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Addition of solid-state fermentation product of yeast ameliorated the effects of high-fat diet on hepatic lipid metabolism, epidermal mucus, intestine and liver health, and gut microbiota of zebrafish

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ABSTRACT

To assessed the effects of solid-state fermentation product of yeast (SFPY) supplementation on high-fat diet (HFD) induced challenges on growth, hepatic lipid metabolism, epidermal mucus, intestine and liver health and gut microbiota in zebrafish (*Danio rerio*), four experimental diets were prepared for one-month-old zebrafish: basal diet (Control), high-fat diet (HFD), 0.5% SFPY (0.5 SFPY) or 1.0% SFPY (1.0 SFPY)-added HFD. After 3 weeks of feeding, the results illustrated that although HFD increased weight gain (WG), corresponding decreased the feed conversation ratio (FCR), it caused negative influences including liver steatosis, intestinal and liver damage in zebrafish. Compared with HFD group, 1.0% SFPY obviously promoted the lysozyme activity and complement 4 (C4) level on epidermal mucus ($P < 0.05$), and significantly reduced liver TAG ($P < 0.05$). Addition of SFPY significantly decrease the lipid synthesis-related genes including *C/EBPα*, *FAS*, *PPARγ*, *ACC1*, *DGAT2* and pro-inflammatory factors including *IL-6*, *IL-1β* in liver ($P < 0.05$), significantly increased the height of gut villi ($P < 0.05$). Moreover, the 1.0 SFPY group significantly reduced the abundance of gut microbiota concluding Proteobacteria, Fusobacteriota, Planctomycetota and improved the abundance of gut Actinobacteriota and Firmicutes ($P < 0.05$). To sum up, the addition of SFPY significantly ameliorated hepatic inflammation and intestinal damage caused by high-fat diet, and positively affected the intestinal microbiota composition of zebrafish.

1. Introduction

With the continuous development of the social economy, people's demand for aquaculture products is increasing (FAO, 2022.). Aquaculture has become one of the most prospective industries in the world (Naylor et al., 2021). However, global feed resources, especially protein resources, have become growing strained (Kim et al., 2019). For protein conservation, diets with low protein, high fat, high sugar and lack of vitamins are increasingly widely used in aquaculture, causing poor quality of fish (Karalazos V et al., 2011; Oliva-Teles, 2012; Wang et al.,

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2021). Particularly, high-fat diets can induce too much hepatic lipid deposition, causing slower growth rate, lipid metabolic disorder, increased feed ratio and decreased resistance to disease in aquacultural species (Catacutan et al., 2001; Xie et al., 2022b; Zhang et al., 2017). Therefore, the "efficient, high-quality, ecological, healthy and safe" green and healthy aquaculture technology is a major concern in aquaculture to fulfill the demand of high-quality animal protein for human consumption.

In previous research, effective solutions for alleviating the negative effects induced by HFD were explored. According to these studies, polyunsaturated fatty acids (Twibell et al., 2000), choline (Lin et al., 1990), methionine (Rumsey, 1991), carnitine (Gaylord and Iii, 2000), phospholipids (Espe et al., 2015) and nucleotides (Ran et al., 2021) have a significant role in reducing fatty liver in fish. In addition to these, probiotics were used as safe feed additives to improve the health of aquatic species. Such as *Lactobacillus rhamnosus* GG (LGG) has been confirmed to ameliorate effectively hepatic lipidosis in fish (Schneider et al., 2014), and exopolysaccharides extracted from LGG through mild sonication and water bath incubation can reduce liver fat as well (Zhang et al., 2019). Yeast application included yeast cell, culture containing yeast cells, metabolites and culture medium (Barnes et al., 2006; Sanderson and Jolly, 1994), yeast enzymolysis products, active powdery yeast and solid-state fermentation yeast culture. Yeast culture is rich in nutrients such as protein (J. Pongpet et al., 2016), which improved feed conversion efficiency, growth performance (Essa et al., 2015), immunity and anti-disease ability of aquaculture animals (Berto et al., 2015; Chao et al., 2015; Essa et al., 2015; Huang et al., 2015), had a positive modulation effect on gut microbiota composition (Liu et al., 2018), and has been widely used as a feed additive for cultured aquatic species (Chaitanawisuti et al., 2011; Shruthi et al., 2022; Wang et al., 2018). Solid-state fermentation (SSF) provides a method of fermentation by microorganisms on a solid substrate substantially without free water (Bhargav et al., 2008). Comparing with submerged fermentation (SMF), SSF has more advantages in a variety of processes including broad resource, low using cost, simple process and high economy. Recently, more and more researches have investigated that the supplementation of solid-state fermentation in aquatic feed improved feed utilization, hepatic and intestinal health, and antiviral immune ability (Wang et al., 2022). In this study, two Saccharomyces cerevisiae, which were isolated from shrimp pond mud and shrimp intestine respectively, were added into solid-state fermentation medium with rice bran, soybean cake powder and corn meal to ferment.

Zebrafish (*Danio rerio*) has become an excellent vertebrate model used for biomedical studying (Hill et al., 2016; Lawrence, 2007; Mingyu et al., 2016; Nath et al., 2015). Its unique features help the research on fish nutrition, metabolism, host-microbe interactions and ultimately fish health (Nadal et al., 2020). Moreover, in our previous research, we used this fish as an animal model to study fatty liver and metabolism dysfunction caused by the addition of HFD (Shen et al., 2009). According to the previous researches, diet supplemented with yeast culture improved the growth performance, immunity, and disease resistant ability of aquatic animals (Min et al., 2018). However, ameliorated influences caused by HFD on hepatic fat deposition, gut health and microbial composition of zebrafish using SFPY is limited. Here, the effects of SFPY supplemented into high-fat diet on growth performance, skin mucus, liver and gut health in zebrafish were observed. Furthermore, the significant role of SFPY on ameliorating the negative effects by HFD on the composition and diversity of gut microbiota were also assessed.

2. Materials and methods

2.1. Solid-state fermentation product of yeast

Saccharomyces cerevisiae GCC-1(CGMCC no. 21819) and GCC-2 (CGMCC no. 21818) were isolated from shrimp pond mud and shrimp intestine, respectively. According to previous study (Yajie Zhao et al., 2022), the first step was to culture the separate primary seed fermentation broth of *S. cerevisiae* GCC-1 and GCC-2 by shaking at 30 °C, 180 r/min for 48 h in yeast extract peptone dextrose medium (YPD). Then, the seed broths were inoculated in new YPD medium at the ratio of 1%, cultured at 30 °C, 180 r/min for 48 h to attain secondary seed fermentation broth. Thereafter, the secondary seed were inoculated into solid-state fermentation at a ratio of 5%, SFPY with 4.76×10^{10} CFU/g was obtained after 96 h solid-state fermentation at 30 °C. Finally, after adding 0 g, 5 g or 10 g SFPY to 1 kg HFD diet, four experimental diets were prepared: basal diet (Control), high-fat diet (HFD), 0.5% SFPY (0.5 SFPY) or 1.0% SFPY (1.0 SFPY)-added HFD.

The ingredients and proximate compositions of the experimental diets were listed in Table 1.

2.2. Zebrafish husbandry

All experiments and animal care procedures were approved by the Feed Research Institute of the Chinese Academy of Agricultural Sciences. Animal Care Committee under the auspices of the China Council for Animal Care (Assurance No. 2020-AF-FRI-CAAS-001).

One-month-old zebrafish with similar initial body weight and in good health were selected. 20 fish per 3 L tank were randomly allocated to the control and experimental groups, with 4 replicates in each group. The feeding experimental period was 3 weeks. During the experiment the fish was cultured in the circulating water system with the water temperature and pH setting at 28–30 °C and 6.8–7.5, respectively and the light condition were 12 h/12 h dark/light period. Zebrafish were fed twice each day at 8:30 am and 4:00 pm with 6% of the fish body weight. Following the above method, after 3 weeks, the fish were weighed after fasting for 24 h to calculate the growth performance, survival rate and feed conversion by previously described (Y. Li et al., 2021).

2.3. Epidermal mucus immunological and antioxidant enzymes analysis

The sample method and assay kits were according to the previous

Table 1
Ingredients and proximate composition of diets for zebrafish (dry matter, g / kg diet).

Ingredient (g / kg diet)	Control	HFD	0.5SFPY	1.0SFPY
Flour	25	20	20	20
Soybean meal	18	19.6	19.6	19.6
Fish meal	45	45	45	45
Choline chloride	2	2	2	2
Monocalcium phosphate	0.2	0.2	0.2	0.2
Soybean oil	1.2	10	10	10
VC phosphate	0.1	0.1	0.1	0.1
Bentonite	6.1	0.7	0.7	0.7
Rice husk meal	1.0	1.0	1.0	1.0
Solid substrates[a]	1.0	1.0	0.5	0
Yeast culture	0	0	0.5	1
Vitamin premix[b]	0.2	0.2	0.2	0.2
Mineral premix[c]	0.2	0.2	0.2	0.2
Total	100	100	100	100
Moisture	3.31%	2.99%	2.90%	2.86%
Crude protein	49.44%	48.46%	48.34%	48.07%
Crude fat	6.97%	15.83%	14.74%	15.03%
Crude ash	13.81%	13.83%	14.19%	14.32%

[a] Containing the following (% solid substrates): soybean meal (30%), rice bran (30%), corn meal (40%)

[b] Containing the following (g/kg vitamin premix): thiamine, 0.438; riboflavin, 0.632; pyridoxine•HCl, 0.908; *d*-pantothenic acid, 1.724; nicotinic acid, 4.583; biotin, 0.211; folic acid, 0.549; vitamin B-12, 0.001; inositol, 21.053; menadione sodium bisulfite, 0.889; retinyl acetate, 0.677; cholecalciferol, 0.116; *dl*-α-tocopherol-acetate, 12.632.

[c] Containing the following (g/kg mineral premix): $CoCl_2$•$6H_2O$, 0.074; $CuSO_4$•5H2O, 2.5; $FeSO_4$•$7H_2O$, 73.2; NaCl, 40.0; $MgSO_4$•7H2O, 284.0; $MnSO_4$•H_2O, 6.50; KI, 0.68; Na_2SeO_3, 0.10; $ZnSO_4$•$7H_2O$, 131.93; Cellulose, 501.09

description (Anran Wang et al., 2022) to detect the superoxide dismutase (SOD), lysozyme activities (LSZ) (Jiancheng, Nanjing), levels of complement 3 (C3) (Jiancheng, Nanjing) and 4 (C4) (Enzyme immune).

2.4. Extraction and detection of triglyceride

After weighting and homogenizing the liver samples with PBS solution, triglyceride was extracted from zebrafish liver and detected by an enzymatic reaction as described previously (Zhang et al., 2019).

2.5. Histological analysis

After rinsing with PBS, the guts and livers were fixed in 4% paraformaldehyde, followed by embedding in paraffin, with sectioning into 5–8 μm. The sections were stained using hematoxylin-eosin after dewaxing. ImageJ (NIH) software was used to measure the villus height of the intestinal images captured by the Leica microscope (Leica DMIL-LED, Germany).

2.6. Intestinal contents sampling and gut microbiota analysis

The gut content of 6 zebrafishes, which were collected 4 h after the last feeding, were mixed into one sample under aseptic surroundings, with 6 replicates per group. After sampling DNA extraction by Fast DNA SPIN Kit for Soil (MP Biomedicals), PCR amplifying the 16 S rRNA V3-V4 region, preparing library, quality inspection and quantification, sequencing is then performed and were analyzed on the Illumina HiSeq platform (Zhang et al., 2019; Wang, A., et al. 2021).

2.7. Quantitative real-time PCR(qRT-PCR) analysis

After isolating the total RNA from zebrafish tissues by Trizol (Invitrogen), transforming 1 μg RNA into cDNA according to the procedure with 42 ℃ for 15 min and 92 ℃ for 3 min qRT-PCR was conducted as previous work (Xie et al., 2021) using ribosomal protein S11 gene as reference gene. All primer sequences were presented in Table 2.

2.8. Statistical analysis

All statistic data were from at least 3 independent experiments and calculated and graphed using Graphpad Prism 5.0 software. The figures were given as mean ± standard error (mean ± SEM). Independent samples t-test was used to analyze the differences. P value which is less than 0.05 was considered as statistical significance., marked with an asterisk (*) in the figure.

3. Results

3.1. Influences of SFPY supplementation on the growth performance of zebrafish

After 3 weeks of feeding trial, there was no significant differences in IBW and SR among all groups ($P > 0.05$) (Fig. 1A), in WG and FCR between HFD and SFPY groups($P > 0.05$) (Fig. 1B-C). WG of the HFD group was significantly higher than that of the control group, corresponding to the FCR decreased significantly($P < 0.05$).

3.2. SFPY increased antioxidant capacity and C4 level in skin mucus

As shown in Fig. 2, except the complement(C3), with supplementation of SFPY in HFD, the activities of lysozyme, superoxide dismutase (SOD) and complement 4 (C4) all showed a continuous increasing trend. In addition, SOD and C4 in 1.0 SFPY were both significantly higher than that of HFD group ($P < 0.05$).

3.3. Dietary SFPY reduced hepatic lipid accumulation caused by high-fat feed

Dietary SFPY ameliorated the liver steatosis triggered by a high fat feed, as indicated by both the TAG content test and tissue HE analysis (Fig. 3A-B). 1.0 SFPY group significantly decreased the TAG content of HFD group which was noticeably higher than that of control group ($P < 0.01$) (Fig. 3A). Consistently, H&E image proved that the addition of SFPY decreased the liver fat droplet accumulation (Fig. 3B), corresponding decreasing significantly the expressions of the lipid synthesis genes including fatty acid synthase (*FAS*), CCAAT enhancer binding protein α (*C/EBPα*), peroxisome proliferator-activated receptor γ (*PPARγ*), acetyl-CoA carboxylase (*ACC*), diacylgycerol acyltransferase 2 (*DGAT2*), contrast with HFD group (Fig. 4A-E).

3.4. Addition of SFPY improved the liver health of zebrafish

Proceeding to evaluate whether SFPY addition could ameliorate liver inflammation or not. The H&E images showed that SFPY supplementation ameliorated hepatic injury triggered by HFD (Fig. 3B). Furthermore, the relative expression of pro-inflammatory including interleukin - 6 (*IL-6*), interleukin - 1β (*IL-1β*) and tumor necrosis factor-α (*TNF-α*) with addition of SFPY were correspondingly reduced(Fig. 5A-C), with IL-6 and IL-1*β* both significantly decreasing compared to the HFD group ($P < 0.05$).

3.5. SFPY increased the villi height of zebrafish

To characterize the effects of SFPY addition on the intestinal health in zebrafish, the intestinal morphology of the fish was examined. The height of the intestinal villi of two SFPY groups was noticeably increased

Table 2
Primer sequences for qPCR.

Gene	Forward primer (5′−3′)	Reverse primer (5′−3′)	GenBank accession No.
RPS11	ACAGAAATGCCCCTTCACTG	GCCTCTTCTCAAAACGGTTG	NM_213377.1
TNFα	AAGGAGAGTTGCCTTTACCG	ATTGCCCTGGGTCTTATGG	NM_212859.2
IL-1β	GGCTGTGTGTTTGGGAATCT	TGATAAACCAACCGGGACA	NM_212844.2
IL-6	TCAACTTCTCCAGCGTGATG	TCTTTCCCTCTTTTCCTCCTG	NM_001261449.1
C/EBPα	AACGGAGCGAGCTTGACTT	AAATCATGCCCATTAGCTGC	NM_131885.2
PPARγ	CCTGTCCGGGAAGACCAGCG	GTGCTCGTGGAGCGGCATGT	NM_131467.1
FAS	GGAGCAGGCTGCCTCTGTGC	TTGCGGCCTGTCCCACTCCT	NC_007123.7
ACC	GCGTGGCCGAACAATGGCAG	GCAGGTCCAGCTTCCCTGCG	XM_021476200.1
DGAT2	CCATACTTGCTGCATATTCC	ATGTCATGATAAACTGCAGC	NM_001030196.1
CPT1	GCATTGACCTTCAGCTCAGC	CTGCCAACACCAGCACGAAC	NM_001044854.1

TNFα, tumor necrosis factor alpha; IL-1β, interleukin-1β; IL-6, interleukin-6; C/EBPα, CCAAT enhancer binding protein α; PPARγ, peroxisome proliferator-activated receptor γ; FAS, fatty acid synthase; ACC, acetyl-CoA carboxylase; DGAT2, diacylgycerol acyltransferase 2; CPT1, Carnitine palmitoyltransferase1;

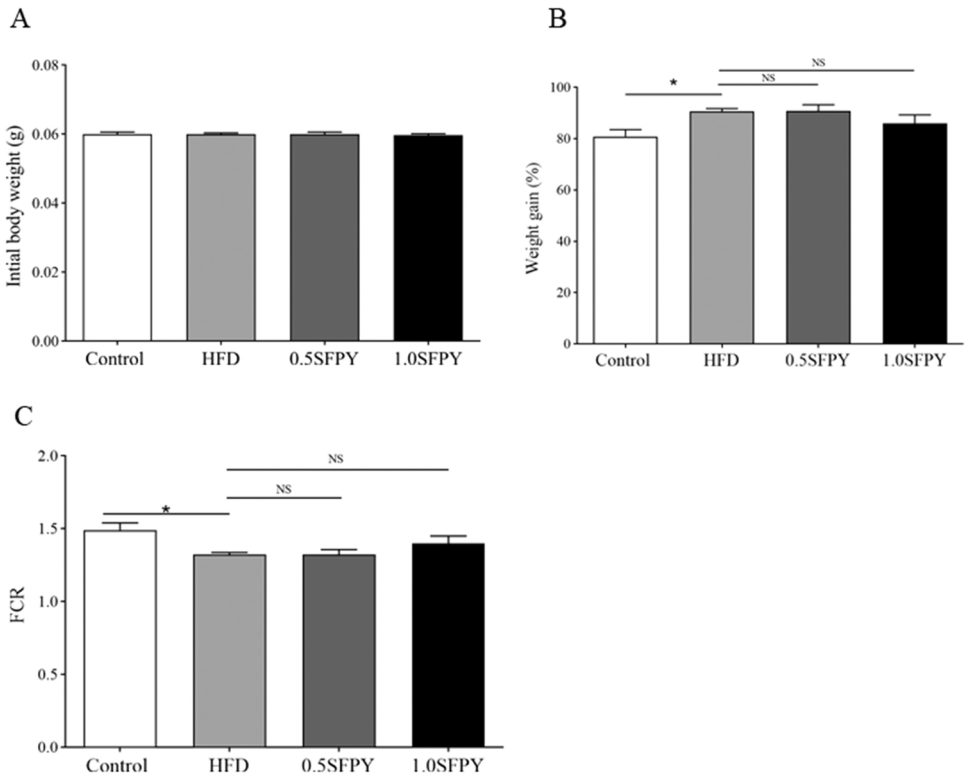

Fig. 1. Effects of HFD, 0.5 SFPY and 1.0 SFPY diets on the initial body weight, survival rate, weight gain (%) and feed conversion ratio of zebrafish. (A) Initial body weight (g), (B) Weight gain (%), (C) Feed conversion ratio(FCR). Data were represented as the means (± SEM). * $P < 0.05$.

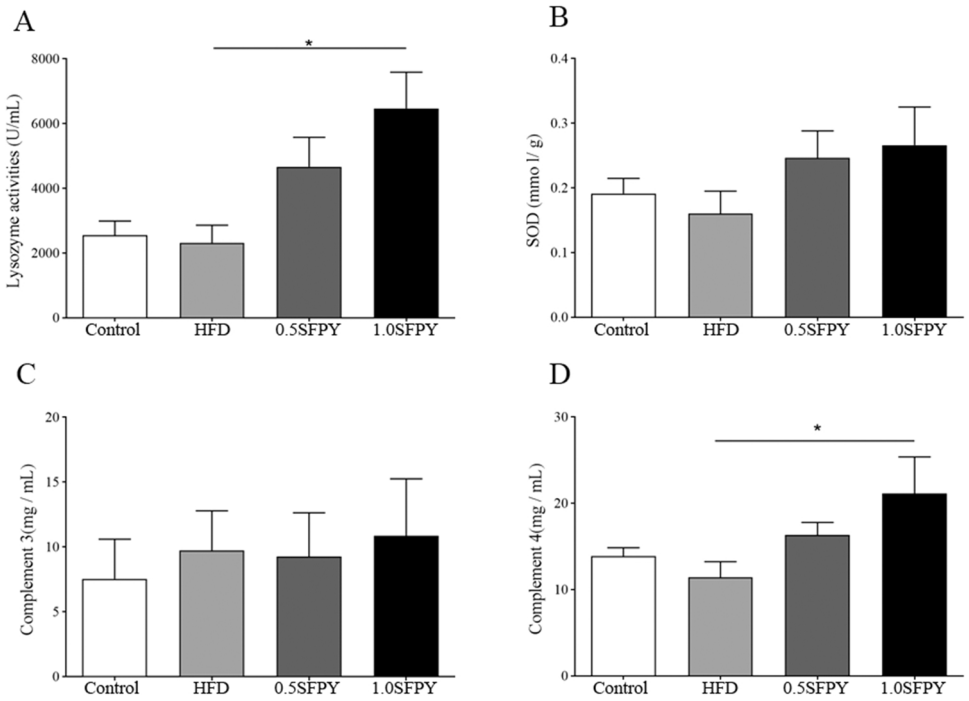

Fig. 2. Effects of HFD, 0.5 SFPY and 1.0 SFPY diets on epidermal mucus total antioxidant capacity, lysozyme, complement 3 and complement 4 levels of zebrafish. (A) Lysozyme activity, (B) superoxide dismutase, (C) Complement 3 level, (D) Complement 4 level of zebrafish fed different diets. Data were represented as the means (± SEM) (n = 6). * $P < 0.05$.

compared with the HFD group (Fig. 6A) ($P < 0.001$). The results showed that the supplementation of SFPY in HFD ameliorated intestinal injury caused by HFD in zebrafish.

3.6. Effects of SFPY supplementation on the gut microbiota profile of zebrafish

High-throughput sequencing technique was used to evaluate the

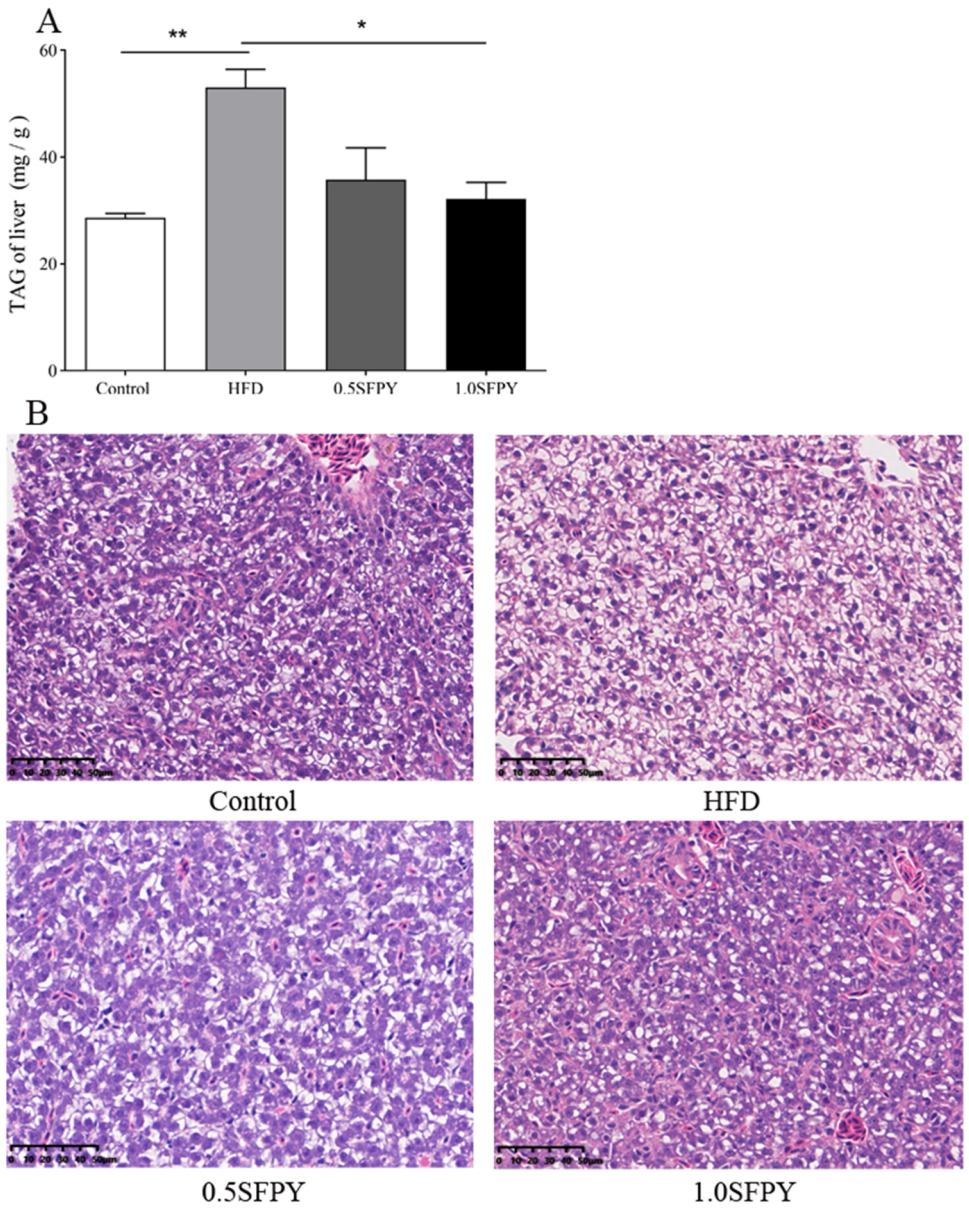

Fig. 3. Effects of HFD, 0.5 SFPY and 1.0 SFPY diets liver of zebrafish. (A) TAG of liver, (B) Representative liver histology image by H&E staining. The scale bar is 50 μm.

effects of dietary SFPY on the intestinal microbiota structure and diversity in zebrafish. The results were presented in (Table 3 & 4, and Fig. 7).

The data of Fig. 7A and Table 3 illustrated that compared with the HFD group, the abundances of Proteobacteria (except 0.5 SFPY), Fusobacteriota, MBNT15, Planctomycetota and Dadabacteria phyla were significantly decreased in two SFPY groups, while the abundances of Actinobacteriota (except 0.5 SFPY) and Firmicutes were increased ($P < 0.05$). Besides, the abundance of Verrucomicrobiota and Chloroflexi of 0.5 SFPY group were obviously reduced ($P < 0.01$).

At the genera level, compared with HFD, the abundance of *Rhodobacter* and *Cetobacterium* were significantly reduced in 0.5 SFPY group and 1.0 SFPY group ($P < 0.01$), respectively. The abundances of *Aeromicrobium* ($P < 0.05$) and *Bacillus* ($P < 0.01$) in the 1.0 SFPY group were obviously higher than that of the HFD group, Staphylococcus higher in 0.5 SFPY group ($P < 0.05$), *Dietzia* higher in two SFPY groups ($P < 0.01$) (Fig. 7B; Table 4).

In addition, The figures of principal coordinate (PCoA) analysis illustrated that the structure of intestinal microbiota between the SFPY groups and HFD were significantly different at the genus level (Fig. 7D), indicating that SFPY supplementation affected the intestinal microbiota profile of zebrafish.

4. Discussion

High-fat feed in aquaculture has many negative influences on host organs and physiological processes. Liver injury and abnormal lipid deposition were caused, intestinal inflammation and imbalance of intestinal microbiota were escalating (Yu et al., 2020; Mohammed et al., 2022; Tang et al., 2019; Yin et al., 2021). Reducing the effects of HFD using different probiotics and postbiotics is now attracting the interest of researchers. Nowadays, Yeast culture has been used being a promising feed additive in various of farmed fish (Barnes et al., 2006). It has been great interest to research the influences of additive culture of yeast on organ and several physiological functions including growth performance (Min et al., 2018), immune reaction (Burgents et al., 2004; Jensen et al., 2008), intestinal health (Ayiku et al., 2020), and gut microbiota (H. Liu et al., 2018) in the past.

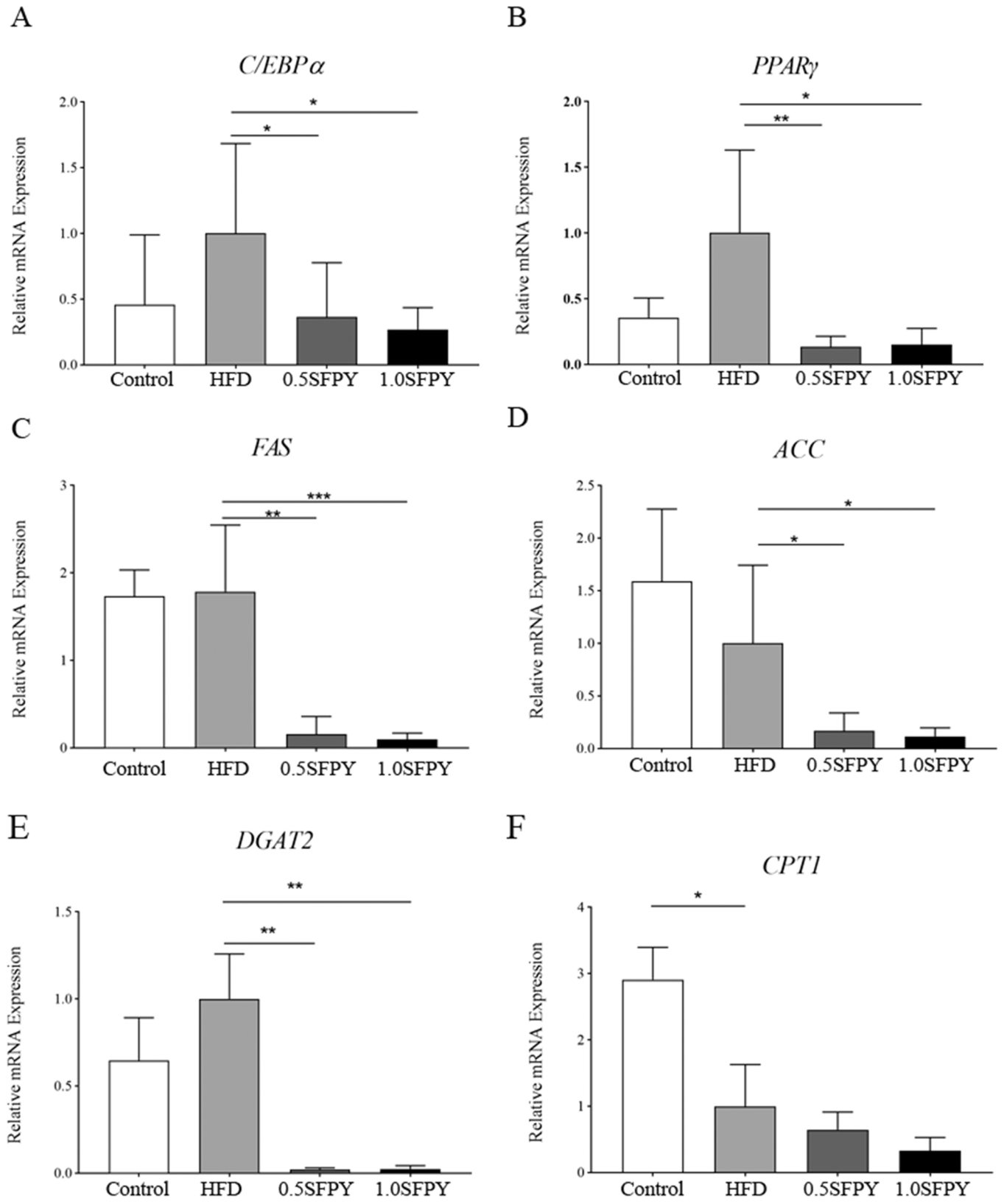

Fig. 4. Effects of HFD, 0.5 SFPY and 1.0 SFPY diets on the relative mRNA expression of genes related to lipometabolism in the liver of zebrafish. (A) *C/EBPα*, (B) *PPARγ*, (C) *FAS*, (D) *ACC*. (E) *DGAT2*, (F) *CPT1*. Data represent the means (± SEM) (n = 6). * $P < 0.05$.

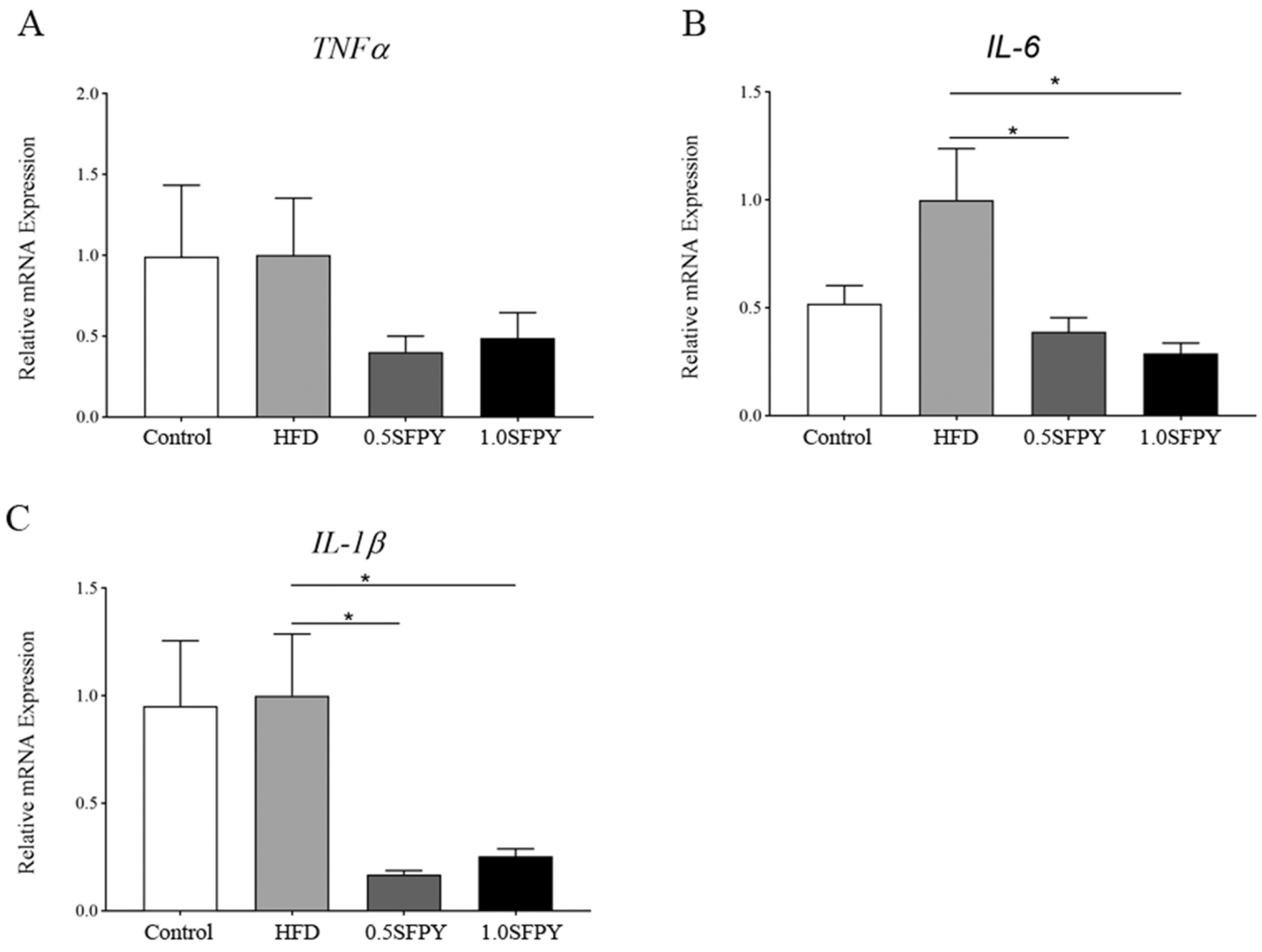

Fig. 5. Effects of HFD, 0.5 SFPY and 1.0 SFPY diets on the relative mRNA expression of inflammation related genes in the liver of zebrafish. (A) *TNFα*, (B) *IL-6*, (C)*IL-1β*. Data are expressed as mean ± SEM (n = 6). * $P < 0.05$.

Dietary yeast culture in aquatic animals has been proved to be positive to the growth performance of varied fish species (Deng et al., 2013; Ruiqiang et al., 2018). The figures of our research also suggested that adding 0.5% and 1% SFPY could increase body weight and reduce FCR. However, Compared with HFD group, addition of SFPY were insignificant differences in the growth performance parameters of zebrafish, suggesting that the addition of SFPY in HFD could raise growth behaviors and efficiency of feed utilization in zebrafish.

As the first defense line defensing against pathogen invasion, the mucus layer on the fish skin is composed of some innate immune components (Subramanian et al., 2007). We measured SOD, T-AOC, LSZ, C3 and C4 levels which are crucial substances in the immunity system of fish (Lvoll et al., 2006; Saurabh and Sahoo, 2010; Xie et al., 2022a; Yajie Zhao et al., 2022) to investigate the effect of SFPY supplementation in innate immune. The result showed that supplementation of SFPY tended to increase the T-AOC of skin mucus compared to the HFD group. Especially, 1.0 SFPY group considerably increased the skin mucus LSZ and C4 levels in zebrafish. All of results illustrated that adding 1.0% SFPY had a certain promoting influence on the immune function of fish.

Studies indicated that HFD has an ability to affect the health of several fish containing grass carp (*Ctenopharyngodon idellus*) (Shi et al., 2017), California perch (*Micropterus salmoides*) (Li et al., 2020), channel catfish (*Ictalurus punctatus*) and blunt snout bream (Desouky et al., 2020; Xiu-Fei Cao et al., 2019). These fish species were easily prone for fatty liver diseases resulting in slow growth, high morbidity and mortality of the fish. Our research found that supplement of SFPY to HFD could reduce adverse effects caused by HFD in zebrafish. We detected hepatic TAG content, HE liver tissue analysis and gene expression levels of lipid metabolism. The content of liver TAG in 1.0 SFPY was obviously decreased. Correspondingly, H&E images confirm that the addition of SFPY decreased liver fat deposition (Fig. 4B). In addition, HDF up-regulated the expression level of lipogenesis genes (*C/EBPα*, *PPARγ*, *ACC*, *FAS*, and *DGAT2*), which is consistent with other reports (Zhang et al., 2019). In contrast, 0.5 and 1.0 SFPY groups(Fig. 4C) saw an opposite trend, indicating an effective function of dietary SFPY in reducing hepatic lipid deposition by inhibiting fatty acids synthesis processes.

Intestine is a critical tissue for nutrient absorption. Intestinal functions are affected by morphology and structures (Gao et al., 2013; Vizcaíno et al., 2014). The length of villi is critical to the function of the gut, which contributes to better absorption of nutrients and promotes growth of fish (Al-Fataftah and Abdelqader, 2014). According to Stephen et al. (Ayiku et al., 2020) yeast culture significantly increased the height and width of intestinal villi which were conductive to promote the growth of the shrimp. In this study, zebrafish villi were lengthened and widen fed with 0.5 and 1.0 yeast culture than HFD diet. In previous study, yeast culture could increase the intestinal villus surface area may be due to mannan oligosaccharides (MOS) and β-glucan (Zhang et al., 2012).

As an organ of digestion and absorption, the zebrafish intestine has a very important impact on growth and immunity (Vizcaíno et al., 2014; Wang et al., 2021). After 10 weeks feeding with yest culture, the intestinal content of grass carp was rich in Fusobacteria, Bacteroidetes,

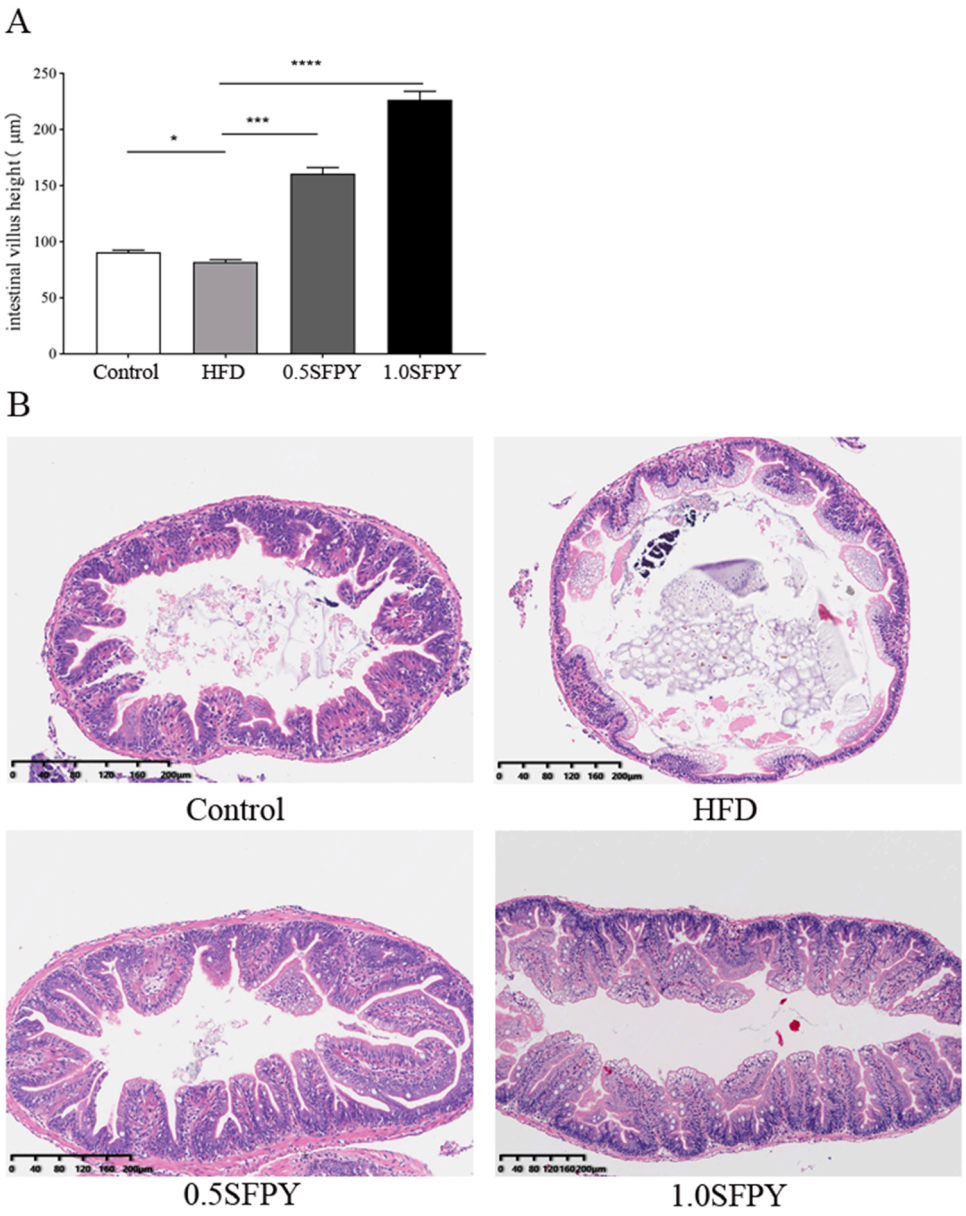

Fig. 6. Effects of HFD, 0.5 SFPY and 1.0 SFPY diets on the H&E-stained sections of the intestine of zebrafish. (A) Intestinal villus height, (B) Representative liver intestinal image by H&E staining. The scale bar is 200 μm.

Firmicutes and Proteobacteria (E. Li et al., 2018). These bacteria promoted many metabolic activities for the hosts (Besten et al., 2013; Fan et al., 2018; Velázquez et al., 1997; Yafei et al., 2019). In the phyla level, Proteobacteria, Actinobacteriota and Firmicutes dominate the gut microbiota in all experimental groups.

After feeding of the fish with SFPY supplemented diet, the abundance of Proteobacteria were decreased, which were consistence with the previous study (Roeselers et al., 2011). Phylum Actinobacteriota had a key role in nutrients absorption and metabolism of the host (Yafei et al., 2019), and their abundances were increased due to supplementation of SFPY. Through analyzing the correlation between the bacterial and animal health, the results showed that SFPY supplementation could modulate the intestine microbial composition to improve the intestinal health and reduce the negative effects by HFD on zebrafish. At the genus level, the percentage of beneficial bacteria including *Bacillus, Dietzia* and *Aeromicrobium* was significantly increased in the 1.0 SFPY group. *Bacillus* was acted as probiotics and create a suitable intestinal micro-ecological environment to enhance the body's resistance against pathogen (Liu et al., 2021). *Dietzia* belongs to phylum *Actinomycetes* has been reported as a probiotic to inhibit the intestinal inflammation in fish (Click, 2011). Besides, *Aeromicrobium* are classified into phylum *Actinomycete*, which could produce a quantity of active secondary metabolits with powerful antibacterial and anti-inflammatory properties (Lee and Kim, 2007). These results suggested that after feeding of zebrafish with SFPY supplemented diet, the gut microbiota would be altered and this change might be contributed to regulate intestinal homeostasis and alleviate intestinal injury of the fish caused by HFD.

5. Conclusion

All in all, the present study demonstrated that while HFD diet could improve weight gain and reduced feed conversion ratio of zebrafish, it would cause negative effects on liver and gut health. The addition of SFPY to high-fat diet not only obtained the high growth caused by HFD, but also ameliorated its effect on liver fat abnormal accumulation, intestinal and liver damage. 1.0 SFPY group significantly reduced hepatic TAG by decreasing the expression of lipogenesis genes, improved the morphology of gut and liver and the composition of gut microbiota, and

Table 3
The relative abundance of main bacteria phyla in the intestinal of zebrafish fed with different diets.

Species name	Control	HFD	0.5 SFPY	1.0 SFPY
Proteobacteria	57.41 ± 5.63	57.53 ± 7.68	29.92 ± 30.12	36.72 ± 7.83 * *
Actinobacteriota	14.20 ± 4.83	9.07 ± 2.80	23.83 ± 14.30	38.5 ± 14.94 * *
Firmicutes	5.79 ± 3.82	6.17 ± 2.43	41.00 ± 29.92 *	10.78 ± 3.36 *
Fusobacteriota	6.39 ± 11.87	7.40 ± 5.91	0.41 ± 0.45 *	0.06 ± 0.04 *
Cyanobacteria	0.48 ± 0.37	1.31 ± 0.92	2.09 ± 3.34	2.76 ± 2.61
MBNT15	1.94 ± 0.53 * *	4.94 ± 1.44	0.10 ± 0.07 * **	0.77 ± 0.92 * *
Planctomycetota	3.20 ± 1.02	3.51 ± 0.93	0.28 ± 0.17 * **	0.74 ± 0.35 * **
Verrucomicrobiota	2.22 ± 0.33	2.84 ± 0.97	0.30 ± 0.39 * **	3.10 ± 4.70
Chloroflexi	2.54 ± 0.37	2.05 ± 0.73	0.28 ± 0.22 * **	1.37 ± 0.80
Bacteroidota	1.32 ± 1.41	1.12 ± 0.74	0.50 ± 0.56	3.35 ± 5.72
Dadabacteria	2.10 ± 0.55	1.74 ± 0.49	0.33 ± 0.27 * **	0.83 ± 0.32**

Values represent the means (± SEM) of 5 replicates. The statistical analyses were done by comparing with HFD group, *p < 0.05, * * p < 0.01, * ** p < 0.001

decreased the relative expression level of pro-inflammatory factors. In addition, SFPY added in HFD increased the level of LSZ, C 4 and SOD in skin mucus. All these figures indicated that addition of SFPY is beneficial to the health of liver and gut and alleviates the negative influences caused by HFD.

CRediT authorship contribution statement

Jie Li: Formal analysis, Investigation, Visualization, Writing – original draft; **Dongmei Xia:** Formal analysis, Investigation, Writing – original draft; **Xiufang Jing:** Formal analysis, Investigation, Writing – original draft; **Yajie Zhao:** Investigation, Visualization, Writing – original draft; **Qiang Hao:** Investigation, Methodology; **Qingshuang Zhang:** Investigation, Methodology; Methodology; **Mingxu Xie:** Methodology; **Yalin Yang:** Methodology; **Chao Ran:** Methodology; **Qiyou Xu:** Methodology; **Chenglong Wu:Zhen Zhang:** Conceptualization,

Table 4
The relative abundance of main bacteria genera in the intestinal of zebrafish fed with different diets.

Species name	Control	HFD	0.5 SFPY	1.0 SFPY
Aeromonas	3.96 ± 14.67	12.08 ± 15.66	6.71 ± 11.32	4.26 ± 3.59
Staphylococcus	1.27 ± 0.74	0.56 ± 0.14	39.34 ± 31.35 *	1.93 ± 1.75
Rhodobacter	9.08 ± 1.65	7.34 ± 2.83	2.33 ± 1.44 * *	4.80 ± 3.59
Gemmobacter	6.72 ± 3.35	5.77 ± 2.47	2.44 ± 2.13	2.99 ± 1.57
Aeromicrobium	0.08 ± 0.03	0.01 ± 0.00	3.98 ± 4.37	16.32 ± 11.64 *
Dietzia	0.71 ± 0.61	0.28 ± 0.31	5.19 ± 2.73 * *	3.07 ± 1.43 * *
Bacillus	0.28 ± 0.14	0.44 ± 0.09	0.29 ± 0.25	6.41 ± 3.21 * *
Cellvibrio	0.08 ± 0.11	0.13 ± 0.19	3.86 ± 8.42	0.02 ± 0.04
Cetobacterium	6.38 ± 11.88	7.40 ± 5.91	0.41 ± 0.45 *	0.06 ± 0.04 * *

Values represent the means (± SEM) of 5 replicates. The statistical analyses were done by comparing with HFD group, *p < 0.05, * * p < 0.01, * ** p < 0.001

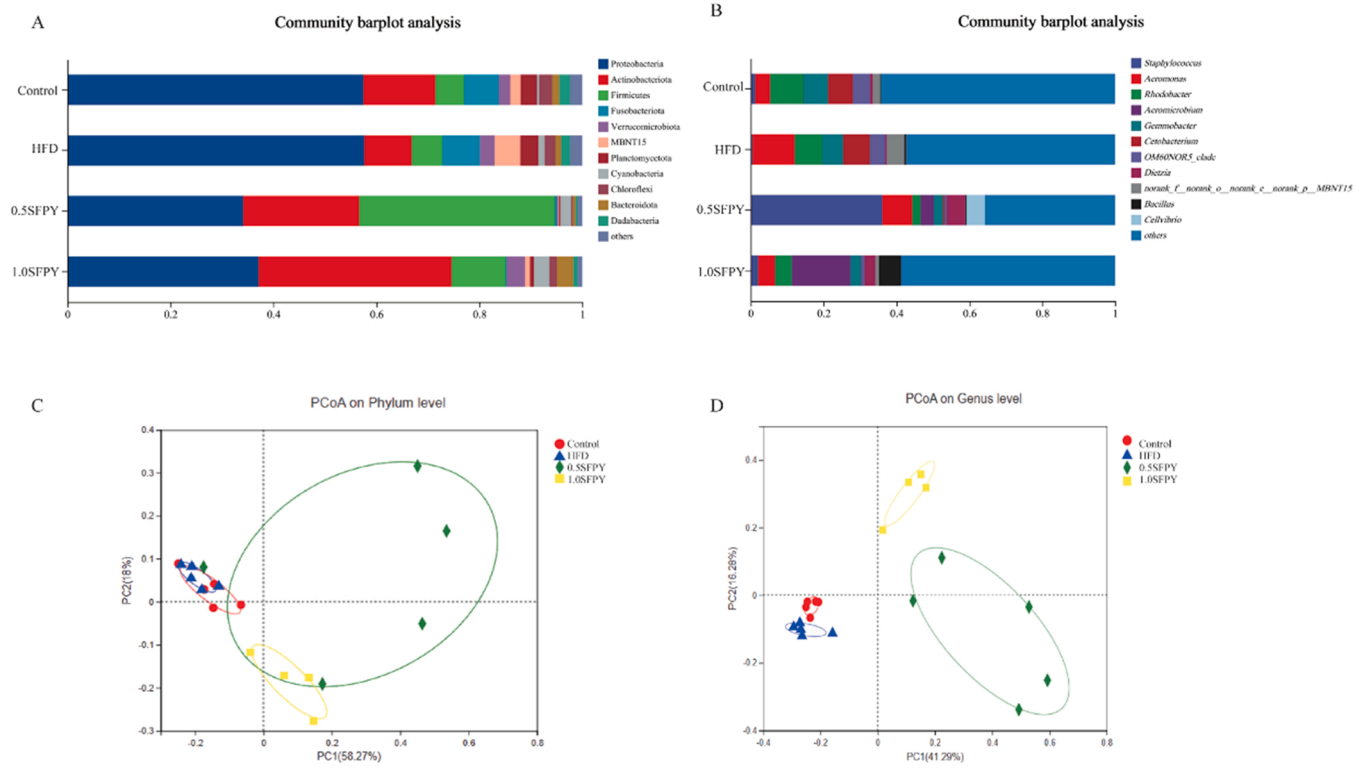

Fig. 7. The intestinal microbiota of zebrafish fed with HFD, 0.5 SFPY and 1.0 SFPY diets. Relative abundance at phylum (A) and genus (B) level of the gut microbiota; Principal coordinates analysis (PCoA) of the intestinal microbiota on phylum (C) and genus (D) level of the gut microbiota.

Methodology, Writing – review & editing, Resources; **Zhigang Zhou:** Conceptualization, Methodology, Writing – review & editing, Resources.

All authors participated in writing draft, reviewing and editing the manuscript. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declared no conflict of interest.

Data Availability

Data will be made available on request.

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