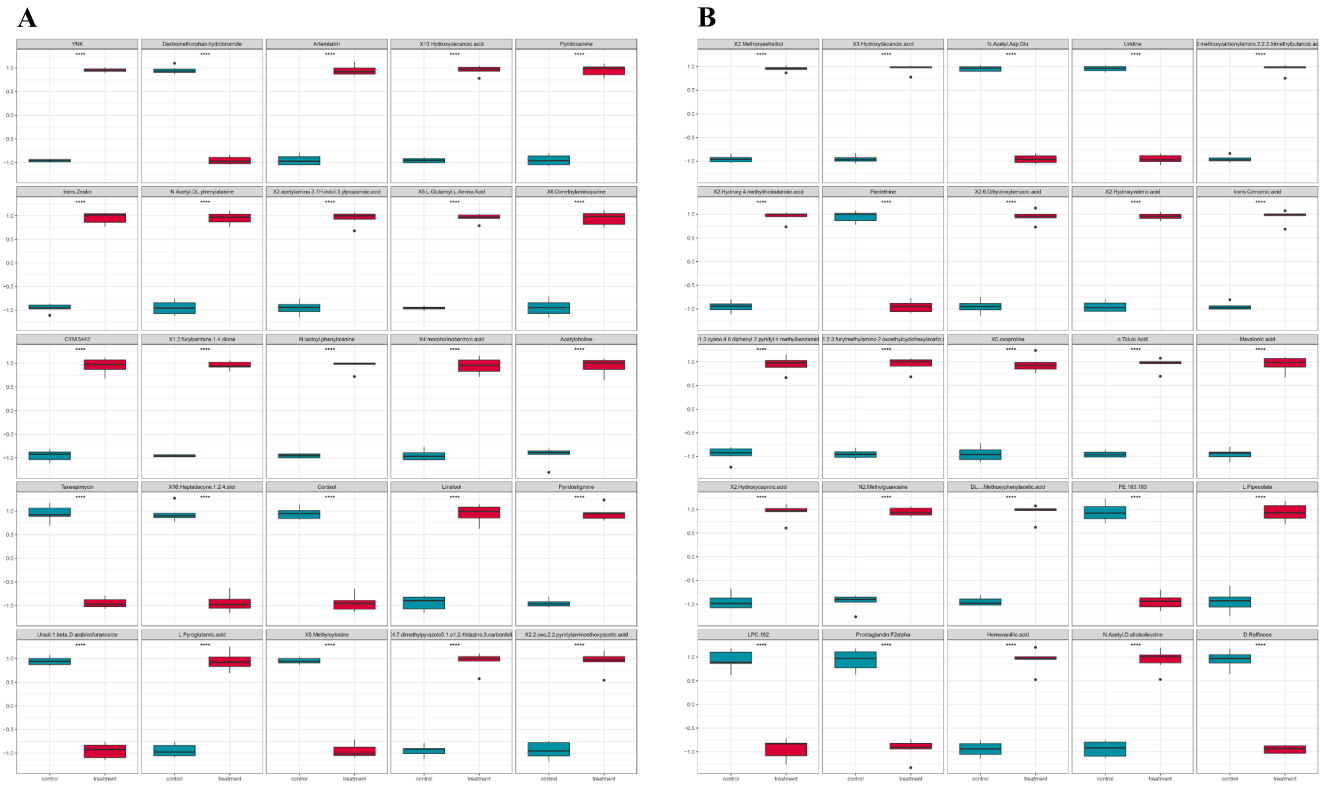


Fig 2. Box diagram of metabolite difference under positive (A) and negative (B) ion mode.

hydroxydecenoic acid, 3-methoxycarbonylamino-2,2,3-trimethylbutanoic acid, 2,6-dihydroxybenzoic acid etc., 7 metabolites were decreased, include *N*-acety-L-Asp-Glu, uridine, pantetheine etc.

3.2. Preventive effects of fermented kiwifruit pulp on mechanical barrier damage of intestinal mucosa

The effect of fermented kiwi pulp and kiwi pulp on intestine barrier function were investigated. Plasma endotoxin content and DAO activity, tight junction protein mRNA expression, intestine and intestinal epithelial cells morphology were determined. Elevated plasma DAO activity is considered to be a marker of impaired intestinal barrier function (Zhang et al., 2022). The plasma DAO activity in control rats were 4.77 U/L, after acute LPS stress it increased to 11.24 U/L ($P < 0.05$), content of LPS group was significantly higher than control group, which indicated that LPS stress caused the increase of plasma DAO content (Fig. 3A). However, the fermented kiwifruit pulp (FKP-LP) suppressed the plasma DAO content increase which caused by LPS.

The mRNA expression (Clauding-1, ZO-1 and Occludin) of intestinal tight junction protein were analyzed as shown in Fig. 3B. The LPS intervention induced the significant declines of the mRNA level of Occludin, compared with control group ($P < 0.05$). However, the fermented kiwifruit pulp (FKP-LP) suppressed the decline of mRNA level of Occludin. In the same way, the fermented kiwifruit pulp (FKP-LP) suppressed the decline of mRNA level of Clauding-1 and ZO-1.

The effects of FKP-LP on morphology were shown in Fig. 3C. In the control group, the structure of colonic mucosa was clear, and the glands were arranged in order. In rats which were injected intraperitoneally with LPS, the glands were disordered and accompanied by a large number of inflammatory cell infiltration, while the fermented kiwifruit pulp (FKP-LP) improved the disorders. Similarly, the transmission electron microscopy of colonic epithelial cells at 10 K magnification. In the control group, the tight junction structure between colonic epithelial cells of rats was clear, and obvious atretic protein was visible (Fig. 3D). Compared with the control group, the tight junction of intestinal epithelial cells in the LPS group were blurred and loose. However, the fermented kiwifruit pulp (FKP-LP) improved the tight junction of intestinal epithelial cells.

3.3. Anti-oxidative effects of fermented kiwifruit pulp on the colon mitochondria

In colonic mitochondria, LPS caused the level of MDA increased from 39.60 nmol/mg prot into 60.85 nmol/mg prot, while supplementation with FKP-LP the content of MDA deceased to 46.73 nmol/mg prot ($P < 0.05$) (shown in Table 1). Compared to normal rats, the activities of GSH-px, *T*-SOD and CAT were decreased by 33.98 %, 25.00 %, and 33.80 %, respectively in LPS injection rats. Administration with fermented kiwifruit the activity of GSH-px, *T*-SOD and CAT were increased to 142.57 U/mg prot, 0.51 U/mg prot, and 30.44 U/mg prot, which showed significant differences ($P < 0.05$) compared to LPS group, showed no significant differences ($P > 0.05$) compared to normal rats. The activity of GSH-Px, CAT, and the content of MDA showed d no significant differences between KP + LP and LPS group. These results indicated kiwifruit fermented with *LP* had more effective effect on improving colonic mitochondria antioxidant.

3.4. Effects of fermented kiwifruit pulp on intestinal mitochondrial function and gene expressions in respiratory chain

We have known that LPS injection induced mitochondria oxidant, and these phenomena were improved by FKP-LP rather than KP + LP. Mitochondria were the main energy provider. Firstly, the contents of ATP, ADP, AMP, and total energy were detected by HPLC, the results were shown in Fig. 4A–D. After LPS injury, the contents of ATP, ADP, AMP and total energy increased compared with control group ($P < 0.05$). However, in FKP-LP group the contents of ATP, ADP, AMP and total energy were decreased to 52.59 ng/g, 3.42 ng/g, 329.43 ng/g, and

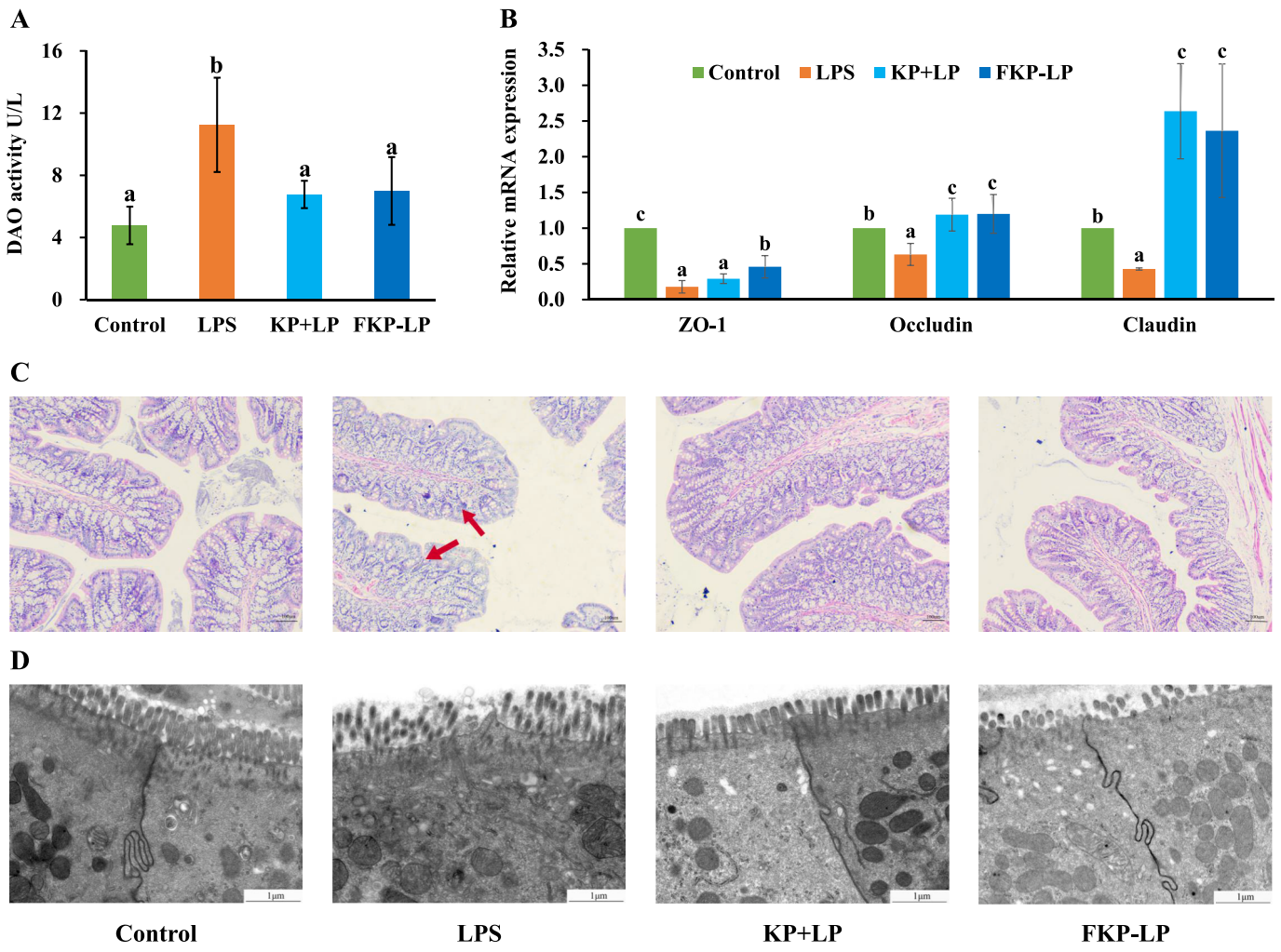


Fig 3. The effects of the fermented kiwifruit on diamine oxidase (DAO) activity (A), the mRNA expression of Clauding-1, ZO-1 and Occludin of intestinal tight junction protein (B), and the HE staining of colon (C) and the transmission electron microscopic image of colonic epithelial cells with tight junctions (D).

Table 1
The effect of *L. plantarum* fermented kiwifruit on colon antioxidant capacity of LPS-stressed rats.

Colonic mitochondria	Control	LPS	KP + LP	FKP-LP
GSH-Px (U/mgprot)	105.63 ± 9.65^{b}	69.74 ± 10.78^{a}	57.27 ± 2.28^{a}	142.57 ± 32.11^{b}
T-SOD (U/mgprot)	0.48 ± 0.04^{b}	0.36 ± 0.04^{a}	0.47 ± 0.08^{b}	0.51 ± 0.06^{b}
CAT (U/mgprot)	26.60 ± 3.66^{bc}	17.61 ± 3.62^{a}	19.23 ± 4.59^{ab}	30.44 ± 7.17^{c}
MDA (nmol/mgprot)	39.60 ± 5.35^{a}	60.85 ± 6.05^{c}	55.67 ± 4.07^{c}	46.73 ± 3.78^{b}

384.85 ng/g respectively, which showed significant difference to LPS rats ($P < 0.05$), while showed no significant difference to normal rats ($P > 0.05$). In KP + LP group, only the content of ADP was decreased to normal value, the contents of ATP, AMP, and total energy showed no significant differences compared to LPS rats.

ATP is produced through the mitochondrial respiratory chain, later the activities of respiratory chain complex enzyme were determined. From Fig. 4E–H, the MRCC III, MRCC IV and MRCC V increased, meanwhile MRCC I decreased significantly in LPS group compared with control group ($P < 0.05$). Whereas the increased activities of the MRCC III, MRCC IV and MRCC V, and the declined activity of the MRCC I were alleviated in KP + LP group and FKP-LP group. Compared with LPS group, the activity of MRCC I was increased to 180.79 U/mg prot, and activities of MRCC III and MRCC V were decreased to 0.64 U/mg prot and 64.30 U/mg prot ($P < 0.05$).

The morphological changes of mitochondria in intestinal epithelial cells were observed by transmission electron microscope. The morphology of mitochondria in the control group was shaped regularly with obvious cristae structure, indicating that the morphology of mitochondria was complete (Fig. 4I). The outer membrane of mitochondria was deformed and broken in the LPS intervention group. After fermented kiwifruit pulp intervention, the mitochondrial damage was alleviated in varying degrees, and the mitochondrial structure of FKP-LP compared to the LPS group was clearer, which was close to the morphology of mitochondria in the control group.

3.5. *Effects of fermented kiwifruit pulp on mitochondrial homeostasis regulation related proteins expression*

Mitochondrial homeostasis is the key to maintaining normal mitochondrial function. Mitochondrial homeostasis was regulated by various proteins, such as AMPK, PGC-1α *et al.* mRNA of AMPK, PGC-1α, NRF-1, NRF-2, TFAM and ULK-2 were analyzed, the results were shown in Fig. 5.

Compared with control group, the LPS injury induced the increase of the relative mRNA expression of AMPK to 1.774 compared with control group ($P < 0.05$) (Fig. 5A), whereas the increase was alleviated in the

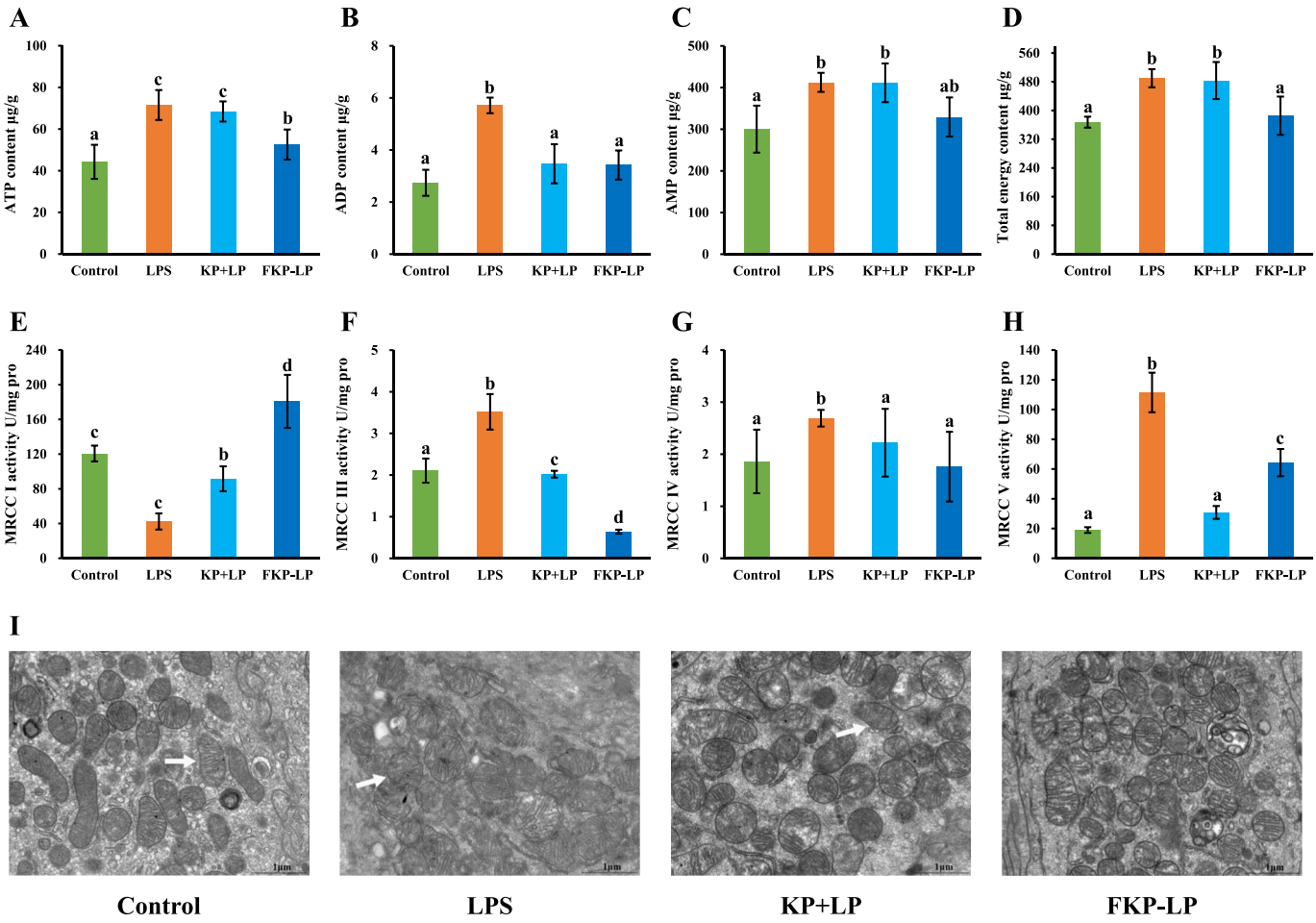


Fig 4. The effects of the fermented kiwifruit on intestinal mitochondrial energy metabolism of ATP (A), ADP (B), AMP (C) and total energy (D), the effects of the fermented kiwifruit on the content of MRCC I (E), MRCC III (F), MRCC IV (G) and MRCC V (H), and the effects of the fermented kiwifruit on the morphology of mitochondria.

KP + LP group (0.232) and FKP-LP group (0.336), which showed significant difference compared with LPS rats and also compared with normal rats ($P < 0.05$).

In addition, the LPS injury induced the increase of the mRNA expression of PGC-1α, NRF-1, NRF-2, TFAM and ULK-2, which were the downstream factors of AMPK. After LPS injury, the relative mRNA expression related to mitochondrial biogenesis, such as PGC-1α, NRF-1, NRF-2, and TFAM were increased significantly ($P < 0.05$). While supplemented with FKP-LP, it deceased to 0.53, 0.65, 0.263, and 2.344, had significantly differences with LPS rats.

ULK-2 is related to mitochondria autophagy. The relative mRNA expression of ULK-2 increased significantly to 12.667 after LPS injury, while supplemented with KP + LP and FKP-LP, it deceased to 4.39 and 1.802, which showed significant difference compared to LPS rats, and also normal rats ($P < 0.05$).

4. Discussion

Lactic acid bacteria fermentation has become an important trend in the development of nutritious and healthy food (Szutowska, 2020). Fermented foods are beneficial to intestinal health because of the lactic bacteria and its metabolites. The beneficial effects of lactic acid bacteria fermented food may play a role in protection of the intestinal barrier (Selhub, Logan, & Bested, 2014). Valero-Cases reported that the fermented tomato juice showed the effect of the improvement of intestinal barrier integrity (Valero-Cases et al., 2017). In present study, the composition changes of fermented kiwifruit pulp were investigated and its preventive effects on intestinal injury and mitochondrial injury were investigated in SD rats.

Firstly, we detected differences constitution between fermented and non-fermented kiwi. After fermentation the antioxidant activity were increased, such as the content of total phenols and flavonoids, and the scavenging activities of DPPH, ABTS and superoxide anion radical were higher in fermented kiwi. These phenomena were consistent with previous studies (Chen et al., 2021). Curiel et al. also reported that lactic acid fermentation could increase the content of total phenolic acid, total flavonoids and anthocyanins, and the content after fermentation is 5–10 times higher than that before fermentation (Curiel et al., 2015). Filannino et al. reported that the metabolic pathway of Lactiplantibacillus plantarum in cherry juice and broccoli juice is closely related to the chemical composition of fruit and vegetable substrates (Filannino, Di Cagno, & Gobbetti, 2018).

The results of non-targeted metabonomics technology (Figs. 1-2) showed that the composition of kiwifruit pulp before and after *Lactiplantibacillus plantarum* fermentation changed significantly and the peptides, hormones and vitamins of kiwifruit pulp increased after fermentation. The specific digestive enzymes will be produced during the growth of lactic acid bacteria, causing corresponding changes in peptides and vitamins. Among the vitamins, VB_6 (pyridoxamine) showed the most significant change, and its content increased significantly after fermentation ($P < 0.05$). Previous study by Hamzehlo has reported that *Lactiplantibacillus* has strong capacity of the production of VB_6 (Hamzehlou, Akhavan Sepahy, Mehrabian, & Hosseini, 2018).

Lipopolysaccharide (LPS) is one of the components of gram-negative

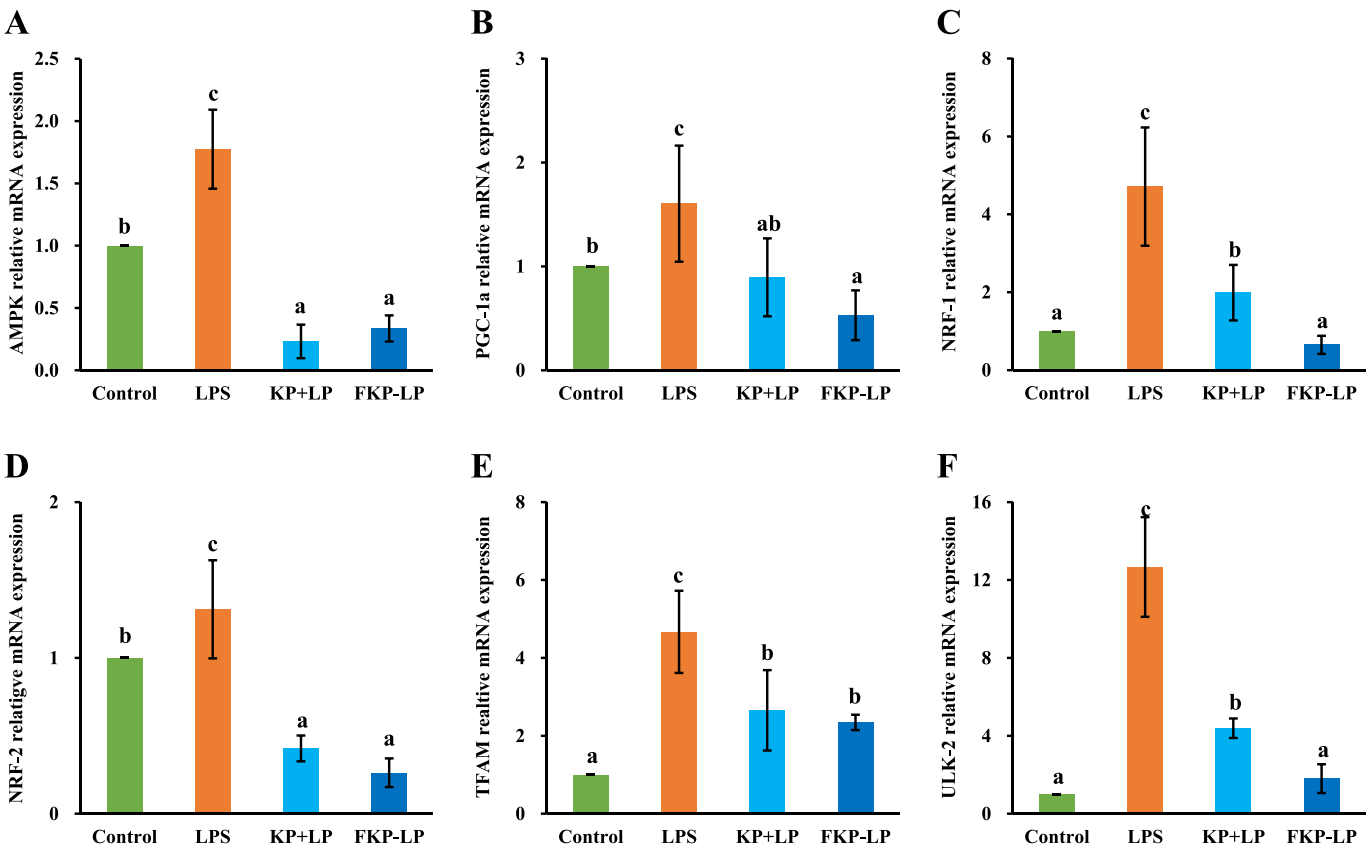


Fig 5. The effects of fermented kiwifruit pulp on the expression of intestinal tight junction protein genes of AMPK (A), PGC-1α (B), NRF-1 (C), NRF-2 (D), TFAM (E) and ULK-2 (F).

bacteria cell walls, such as *Escherichia coli*, which could increase the intestinal permeability (Stephens & von der Weid, 2019). Diamine oxidase (DAO) is a highly active intracellular enzyme in the villi of the upper intestinal mucosa of humans and mammals, which plays an important role in the metabolism of histamine and various polyamines (Luk, Bayless, & Baylin, 1980). Our results had shown that administration with fermented kiwi (FKP-LP) or non-fermented kiwi (KP + LP) all could suppressed the plasma DAO activity, which was increase which caused by LPS (Fig. 3A). It's indicated either fermented kiwi or non-fermented kiwi had positive effect on intestinal protection. Later, mRNA of tight junction protein, morphological by H&E and transmission electron microscopy were detected (Fig. 3C and D).

The colon after LPS injury showed morphological changes, such as gland disorder and inflammatory cell infiltration, which were improved in the fermented kiwifruit pulp group. The tight junctions of colonic epithelial cells could be clearly observed under transmission electron microscopy. LPS caused intestinal tight junctions to break or even disappear, which was alleviated in the kiwi pulp intervention group. This was verified by the relative mRNA expression levels of intestinal tight junction proteins Occludin, claudin-1 and ZO-1 (Fig. 3B). Fermented kiwifruit pulp can relieve the injury of the intestinal mucosa mechanical barrier by increasing the expression of Clauding-1, ZO-1 and Occludin. Previous study has reported that the fermented foods can increase the expression of intestinal tight junctions and maintain the integrity of intestinal tract morphology and function. Woo *et al.* found that fermented barley could enhance the integrity of intestinal mechanical barrier by upregulating the expression of tight junction protein in intestinal epithelial cells, to prevent intestinal mucosal permeability damage caused by DSS (Woo et al., 2016). The results in this study indicated that the kiwifruit pulp after fermentation had a certain preventive effect on the stress damage of intestinal mucosal mechanical barrier. Its preventive effect is mainly to increase the expression of tight junction protein related genes in intestinal epithelial cells, to maintain the structural integrity of intestinal mucosal mechanical barrier.

Oxidative damage is an important cause of intestinal injury induced by LPS. Mitochondria was the main place, which production of free radicals, however, it was easily be injured by free radical (Xu et al., 2019). Then, the antioxidant activity in colonic mitochondria was detected (Table 1). The fermented kiwifruit pulp intervention could improve the damage of mitochondria caused by LPS, through effectively inhibit the expression of MDA in intestinal tract and intestinal mitochondria after LPS injury, and increase the expression of GSH-Px, SOD and CAT. Li et al. reported that *Lactiplantibacillus plantarum* fermented soymilk could effectively upregulate catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px) levels and decrease malondialdehyde (MDA) content in the liver, brain, and serum (Li et al., 2021), which was consistent with our result in this study. Musa et al. also found that *Lactobacilli*-fermented cow's milk attenuated the reduction of antioxidants (SOD and GPx) and increment of MDA, which induced by LPS (Musa et al., 2017).

The previous results showed that the addition of fermented and non-fermented kiwifruit could alleviate the oxidative damage of mitochondria. Next, we determined the structure and function of mitochondria (Fig. 4). Providing energy is the main function of mitochondria and is produced through the mitochondrial respiratory chain. The mitochondrial respiratory chain is located on mitochondrial inner membrane, consists of five complexes, NADH-Q dehydrogenase (MRCC I), succinate-Q dehydrogenase (MRCC II), UQ-cytochrome *C* oxidoreductase (MRCC III), cytochrome *C* oxidase (MRCC IV), and ATPase (MRCC V). In this study, the respiratory chain complex enzyme activity in LPS group (MRCC III, MRCC IV and MRCC V) increased, and its consistent with the increase of ATP, ADP, AMP, and total energy. While the intervention of fermented kiwifruit pulp inhibited the increase in varying degrees (Fig. 4E–H), which indicated that fermented kiwifruit

pulp might reduce the stress reaction by LPS. It has been reported that the lipopolysaccharide was able to promote ATP release from macrophage cells (Sperlágh, Haskó, Németh, & Vizi, 1998). Peters et al. also observed that increased extracellular ATP concentrations following LPS incubation (Peters et al., 2015). Hoshino et al. found that the extracellular concentration of ATP was increased soon after stimulation with LPS and peaked at 10 to 20 min in THP-1 human monocytes (Hoshino et al., 2013). Imura et al. reported that lipopolysaccharide increased the ionomycin-induced release of ATP, which was dependent on the increase in vesicular nucleotide transporter (Imura et al., 2013).

Mitochondrial form and function are intimately connected in normal cells, playing an essential role of meeting the energy requirements of the cell. Numerous cellular processes are dependent upon healthy mitochondria for an adequate energy supply. From the view of the morphology of mitochondria, the outer membrane of mitochondria was deformed and broken caused by LPS. After fermented kiwifruit pulp intervention, the mitochondrial damage and mitochondrial stress (as shown by lower energy production and respiratory chain activity, compared to LPS) was alleviated, and the mitochondrial structure were improved (Fig. 4I). AMPK is the control center for energy metabolism in cells, and play a key role in controlling mitochondrial homeostasis (Li et al., 2016). Then, AMPK and its downstream molecules were determined. Firstly, AMPK could regulation mitochondrial biogenesis to increase the number of mitochondria. PGC-1α is an important downstream molecule, when PGC-1α is activated by AMPK, it increased the expression of NRF1/NRF2-TFAM. TFAM a regulator of mitochondrial DNA replication and transcription, increased TFAM promote mitochondrial biogenesis and increase the number of mitochondria. Secondly, AMPK could influence mitochondria autophagy. Mitochondria autophagy is a manner that to clearance the damaged mitochondria, ensuring mitochondrial quality. ULK is an important molecule, which can initiate mitochondrial autophagy, and it can be activated by AMPK.

The role of AMPK in LPS treatment is controversial. Some studies reported that LPS could increase AMPK expression. Chang et al. reported that LPS induced cPLA2 gene expression via activation of AMPK in preadipocytes (Chang et al., 2019). Chen et al. reported that LPS treatment led to a dramatic increase in autophagosome formation, which was mediated through the AKT-mTOR and AMPK-ULK1 pathway by increasing AMPK expression (Chen, Liu, Yang, & Ling, 2017). In this study, LPS injury increased AMPK and its downstream molecules (PGC-1α, NRF-1, NRF-2, TFAM and ULK-2) expression (Fig. 5), as well as ATP production. The reason for this phenomenon may be that high doses of LPS were injected, after 48 h of this acute LPS stress animals were slaughtered, at this time rats maybe in an acute stress period, in order to cope with injury compensatory pathways were initiated, such as increased mitochondria biogenesis and autophagy, and ATP production. When early intervention by FKP, the stress response of rats induced by LPS were decreased, lowered ATP production, and mitochondria biogenesis and autophagy related protein's mRNA expression.

Some articles reported increased AMPK expression may improve the injury. Chang et al. reported that 6-Gingerol could modulate proinflammatory responses in dextran sodium sulfate (DSS)-treated Caco-2 cells and experimental colitis in mice through AMPK activation (Chang & Kuo, 2015). Cao et al. reported that curcumin could ameliorate oxidative stress-induced intestinal barrier injury and mitochondrial damage by promoting Parkin dependent mitophagy through AMPK signal pathway (Cao et al., 2020). In our study, supplementation FKP the expression of AMPK and its downstream molecules were decreased, that maybe due to animals' status, because LPS increased AMPK expression.

5. Conclusions

In conclusion, we demonstrated that *Lactiplantibacillus plantarum* fermentation could improve the antioxidant capacity, change the composition of kiwifruit pulp, and fermented kiwifruit pulp could relieve the LPS injury of the intestine targeting mitochondria. The mechanism might contribute to reduced mitochondrial stress response, which regulated by AMPK pathway and its downstream factors, including PGC-1α, NRF-1, NRF-2, TFAM and ULK-2. These findings spotlight the protective role of fermented kiwifruit pulp on the intestinal damage, which provides theoretical support for fermented foods on intestinal health.

CRediT authorship contribution statement

Yun Ma: Formal analysis, Writing – original draft, Writing – review & editing. **Xiao Chen:** Validation, Investigation. **Ruiyu Xu:** Validation, Investigation. **Hongyan Niu:** Validation, Investigation. **Qun Huang:** Writing – review & editing. **Yan Zhou:** Conceptualization, Funding acquisition, Project administration, Writing – review & editing.

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.

Data availability

Data will be made available on request.

Acknowledgments

We would like to thank all members of the present study group for their ideas, suggestions, participation and support. This work was supported by National Natural Science Foundation of China (NSFC) (32060537), the Science and Technology Support Project in Guizhou Province (Qian ke he Jichu ZK[2022]360).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fochx.2023.101025.

References

Cao, S., Wang, C., Yan, J., Li, X., Wen, J., & Hu, C. (2020). Curcumin ameliorates oxidative stress-induced intestinal barrier injury and mitochondrial damage by promoting Parkin dependent mitophagy through AMPK-TFEB signal pathway. *Free Radical Biology and Medicine, 147*, 8–22. https://doi.org/10.1016/j.freeradbiomed.2019.12.004

Carr, F. J., Chill, D., & Maida, N. (2002). The lactic acid bacteria: A literature survey. *Critical Reviews in Microbiology, 28*(4), 281–370. https://doi.org/10.1080/1040-840291046759

Chang, C. C., Sia, K. C., Chang, J. F., Lin, C. M., Yang, C. M., Huang, K. Y., & Lin, W. N. (2019). Lipopolysaccharide promoted proliferation and adipogenesis of preadipocytes through JAK/STAT and AMPK-regulated cPLA2 expression. *International Journal of Medical Sciences, 16*(1), 167–179. https://doi.org/10.7150/ijms.24068

Chang, K.-W., & Kuo, C.-Y. (2015). 6-Gingerol modulates proinflammatory responses in dextran sodium sulfate (DSS)-treated Caco-2 cells and experimental colitis in mice through adenosine monophosphate-activated protein kinase (AMPK) activation. *Food & Function, 6*(10), 3334–3341. https://doi.org/10.1039/c5fo00513b

Chen, M., Liu, J., Yang, W., & Ling, W. (2017). Lipopolysaccharide mediates hepatic stellate cell activation by regulating autophagy and retinoic acid signaling. *Autophagy, 13*(11), 1813–1827. https://doi.org/10.1080/15548627.2017.1356550

Chen, S., Zhang, C., He, B., He, R., Xu, L., Zhang, S., & Singh, A. (2021). The role of lncRNAs in regulating the intestinal mucosal mechanical barrier. *BioMed Research International, 2021*, 1–13. https://doi.org/10.1155/2021/2294942

Chen, X., Yuan, M., Wang, Y., Zhou, Y., & Sun, X. (2021). Influence of fermentation with different lactic acid bacteria and in vitro digestion on the change of phenolic compounds in fermented kiwifruit pulps. *International Journal of Food Science & Technology, 57*(5), 2670–2679. https://doi.org/10.1111/ijfs.15316

Curiel, J. A., Pinto, D., Marzani, B., Filannino, P., Farris, G. A., Gobbetti, M., & Rizzello, C. G. (2015). Lactic acid fermentation as a tool to enhance the antioxidant properties of Myrtus communis berries. *Microbial Cell Factories, 14*(1), 67. https://doi.org/10.1186/s12934-015-0250-4

Feng, S., Dai, Z., Liu, A., Wang, H., Chen, J., Luo, Z., & Yang, C. S. (2017). β-Sitosterol and stigmasterol ameliorate dextran sulfate sodium-induced colitis in mice fed a high

fat Western-style diet. *Food & Function, 8*(11), 4179–4186. https://doi.org/10.1039/C7FO00375G

Filannino, P., Azzi, L., Cavoski, I., Vincentini, O., Rizzello, C. G., Gobbetti, M., & Di Cagno, R. (2013). Exploitation of the health-promoting and sensory properties of organic pomegranate (Punica granatum L.) juice through lactic acid fermentation. *International Journal of Food Microbiology, 163*(2), 184–192. https://doi.org/10.1016/j.ijfoodmicro.2013.03.002

Filannino, P., Bai, Y., Di Cagno, R., Gobbetti, M., & Gänzle, M. G. (2015). Metabolism of phenolic compounds by Lactobacillus spp. during fermentation of cherry juice and broccoli puree. *Food Microbiology, 46*, 272–279. https://doi.org/10.1016/j.fm.2014.08.018

Filannino, P., Di Cagno, R., & Gobbetti, M. (2018). Metabolic and functional paths of lactic acid bacteria in plant foods: Get out of the labyrinth. *Current Opinion in Biotechnology, 49*, 64–72. https://doi.org/10.1016/j.copbio.2017.07.016

Gleeson, J. P. (2017). Diet, food components and the intestinal barrier. *Nutrition Bulletin, 42*(2), 123–131. https://doi.org/10.1111/nbu.12260

Hamzehlou, P., Akhavan Sepahy, A., Mehrabian, S., & Hosseini, F. (2018). Production of vitamins B3, B6 and B9 by lactobacillus isolated from traditional yogurt samples from 3 Cities in Iran, Winter 2016. *Applied Food Biotechnology, 5*(2), 107–120. https://doi.org/10.22037/afb.v5i2.18905

Hoshino, Y., Sakaki, H., Tsukimoto, M., Harada, H., Moriyama, Y., & Kojima, S. (2013). Autocrine regulation of macrophage activation via exocytosis of ATP and activation of P2Y11 receptor. *PLoS One, 8*(4). https://doi.org/10.1371/journal.pone.0059778

Imura, Y., Morizawa, Y., Komatsu, R., Shibata, K., Shinozaki, Y., Kasai, H., … Koizumi, S. (2013). Microglia release ATP by exocytosis. *Glia, 61*(8), 1320–1330. https://doi.org/10.1002/glia.22517

König, J., Wells, J., Cani, P. D., García-Ródenas, C. L., MacDonald, T., Mercenier, A., … Brummer, R. J. (2016). Human intestinal barrier function in health and disease. *Clinical and Translational Gastroenterology, 7*(10), e196.

Kwaw, E., Ma, Y., Tchabo, W., Apaliya, M. T., Wu, M., Sackey, A. S., … Tahir, H. E. (2018). Effect of lactobacillus strains on phenolic profile, color attributes and antioxidant activities of lactic-acid-fermented mulberry juice. *Food Chemistry, 250*, 148–154. https://doi.org/10.1016/j.foodchem.2018.01.009

Li, C., Ding, Q., Nie, S.-P., Zhang, Y.-S., Xiong, T., & Xie, M.-Y. (2014). Carrot juice fermented with Lactobacillus plantarum NCU116 ameliorates Type 2 diabetes in rats. *Journal of Agricultural and Food Chemistry, 62*(49), 11884–11891. https://doi.org/10.1021/jf503681r

Li, C., Fan, Y., Li, S., Zhou, X., Park, K.-Y., Zhao, X., & Liu, H. (2021). Antioxidant effect of soymilk fermented by Lactobacillus plantarum HFY01 on D-galactose-induced premature aging mouse model. *Frontiers in Nutrition, 8*. https://doi.org/10.3389/fnut.2021.667643

Li, L., Xiao, L., Hou, Y., He, Q., Zhu, J., Li, Y., … Zhao, Y. (2016). Sestrin2 silencing exacerbates cerebral ischemia/reperfusion injury by decreasing mitochondrial biogenesis through the AMPK/PGC-1α pathway in rats. *Scientific Reports, 6*(1), 30272. https://doi.org/10.1038/srep30272

Luk, G. D., Bayless, T. M., & Baylin, S. B. (1980). Diamine oxidase (histaminase). A circulating marker for rat intestinal mucosal maturation and integrity. *Journal of Clinical Investigation, 66*(1), 66–70. https://doi.org/10.1172/jci109836

Luo, W., Zhao, M., Yang, B., Shen, G., & Rao, G. (2009). Identification of bioactive compounds in Phyllenthus emblica L. fruit and their free radical scavenging activities. *Food Chemistry, 114*(2), 499–504. https://doi.org/10.1016/j.foodchem.2008.09.077

Musa, N. H., Mani, V., Lim, S. M., Vidyadaran, S., Abdul Majeed, A. B., & Ramasamy, K. (2017). Lactobacilli-fermented cow's milk attenuated lipopolysaccharide-induced neuroinflammation and memory impairment in vitro and in vivo. *Journal of Dairy Research, 84*(4), 488–495. https://doi.org/10.1017/S0022029917000620

Peters, E., Geraci, S., Heemskerk, S., Wilmer, M. J., Bilos, A., Kraenzlin, B., … Masereeuw, R. (2015). Alkaline phosphatase protects against renal inflammation through dephosphorylation of lipopolysaccharide and adenosine triphosphate. *British Journal of Pharmacology, 172*(20), 4932–4945. https://doi.org/10.1111/bph.13261

Re, R., Pellegrini, N., Proteggente, A., Pannala, A., Yang, M., & Rice-Evans, C. (1999). Antioxidant activity applying an improved ABTS radical cation decolorization assay. *Free Radical Biology and Medicine, 26*(9), 1231–1237. https://doi.org/10.1016/S0891-5849(98)00315-3

Richardson, D. P., Ansell, J., & Drummond, L. N. (2018). The nutritional and health attributes of kiwifruit: A review. *European Journal of Nutrition, 57*(8), 2659–2676. https://doi.org/10.1007/s00394-018-1627-z

Selhub, E. M., Logan, A. C., & Bested, A. C. (2014). Fermented foods, microbiota, and mental health: Ancient practice meets nutritional psychiatry. *Journal of Physiological Anthropology, 33*(1), 2. https://doi.org/10.1186/1880-6805-33-2

Septembre-Malaterre, A., Remize, F., & Poucheret, P. (2018). Fruits and vegetables, as a source of nutritional compounds and phytochemicals: Changes in bioactive compounds during lactic fermentation. *Food Research International, 104*, 86–99. https://doi.org/10.1016/j.foodres.2017.09.031

Singh, U., Kunwar, A., Srinivasan, R., Nanjan, M. J., & Priyadarsini, K. I. (2009). Differential free radical scavenging activity and radioprotection of caesalpinia digyna extracts and its active constituent. *Journal of Radiation Research, 50*(5), 425–433. https://doi.org/10.1269/jrr.08123

Sperlágh, B., Haskó, G., Németh, Z., & Vizi, E. S. (1998). ATP released by LPS increases nitric oxideproduction in raw 264.7 macrophage cell line viaP2Z\P2X7 receptors fn1fn1 Due to circumstances beyond the Publishers control, this article appears with out he authors corrections. *Neurochemistry International, 33*(3), 209–215. https://doi.org/10.1016/S0197-0186(98)00025-4

Stephens, M., & von der Weid, P.-Y. (2019). Lipopolysaccharides modulate intestinal epithelial permeability and inflammation in a species-specific manner. *Gut Microbes, 11*(3), 421–432. https://doi.org/10.1080/19490976.2019.1629235

Szutowska, J. (2020). Functional properties of lactic acid bacteria in fermented fruit and vegetable juices: A systematic literature review. *European Food Research and Technology, 246*(3), 357–372. https://doi.org/10.1007/s00217-019-03425-7

Turner, J. R. (2009). Intestinal mucosal barrier function in health and disease. *Nature Reviews Immunology, 9*(11), 799–809. https://doi.org/10.1038/nri2653

Valero-Cases, E., Roy, N. C., Frutos, M. J., & Anderson, R. C. (2017). Influence of the fruit juice carriers on the ability of Lactobacillus plantarum DSM20205 to improve in vitro intestinal barrier integrity and its probiotic properties. *Journal of Agricultural and Food Chemistry, 65*(28), 5632–5638. https://doi.org/10.1021/acs.jafc.7b01551

Verón, H. E., Gauffin Cano, P., Fabersani, E., Sanz, Y., Isla, M. I., Fernández Espinar, M. T., … Torres, S. (2019). Cactus pear (Opuntia ficus-indica) juice fermented with autochthonous Lactobacillus plantarum S-811. *Food & Function, 10*(2), 1085–1097. https://doi.org/10.1039/c8fo01591k

Woo, J. K., Choi, S., Kang, J.-H., Kim, D. E., Hurh, B.-S., Jeon, J.-E., … Oh, S. H. (2016). Fermented barley and soybean (BS) mixture enhances intestinal barrier function in dextran sulfate sodium (DSS)-induced colitis mouse model. *BMC Complementary and Alternative Medicine, 16*(1), 498. https://doi.org/10.1186/s12906-016-1479-0

Xu, Y., Charles, M. T., Luo, Z., Mimee, B., Tong, Z., Véronneau, P. Y., … Rolland, D. (2019). Ultraviolet-C priming of strawberry leaves against subsequent Mycosphaerella fragariae infection involves the action of reactive oxygen species, plant hormones, and terpenes. *Plant, Cell & Environment, 42*(3), 815–831. https://doi.org/10.1111/pce.13491

Zhang, L. L., Wang, Y. M., Xu, M., Wu, D. M., Chen, J. H., & Yan, X. P. (2013). Antioxidant activity, phenol and flavonoid contents of fourteen mulberry varieties leaves. *Advanced Materials Research, 781–784*, 1454–1459. https://doi.org/10.4028/www.scientific.net/AMR.781-784.1454

Zhang, X., Peng, B., Zhang, Y., Zhang, Y., Lu, X., & Cao, Y. (2022). Biliary drainage reduces intestinal barrier damage in obstructive jaundice by regulating autophagy. *Contrast Media & Molecular Imaging, 2022*, 3301330. https://doi.org/10.1155/2022/3301330