Lipid metabolic disorders and physiological stress caused by a high-fat diet have lipid source-dependent effects in juvenile black seabream Acanthopagrus schlegelii

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Abstract This study was conducted to evaluate the effects of different dietary lipid sources on growth performance, lipid metabolism, and physiological stress responses including oxidative stress (OS) and endoplasmic reticulum stress (ERS) of juvenile Acanthopagrus schlegelii (initial weight 0.88 ± 0.01 g) fed a high-fat diet (HFD). Four isonitrogenous and isolipidic experimental diets containing different lipid sources were formulated: fish oil (FO), palm oil (PO), linseed oil (LO), and soybean oil (SO), respectively. Results indicated that fish fed HFD supplemented with FO significantly improved growth than SO treatment. The high concentrations of aspartate aminotransferase and alanine transaminase were found in HFD supplemented with SO. Fish fed dietary LO supplementation showed significantly lower serum cholesterol, triglyceride, low-density lipoprotein, and high-density lipoprotein contents than those in SO group. Likewise, hepatic paraffin section analysis indicated that HFD with PO or SO supplementation increased fat drop. The expression levels of peroxisome proliferators-activated receptor alpha (ppara) and silent regulator 1 (sirt1) were significantly elevated by HFD with FO or LO supplementation. Additionally, the key marker of OS malonaldehyde was significantly increased in FO and SO groups. ERS-related genes were activated in dietary PO or SO supplementation and, hence, triggering inflammation and apoptosis by promoting the expression levels of nuclear factor kappa B (nf-kb) and c-Jun N-terminal kinase (jnk). Overall, the present study reveals that lipid metabolic disorders and physiological stress caused by a HFD have significant lipid source-dependent effects, which have important guiding significance for the use of HFD in marine fish.

Keywords Apoptosis · High-fat diet · Lipid metabolism · Lipid source · Physiological stress response

Abbreviations

ALT · Alanine transaminase
AST · Aspartate aminotransferase
atf6 · Activating transcription factor 6
bax · Bcl2-associated X
bcl-2 · B cell leukemia 2
Cu/Zn-sod · Cu-Zn superoxide dismutase
DHA · Docosahexaenoic
EPA · Eicosapentaenoic acid
ERS · Endoplasmic reticulum stress
Introduction

Lipids not only can provide large amounts of energy and essential fatty acids but can also promote absorption of fat-soluble vitamins (Miranda-Díaz et al. 2020; Anvith and Sankar 2015). Recently, high-fat diet (HFD) is popularly used in marine fish due to its protein-sparing effect and, hence, reduces feed cost and nitrogen and phosphorus emissions (Boujard 2004; Jin et al. 2021; Wang et al. 2019). Nevertheless, HFD can cause lipid metabolic disorders (e.g., hepatic steatosis, lipotoxic injury) and physiological stress responses (e.g., oxidative stress (OS), endoplasmic reticulum stress (ERS)) (Cao et al. 2019a; Qian et al. 2021), triggering inflammation and apoptosis (Jin et al. 2021; Xie et al. 2021), therefore, leading to the promotion and use of HFD in aquaculture facing great challenges.

Generally, different lipid sources have different characteristic fatty acid profiles (Jin et al. 2017). Fish oil (FO) is rich in long-chain polyunsaturated fatty acids (LC-PUFAs), especially rich in eicosapentaenoic acid (20:5n-3, EPA) and docosahexaenoic acid (22:6n-3, DHA), which is the main lipidic source in marine fish diets (Nasopoulou and Zabetakis 2012). However, with the development of global aquaculture, the limited and unstable supply of FO results in price increases and, consequently, leading many vegetable oils (VOs) being used to substitute FO in aquaculture industries (Milián-Sorribes et al. 2021). VOs as promising alternative sources of FO have attracted wide ranges of attention because of their relatively better economic value, high availability, and steadily increasing production (Gou et al. 2021; Nasopoulou and Zabetakis 2012). The most common VOs used for aquaculture have been soybean oil (rich in 18:2n-6, SO), linseed oil (rich in 18:3n-3, SO), rapeseed oil (rich in 18:1n-9), sunflower oil (rich in 18:2n-6), palm oil (rich in 16:0 and 18:1n-9), and olive oil (rich in 18:1n-9) (Nasopoulou and Zabetakis 2012).

FO is thought to play vital roles in anti-thrombotic and anti-inflammatory (Din et al. 2004; Rennie et al. 2003). Interestingly, previous studies elucidated that FO could prevent metabolic dysfunction ameliorate hepatic inflammation induced by HFD in mice (Philp et al. 2015; Yuan et al. 2016). However, replacing FO in feed with VOs can affect the health of aquatic animals through modification of immune function and interference with normal function of the endocrine system (Naylor et al. 2021), since n-3 LC-PUFAs (e.g., DHA and EPA) are lacking in VOs (Turchini et al. 2009). On the other hand, when compared to fish fed with FO diet, dietary VOs had lower superoxide production (Lin and Shiau 2007; Mourente et al. 2007). Nonetheless, there is barely study on the influence of HFD supplemented with VOs, whether there are different effects on lipid metabolism and
physiological responses caused by HFD supplemented with various lipid sources remain unknown.

Black seabream (*Acanthopagrus schlegelii*) is a popular and commercially important marine fish species that inhabits coastal and estuarine waters of China and some other countries such as Japan and South Korea in Asia, and it has been regarded as an excellent marine fish species since it exhibits rapid growth, high disease resistance, and can tolerate a wide range of environmental conditions (Li et al. 2022). Different lipid sources vary in fatty acid profiles and contents; obviously, they have different effects on growth performance and lipid metabolism of aquatic animals (Jin et al. 2017). It is accepted that HFD intake leads to lipid accumulation, lipid metabolic disorders, physiological stress responses (including OS and ERS), inflammation, and apoptosis, but the issue of lipid sources seems to be overlooked in many studies. Hence, this study aimed to evaluate the effects of HFD supplemented with four different lipid sources (FO, PO, LO, and SO) on growth performance, lipid metabolism, and physiological responses in *A. schlegelii*, and provide further insight into the theoretical basis for the use of HFD in marine fish.

**Materials and methods**

**Diet preparation**

Four isoproteic (40% crude protein) and isolipidic (18% crude lipid) diets were formulated with FO (rich in LC-PUFAs, control group), palm oil (PO, rich in palmitic acid and oleic acid, 16:0 and 18:1n-9), soybean oil (SO, rich in linoleic acid, 18:2n-6), and linseed oil (LO, rich in linolenic acid, 18:3n-3) as main lipid sources and proximate composition of the experimental diets are showed in Table 1. The experimental diets were produced as follows: the ground ingredients were mixed in a Hobart type mixer and cold-extruded pellets produced (F-26, Machine factory of South China University of Technology) with pellet strands cut into uniform sizes (2 mm and 4 mm diameter pellets) (G-250, Machine factory of South China University of Technology). Pellets were heated for 4 h at 50 °C to approximately 10% moisture, sealed in vacuum-packed bags, and stored at −20 °C until used in the feeding trial.

| **Table 1** Ingredients and proximate composition of the experimental diets (air-dry basis, %) |
|---------------------------------------------------------------|
| **Ingredient** | **Experimental diets** |
| | FO | PO | LO | SO |
| Fish meal | 26.00 | 26.00 | 26.00 | 26.00 |
| SPC | 10.00 | 10.00 | 10.00 | 10.00 |
| SM | 16.00 | 16.00 | 16.00 | 16.00 |
| Wheat meal | 28.30 | 28.30 | 28.30 | 28.30 |
| Fish oil | 13.50 | 0.00 | 0.00 | 0.00 |
| Palm oil | 0.00 | 13.50 | 0.00 | 0.00 |
| Linseed oil | 0.00 | 0.00 | 13.50 | 0.00 |
| Soybean oil | 0.00 | 0.00 | 0.00 | 13.50 |
| Soybean lecithin | 1.00 | 1.00 | 1.00 | 1.00 |
| Vitamin premix | 1.00 | 1.00 | 1.00 | 1.00 |
| Mineral premix | 2.00 | 2.00 | 2.00 | 2.00 |
| Choline chloride | 0.20 | 0.20 | 0.20 | 0.20 |
| Ca(H2PO4)2 | 2.00 | 2.00 | 2.00 | 2.00 |
| Sum | 100.00 | 100.00 | 100.00 | 100.00 |
| **Proximate composition (%)** |  |
| Dry matter | 92.90 | 91.73 | 92.41 | 92.82 |
| Crude protein | 39.18 | 39.65 | 39.67 | 38.70 |
| Crude lipid | 18.73 | 18.44 | 18.69 | 18.63 |
| Ash | 9.33 | 9.11 | 9.56 | 9.58 |

All ingredients were purchased from Ningbo Tech-Bank Feed Co. Ltd., Ningbo, China

*Vitamin premix based on Zhou et al. (2011)*

Mineral premix (g kg⁻¹ premix): FeC6H5O7, 11.43; ZnSO4·7H2O, 11.79; MnSO4·H2O (99%), 2.49; CuSO4·5H2O (99%), 1.06; MgSO4·7H2O (99%), 27.31; KH2PO4, 232.3; NaH2PO4, 228.39; C6H10CaO6·5H2O (98%), 34.09; CoCl2·6H2O (99%), 0.54; KIO3 (99%), 0.06; zeolite, 449.66

Fish feeding and experimental conditions

A 6-week feeding trial was conducted on juvenile *A. schlegelii* with an initial weight of 0.88 ± 0.01 g obtained from a local commercial hatchery (Xiangshan Bay, Ningbo, China). Prior to the start of the feeding trial, *A. schlegelii* juveniles were firstly acclimated to the experimental facilities and fed with a commercial diet (45% protein, 12% crude lipid, Ningbo Tech-Bank Corp.) for 2 weeks. A total of 240 *A. schlegelii* juveniles were randomly allocated to 12 tanks (400 L) corresponding to triplicate tanks for each of the four dietary treatments. The feeding trial was carried out with a completely randomized design. During the experimental period, fish were hand-fed to apparent satiation twice daily at 08:00
and 18:00 for 6 weeks. Water quality parameters were measured and the values were as follows: temperature (28.6-33.7 °C), salinity (28.5-30.8 psu), dissolved oxygen (5.1-7.8 mg/L), and pH (8.0-8.1 mg/L) (YSI, Yellow Springs, OH, USA).

Sample collection

At the end of feeding trial, fish were sampled 12 h after the last feed. All fish were euthanized (Eugenol at 10 mg/L, Sinopharm Chemical Reagent Co., Ltd.) and all fish in each tank were weighed and counted individually to calculate the parameters of growth performance and feed utilization. All analyses were performed on a per tank basis (n=3) with samples from each tank being derived from pooled fish. Firstly, blood samples were taken from the caudal vasculature of 10 fish per tank using a 1 mL syringe, and stored at 4 °C for 24 h for collecting serum samples by centrifugation at 956×g for 10 min at 4 °C to test biochemical indices. Then, liver samples were obtained and stored at −80 °C for analyzing enzyme activities (pools of 3 fish per tank) and gene expression (pools of 3 fish per tank). In addition, fresh liver tissues (blood has not been drawn) were collected from one fish per tank and stored in 4% formaldehyde for histological analyses.

Assay of proximate composition

Moisture, protein, crude lipid, and ash contents of diets were determined by standard AOAC (2006) methods. Moisture content was measured by drying the diet samples to constant weight at 105 °C. Crude protein (N×6.25) was determined according to the Dumas combustion method with a protein analyzer (FP-528, Leco, USA). Total lipid was extracted via the ether extraction method using a Soxtec System HT (Soxtec System HT6, Tecator, Sweden) and a muffle furnace (550 °C for 8 h) was used to measure ash content.

Serum and liver biochemical indices analysis

Total cholesterol (TC) and triacylglycerol (TG) concentrations in serum were measured using an automatic biochemistry analyzer (VITALAB SELECTR A Junior Pros, Netherlands). Liver samples were homogenized in nine volumes (w/v) of ice-cold physiological saline 0.89% (w/v), and then centrifuged at 956×g for 10 min at 4 °C. The activity or contents of superoxide dismutase (SOD), glutathione peroxidase (GSH-px), glutathione (GSH), and malondialdehyde (MDA) were assayed according to the manufacturer’s instructions (Nanjing Jiancheng Bioengineering Institute, China) using Multiskan spectrum (Thermo, USA).

Histological analysis

Fresh liver tissue was fixed in 4% paraformaldehyde before paraffin sections were prepared (Servicebio, China). Briefly, after fixation for 24 h, liver samples were trimmed appropriately in a fume hood before being dehydrated in ethanol with concentration increasing incrementally from 75 to 100%. Liver samples were then embedded in paraffin, sliced into sections of 4 mm using a microtome, and stained with hematoxylin and eosin (H&E), and images acquired under a microscope (Nikon Eclipse CI, Tokyo, Japan).

Assay of reverse-transcriptase quantitative PCR

Total RNA was extracted from the liver by using Trizol reagent according to manufacturer’s instructions (Vazyme, China). The quality and quantity of extracted RNA were assessed by gel electrophoresis (1.0% denaturing agarose) and spectrophotometer NanoDrop 2000 (Thermo Fisher Scientific, USA), respectively. HiScript® II Q RT SuperMix for qPCR (+gDNA wiper) (Vazyme) was used to prepare cDNA from 1000 ng of DNAase-treated RNA using the protocol supplied by the manufacturer. The housekeeping gene β-actin was used as a reference gene because it is stable across the experimental treatments. Primer Premier 5.0 was used for designing specific primers for the housekeeping and target genes (Table 2). Amplification and qPCR were carried out in a Lightcycler 96 Instrument (Roche, Switzerland). The qPCR was carried out in reaction volume of 20 μL, containing 0.4 μL of each primer, 10 μL of double concentrated SYBR qPCR Green Master Mix (Vazyme), 0.8 μL of 1/10 diluted cDNA, and 8.4 μL diethyl pyrocarbonate-treated water. The real-time PCR conditions were as follows: 95 °C for 2 min, 45 cycles of 95 °C for 10 s, 58 °C for 10 s, and 72 °C for 20 s. Standard calibration curves were
Table 2 Primers for real-time quantitative PCR of black seabream (*Acanthopagrus schlegelii*)

| Gene       | Nucleotide sequence (5’–3’) | Size (bp) | GenBank reference or publication |
|------------|-----------------------------|-----------|---------------------------------|
| sirt1      | F: TGGATGAAACTGTAGGAAACC    | 238       | MN871952                        |
|            | R: ACAAATGGACTGGGA          |           |                                 |
| pparα      | F: ACGAGCCTTCCTCCTCCC       | 183       | KX066234                        |
|            | R: GCCCTCCCCCTGGTTTATTC      |           |                                 |
| Srebp-1    | F: TGGGGGTAGAGGTAGTAG       | 247       | KX066235                        |
|            | R: GTGAGGGTCTGAGTGTTGGA      |           |                                 |
| grp78      | F: AACAGCTGACCTCTAAACC      | 164       | MT451934                        |
|            | R: ATGTCTTCATCTGGCCACCA      |           |                                 |
| aif6       | F: CCTTTGGTTTCTCTCCAG       | 222       | MT512507                        |
|            | R: CCGTACTCTCACAGTCAAATGC   |           |                                 |
| xbp1       | F: TGATACGGAAGACGAGACC      | 235       | MW589390                        |
|            | R: TTCTGTCTCCTGGCTCTTG       |           |                                 |
| ire1α      | F: AGAGGTCTGGTGATGTTG       | 181       | OL361769                        |
|            | R: GTCCCCTCTAGGGAAGAGT       |           |                                 |
| nrf-κb     | F: AGCCCAAGGCACCTAGACAG     | 196       | MK922543                        |
|            | R: GTTCTGGGCAGCTGAGGAGG      |           |                                 |
| tnf-α      | F: GGGCAGACAGACAGGGCAAGA    | 172       | MK922542                        |
|            | R: TCAGCCGCAAGGTATCTCTC      |           |                                 |
| il-1β      | F: CATCTGGAGGGCGTGGA         | 231       | JQ973887                        |
|            | R: CGGTGGTTGGGGAGGA          |           |                                 |
| tgfβ-1     | F: GGGTTTCAAACCTCGGC        | 209       | Xue et al. (2008)               |
|            | R: TTGTCTGCGAGGCTG          |           |                                 |
| il-10      | F: TGCTAAACGGCTCTTGCAAG     | 214       | OL321594                        |
|            | R: GGCATCCCTGGCTCTCACTC      |           |                                 |
| caspase7   | F: GTTTGCTACTCCACTGTTGC     | 152       | OL321593                        |
|            | R: TGCCACACATGAGTGTGGCT      |           |                                 |
| caspase9   | F: CCATTGTTTTCTGACAGTCC     | 214       | OL321594                        |
|            | R: GAGATGATCTGGGCTGCGGC      |           |                                 |
| bcl-2      | F: GCTCCAAAGCAGTCAACC       | 203       | OL420679                        |
|            | R: TGACCTGGAAGAACCGAGCTT     |           |                                 |
| bax        | F: AAGTGGATGAGCAAGAGTGAGG   | 232       | OL321596                        |
|            | R: ATGCAATCTGTTGCTGGAGA      |           |                                 |
| jnk        | F: ATAGCGTGTGGCTGGGAAA       | 171       | OK315340                        |
|            | R: CGCAGACATGAAACAGCCCA      |           |                                 |
| gpx        | F: TCTGAGATCAGTGCCCTCCTG    | 257       | OL321587                        |
|            | R: TCTGAAAGTTCAGGCCCTCA      |           |                                 |
| Cu/Zn-sod  | F: CACGGTAAAGAATCAGTGCGG    | 202       | OL321588                        |
|            | R: TCTCTGCTGAGCTCTCTTTTT     |           |                                 |
| Mn-sod     | F: TCTTTTCTCTCTGTACCCAGC     | 247       | OL321589                        |
|            | R: GCAAAGGGAGATGTCAGACGC     |           |                                 |
| β-actin    | R: ATGAGGTAGTCTGTAGGTCG      | 212       | Jiao et al. (2006)              |

1 sirt1, silent regulator 1
2 pparα, peroxisome proliferation-activated receptor alpha
3 Srebp-1, sterol regulatory element-binding protein-1
4 grp78, glucose-regulated protein 78
5 aif6, activating transcription factor 6
generated using six different dilutions (in triplicate) of the cDNA samples, and the amplification efficiency of all genes was analyzed using the equation $E = 10^{(–1/Slope)} - 1$, which were approximately equal and ranged from 89 to 103%. The expression levels of the target genes were calculated using the $2^{-\Delta\Delta Ct}$ method described.

Calculations and statistical analysis

Final weight (FW) = total final weight/final fish number.

Weight gain (WG) = WG (%) = $100 \times ((\text{final body weight}) - (\text{initial body weight})) / (\text{initial body weight})$.

Specific growth ratio (SGR) = SGR (%) = $100 \times (\text{Ln (final body weight)} - \text{Ln (initial body weight)})/42$ days.

Survival rate (SR): SR (%) = $100 \times (\text{final fish number}/\text{initial fish number})$.

The homogeneity of variances (Levene’s test) was checked prior to one-way analysis of variance (ANOVA) followed by Tukey’s HSD test at a significance level of $P < 0.05$ (IBM SPSS Statistics 20, USA).

Results

Growth performance and survival

The effects of HFD supplemented with different lipid sources on growth performance of *A. schlegelii* juveniles are presented in Table 3. Fish fed FO diet showed higher final weight (FW), weight gain (WG), and specific growth rate (SGR) than those fed the other diets, and significantly higher than SO group ($P < 0.05$). However, survival rate (SR) did not show any significant differences among treatments ($P > 0.05$).

Serum biochemical indices and hepatic histological analysis

The highest contents of alanine aminotransferase (ALT) and aspartate transaminase (AST) in serum were observed in fish fed HFD supplemented with SO ($P < 0.05$), and there were no significant differences with other treatment ($P > 0.05$) (Fig. 1A). Similar results were found for total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) contents in serum that significantly increased by dietary SO supplementation ($P < 0.05$); in contrast, all these indices were decreased in LO group, and significantly lower than fish fed HFD supplemented with PO or SO increased the number and area of vacuolar fat drops and, hence, induced hepatic fat pathological change. The symptoms are relatively mild in HFD containing n-3 PUFA (FO and LO groups) as the shape of hepatocytes was more

Table 2 (continued)

6 xbp1, X-box binding protein 1  
7 ire1α, inositol requiring enzyme-1  
8 nf-kb, nuclear factor kappa B  
9 tfn-α, tumor necrosis factor α  
10 il-1β, interleukin-1 β  
11 tgfβ-1, transforming growth factor β 1  
12 il-10, interleukin-10  
13 bcl-2, B cell leukemia2  
14 bax, bcl2-associated X  
15 jnk, c-Jun N-terminal kinase  
16 gpx, glutathione peroxidase  
17 Cu/Zn-sod, Cu, Zn-superoxide dismutase  
18 Mn-sod, Mn-superoxide dismutase
regular and fewer vacuolar lipid droplets were observed (Fig. 1C).

The key markers of lipid metabolism

The regulatory effects of HFD supplemented with different lipid sources on expression levels of lipid metabolism relevant genes are shown in Fig. 2. The gene expression levels of sterol regulatory element-binding protein-1 (srebp-1) did not show any significant differences among treatments (P > 0.05). However, fish fed HFD containing PO or SO markedly downregulated silent regulator 1 (sirt1) and peroxisome proliferators-activated receptor alpha (ppara) expression levels (P < 0.05), whereas contrary results were found in FO and LO groups that significantly upregulated the expression levels of sirt1 and ppara (P < 0.05).

Oxidation and antioxidant parameters in the liver

The effects of HFD supplemented with different lipid sources on oxidation and antioxidant parameters are presented in Fig. 3. The glutathione peroxidase (GSH-px) and content of glutathione (GSH) were not significantly different among treatments (P > 0.05). The activity of superoxide dismutase (SOD) was markedly higher in fish fed HFD with FO or PO supplementation than those in PO and SO groups (P < 0.05). Moreover, the significantly higher contents of malondialdehyde (MDA) were recorded in fish fed HFD supplemented with FO or SO compared to dietary PO and LO treatments (P < 0.05) (Fig. 3A). Similar patterns were found for the relative mRNA expression levels of hepatic antioxidant genes, where the expression levels of Cu-Zn superoxide dismutase (Cu/Zn-sod) and Mn superoxide dismutase (Mn-sod) were upregulated by HFD supplemented with FO compared to fish fed with dietary PO or SO supplementation (P < 0.05), while no statistical differences of glutathione peroxidase (gpx) expression levels were found among treatments (P > 0.05) (Fig. 3B).

The key markers of ERS in the liver

The regulation of HFD supplemented with different lipid sources on gene expression levels related to ERS are shown in Fig. 4. The significantly higher expression levels of glucose regulated protein 78 (grp78), activating transcription factor 6 (atf6), inositol requiring enzyme-1 α (ire1α), and X-box binding protein 1 (xbp-1) in liver were all found in fish fed HFD supplemented with SO than those in FO or LO treatments (P < 0.05), but showed no marked differences with dietary PO supplementation (P > 0.05), except for grp78.

Table 3 Effects of different high-fat diet on growth performance, feed utilization of juvenile black seabream (Acanthopagrus schlegelii)

| Parameter          | Experimental diets | ANOVA |
|--------------------|--------------------|-------|
|                    | FO                | PO    | LO    | SO    | p-value |
| IW (g) 1           | 0.87± 0.00        | 0.87± 0.01 | 0.88± 0.00 | 0.88± 0.00 | 0.596 |
| FW (g) 2           | 4.74± 0.04b       | 4.53± 0.02ab | 4.46± 0.07ab | 4.34± 0.08a | 0.015 |
| WG (%) 3           | 439.03± 6.3b      | 419.06± 3.36ab | 408.34± 9.83ab | 392.37± 10.89a | 0.021 |
| SGR (%/d) 4        | 6.02± 0.04b       | 5.88± 0.02ab | 5.81± 0.07ab | 5.69± 0.08a | 0.023 |
| SR (%) 5           | 80.00± 2.89       | 86.67± 1.67 | 88.33± 7.26 | 86.67± 7.26 | 0.713 |

Values are presented as the mean±standard error (n = 3). Mean values for the same column with different letters were significantly different (P < 0.05)

1IW initial weight
2FW final weight
3WG weight gain
4SGR specific growth ratio
5SR survival rate
Fig. 1  Effects of high-fat diet supplemented with different lipid sources (FO, fish oil; PO, palm oil; LO, linseed oil; SO, soybean oil) on serum biochemical indices and lipid accumulation in liver of juvenile black seabream (Acanthopagrus schlegelii). (A) Serum aspartate aminotransferase (AST) and alanine transaminase (ALT) contents. (B) Serum high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triacylglycerol (TG), and total cholesterol (TC) contents. (C) Paraffin section of the liver with hematoxylin and eosin staining (×400, bar = 20 μm). Values are presented as the means (n = 3), with standard errors represented by vertical bars. Mean values for the same column with different superscript letters were significantly different (P < 0.05). F, fat drop; N, nucleus.
The key markers of inflammation in liver

The regulation of HFD supplemented with different lipid sources on gene expression levels related to inflammatory response were determined (Fig. 5). The relative expression levels of tumor necrosis factor $\alpha$ ($tnf\alpha$), interleukin-1$\beta$ ($il-1\beta$), and nuclear factor kappa B ($nf-kb$) significantly upregulated by HFD supplemented with PO compared to FO and LO groups ($P < 0.05$), but did not show any statistical differences with PO treatment ($P > 0.05$). In contrast, relative expression levels of transforming growth factor $\beta$ ($tgf\beta$) and interleukin-10 ($il-10$) significantly decreased in fish fed HFD with PO or SO supplementation compared to FO and LO treatments ($P < 0.05$), but no significant differences were found between SO and PO groups ($P > 0.05$).

Apoptotic markers in the liver

The regulation of HFD supplemented with different lipid sources on gene expression levels related to apoptosis are presented in Fig. 6. The relative expression levels of c-Jun N-terminal kinase ($jnk$), pro-apoptosis genes including $bcl2$-associated X ($bax$), $caspase7$, and $caspase9$ all upregulated in fish fed dietary PO or SO supplementation ($P < 0.05$), while the expression level of anti-apoptosis gene B cell leukemia 2 ($bcl-2$) was markedly decreased ($P < 0.05$). Opposite results were recorded in FO and LO treatments, where showed low expression levels of $jnk$, $bax$, $caspase7$, and $caspase9$ and high expression levels of $bcl-2$.

Discussion

Growth is the most commonly used indicator to evaluate the changes in dietary content of a nutrient (National Research Council (NRC), 2011). As expected, the highest values of FW, WG, and SGR were found in fish fed HFD supplemented with FO, but showed no significantly differences with PO or LO supplementation. These results were similar to previous reports on some other marine fish, suggesting that dietary LO could completely replace FO for Diplodus puntazzo (Piedecausa et al. 2007), Solea senegalensis (Benítez-Dorta et al. 2013), and Oncorhynchus mykiss (Turchini et al. 2018; Yıldız et al. 2020) without impacting on growth. Most studies concluded that when dietary FO was completely replaced by PO, the growth indicators could be decreased, which have been confirmed in Nibea coilbor (Huang et al. 2016) and Larimichthys crocea (Mu et al. 2020). However, a previous study reported that
PO partially or totally replaced FO in diet had no negative impact on growth performance in *O. niloticus* (Larbi Ayisi et al. 2018), which was in consistence with the present study. Additionally, in this study, the low growth performance was observed in fish fed SO supplementation, which probably due to the high proportion of SO replacing FO in the diet. To some extent, this result was in accordance with some previous studies for *A. schlegelii* (Jin et al. 2017), *Megalobrama amblycephala* (Li et al. 2016), *Misgurnus Anguillicaudatus* (Li et al. 2018), *Scophthalmus maximus* (Peng et al. 2014), *Cynoscion parvipinnis* (González-Félix et al. 2016), and *L. crocea* (Mu et al. 2018), indicating that replacing dietary FO with a high percentage of SO could depress growth performance. In this study, SR did not show any statistical differences among treatments, indicating that *A. schlegelii* fed HFD with different lipid sources could not impact on SR, which has been confirmed in a previous study in *A. schlegelii* (Jin et al. 2017; Wang et al. 2019). In sum, the present study indicated that the growth performance did not impact by HFD supplemented with FO, PO, or LO, but suppressed by HFD with SO supplementation.

In the present study, vacuolar fat droplets were observed in all treatments; this could be contributed to HFD intake. It has been suggested that when fish fed with HFD could cause cellular swelling,

![Graph A](image1)

![Graph B](image2)

**Fig. 3** Effects of high-fat diet supplemented with different lipid sources (FO, fish oil; PO, palm oil; LO, linseed oil; SO, soybean oil) on oxidative stress and antioxidant capacity in liver of juvenile black seabream (*Acanthopagrus schlegelii*). (A) Oxidation and antioxidant parameters in liver. (B) Relative mRNA expression levels involved in antioxidant capacity in liver. FO group was set as the reference group, and the mRNA expression levels of target genes were normalized relative to the expression of β-actin. Values are presented as the means (*n* = 3), with standard errors represented by vertical bars. Mean values for the same column with different superscript letters were significantly different (*P* < 0.05). GSH, glutathione; GSH-px/gpx, glutathione peroxidase; MDA, malonaldehyde; SOD, superoxide dismutase; CuZn-sod, Cu/Zn superoxide dismutase; Mn-sod, Mn superoxide dismutase.
nuclear translocation, and lipid droplet accumulation (Cao et al. 2019b; Lu et al. 2014) which has been reported in M. amblycephala (Lu et al. 2017) and Pseudosciaena crocea R. (Wang et al. 2015). Moreover, when compared to FO and LO groups, hepatic paraffin section of fish fed HFD with PO or
SO supplementation showed more clear liver injury including the presence of irregularly shaped cells, severe lipid vacuolization, and obvious hepatocyte nucleus polarization. These pathologies might be linked to suppress lipoprotein secretion and fatty acid oxidation and, consequently, resulted in a vicious cycle (Du et al. 2008). Kikuchi et al. (2009) demonstrated that the increasing TG, TC, and LDL-C concentrations in serum might be a symptom of declined health status of fish. Hence, these serum biochemical indices have been determined in this study; results indicated that serum TG, TC, and LDL-C contents were significantly enhanced by fish fed HFD supplemented with PO or SO. These results were similar to a previous study in (Gou et al. 2021), suggesting that PO or SO intake could aggravate the damage degree of the liver and prevent it to secret lipid to the circulatory system. ALT and AST are two common indexes in serum for diagnosing liver function and health (Boone et al. 2005; Metón et al. 1999). Generally, when liver cells were damaged, these two transaminases would be allowed to enter blood and, hence, increased the activities of ALT and AST in serum (Racicot et al. 1975). Indeed, in this study, the higher content of AST and ALT in serum were found in dietary SO supplementation, indicating that HFD supplemented with SO had adverse effects on the liver function of A. schlegelii. These findings suggested that regardless of lipid sources, fish fed with HFD could increase vacuolar fat droplets, whereas HFD with PO or SO supplementation showed more ability to induce liver injury and may cause lipid metabolic disorders in A. schlegelii.

Liver is a metabolic organ, which is a primary site for lipid uptake, synthesis, and secretion (Berghé 1991). PPARα is one of hepatic nuclear receptors and transcriptional coactivators; it plays a vital role in the liver’s ability to respond to nutrients and hormones (Francis et al. 2003) and regulates the gene expression of fatty acid catabolism (Cantó and Auwerx 2009). SIRT1 is a highly conserved NAD+-dependent protein deacetylase, which can promote oxidation of fatty acids in the liver and positively regulate the transcriptional activity of PPARα (Lomb et al. 2010; Prola et al. 2017). Chen et al. (2008) reported that liver-specific knock-down of SIRT1 in mice gain more weight when fed a HFD and lead to hepatic steatosis. Besides, SREBP-1 is a positive regulator of lipid anabolism, which may also be negatively regulated by SIRT1 (Shimano 2009). Therefore, the hepatic gene expression levels of sirt1, ppara, and srebp-1 were determined through qPCR in this study.
were determined; herein, results indicated that the mRNA expression levels of *ppara* and *sirt1* were markedly activated by HFD with FO or LO supplementation, but downregulated by dietary PO or SO supplementation. To some extent, these results were in accordance with some studies in fish for *O. macrolepis* (Gou et al. 2021; Peng et al. 2017), *M. amblycephala* (Li et al. 2016), and *A. schlegelii* (Jin et al. 2017) that dietary SO downregulated the expression levels of *ppara* than fish fed HFD with FO supplementation. Nevertheless, the gene expression level of *srebp-1* showed no significant differences among treatment, suggesting that the lipogenesis may not be affected by HFD supplemented with different lipid sources. These findings revealed that when compared to PO and SO treatments, dietary FO or LO supplementation (rich in n-3 PUFA) can alleviate fat deposition in liver appropriately by activating *sirt1/ppara* pathway.

Recently, many studies have concluded that HFD could cause OS and damage antioxidant defense system (Guo et al. 2019; Lu et al. 2017). MDA is a common biomarker of lipid peroxidation in fish (Ji et al. 2021); in the current study, the serum MDA concentration were significantly increased by dietary FO or SO supplementation. Besides, SOD including Cu/Zn-SOD and Mn-SOD play central roles in reactive oxygen species scavenging systems by converting O$_2^-$ to H$_2$O$_2$. Next, the H$_2$O$_2$ can be catalyzed to H$_2$O and O$_2$ by other antioxidative enzymes, for instance, GSH-px (Wang et al. 2018). In the current study, HFD supplemented with FO or LO markedly activated SOD activities; accordingly, the high expression levels of *Mn-sod* and *Cu/Zn-sod* were recorded in dietary FO and LO supplementation. Nevertheless, the GSH-px activity as well as its gene expression level did not affect by HFD supplemented with different lipid sources. Previous studies revealed that high levels of LC-PUFAs in feed are the main cause of lipid peroxidation and induce OS (Jin, et al. 2017; Yuan et al. 2019); this probably account for the high MDA content in dietary FO supplementation, with regard high content of MDA in SO group, which might be attributed to the decreased *sirt1* expression level, since deletion of SIRT1 in liver could significantly increase OS (Singh and Ubaid 2020). Collectively, these findings elucidated that when fish fed HFD with LO supplementation could relieve OS when compared with the other treatments, which also has been confirmed in *O. niloticus* (Peng et al. 2016).

Accumulated lipids may disrupt the signaling mechanisms and pathways, so can cause cellular dysfunction and cell death (Yilmaz 2017). ER is most notable for its pivotal roles in lipid biosynthesis, and protein sorting and processing; it can regulate diverse cellular processes including inflammatory and insulin signaling, nutrient metabolism, and cell proliferation and death via a signaling pathway called the unfolded protein response (UPR) (Pagliassotti et al. 2016; Yoshida 2007). It has been reported that excess of nutrients or energy may cause ERS (Fu et al. 2011). GRP 78 is considered to be a marker molecule of ERS (Yao et al. 2021). Besides, IRE1 and ATF6 are two sensor proteins ERS; these proteins could be activated during different stress conditions. Then, the activated IRE1 could lead to splicing of transcription factor XBP1 mRNA, spliced form of XBP1 translocate to the nucleus participate in the UPR (Yilmaz 2017). In this study, the mRNA expression levels of *ire1a, grp78, atm6*, and *xbp1* were measured; results indicated that dietary SO supplementation dramatically upregulated all these genes’ expression levels when compared to HFD supplemented with FO or LO, but showed no significantly different with PO group, except for *grp78*. These results indicated that HFD supplemented with PO or SO which are rich in saturated fatty acid (SFA), monounsaturated fatty acid (MUFA), or 18:2n-6 could be easy to cause ERS; in turn, there is evidence that ERS can induce excessive lipid accumulation (Fang et al. 2021); this could also explain why the dietary PO or SO supplementation had large lipid accumulation.

There is evidence that IRE1$\alpha$ might play a central role in linking ERS signaling to inflammatory-response signaling (Zhang and Kaufman 2008). Furthermore, in response to ERS, nuclear translocation of NF-$\kappa$B would be activated by the autophosphorylation of IRE1$\alpha$ (Davis 2000; Hu et al. 2006). The transcription factor NF-$\kappa$B serves as a pivotal mediator of inflammatory responses; it can induce the expression of various pro-inflammatory genes including those encoding TNF-$\alpha$, IL-1$\beta$, IL-6, etc. (Liu et al. 2017). On the contrary, TGF-$\beta$1 and IL-10 are considered to be important anti-inflammatory cytokines (Levin and Godukhin 2011). In this study, the expression levels of *nf-$\kappa$b* and pro-inflammatory cytokines including *tnf-$\alpha*$ and *il-1$\beta$* were markedly upregulated by dietary...
SO supplementation than other treatments, except for HFD supplemented with PO. Contrary results were found in the anti-inflammatory markers \textit{tgfβ-1} and \textit{il-10}, which were downregulated in HFD with PO or SO supplementation. These findings were confirmed in \textit{L. crocea} (Li et al. 2019; Mu et al. 2020) that high levels of dietary SO or PO induced inflammatory response. Moreover, our previous studies have showed that \textit{A. schlegelii} fed HFD supplemented with palmitic acid (16:0) could cause inflammation by activated \textit{nf-kb} (Jin et al. 2019a, 2019b, 2020, 2021). Therefore, these findings suggested that fish fed HFD supplemented with PO or SO (rich in SFA and MUFA or n-6 PUFA) had more ability to cause inflammation than dietary FO or LO (rich in n-3 PUFA) supplementation (rich in n-3 PUFA).

JNK plays a pivotal role in apoptotic pathways that activate apoptotic signaling by the upregulation of pro-apoptotic genes including initiator caspase (caspase 2, 8, 9, and 10) and effector caspases (caspase 3, 6, and 7) (Dhanasekaran and Reddy 2008; Shi 2002). Additionally, Pattingre et al. (2005) reported that Bcl-2 is an anti-apoptotic protein that plays a crucial role in inhibiting apoptosis. In the present study, the high expression levels of \textit{jnk} and the apoptotic cytokines including \textit{bax}, \textit{caspase 7}, and \textit{caspase 9} were observed in HFD supplemented with PO or SO, whereas the expression level of anti-apoptotic marker \textit{bcl-2} markedly downregulated by PO or SO supplementation. Similar results were previously reported for \textit{M. amblycephala} (Lu et al. 2017) and \textit{O. niloticus} (Jia et al. 2020) fed HFD supplemented with high levels of SO and lard oil (rich in SFA and MUFA), respectively. In sum, these results revealed that when compared to SO or LO supplementation (rich in n-3 PUFA), fish fed HFD supplemented with PO or SO (rich in SFA, MUFA, or n-6 PUFA) had more ability to induce apoptosis by elevating the gene expression level of \textit{jnk}.

**Conclusion**

Overall, the current study revealed that fish fed HFD with PO or SO (rich in SFA, MUFA, or n-6 PUFA) supplementation had more ability to cause lipid accumulation, liver injury, lipid metabolic disorders, ERS, inflammatory response, and apoptosis, whereas these adverse effects were mild in HFD supplemented with FO or LO (rich in n-3 HUFA). Specifically, when compared to dietary PO or SO supplementation, HFD supplemented with FO or LO showed slight lipid deposition by upregulating the gene expression levels of \textit{ppara} and \textit{sirt1}, and promoted antioxidant ability through increased the levels of SOD activity and its gene expression levels. Furthermore, compared to the FO and LO treatments, HFD supplemented with PO or SO increased gene expression related to ERS, triggering inflammatory response and apoptosis through upregulating the key gene expression levels of \textit{nf-kb} and \textit{jnk}, respectively. These findings clearly elucidate that lipotoxic injury including lipid metabolic disorders and physiological stress responses caused by a HFD have significant lipid source-dependent effects, which probably due to different fatty acid compositions, and provide guiding significance for the use of HFD in marine fish that lipid sources which are rich in SFA, MUFA, or n-6 PUFA should be used with caution in HFD.

**Author contribution** Qicun Zhou and Min Jin: conceptualization, methodology, validation and supervision; Yuedong Shen, Xuejiao Li, Yangguang Bao, and Tingting Zhu: formal analysis, software, validation; Zhaoxun Wu, Bingqian Yang, and Lefei Jiao: resources; Yuedong Shen: writing—original draft; Qicun Zhou and Min Jin: writing—reviewing and editing. All authors read and approved the final manuscript.

**Funding** This research was supported by the National Natural Science Foundation of China (31802303), National Key R & D Program of China (2018YFD0900040), Scientific Research Foundation of Ningbo University (XYL20007), Fundamental Research Funds for the Provincial Universities of Zhejiang (SILY2021007), the Open Fund of Zhejiang Provincial Top Key Discipline of Aquaculture in Ningbo University, and K. C. Wong Magna Fund in Ningbo University.

**Data availability** All data generated or analyzed during this study are included in this published article.

**Declarations**

**Ethical approval** Animal experimentation within the present study was conducted in accordance with the Animal Research Institute Committee guidelines of Ningbo University, China, and approved by the Committee of Animal Research Institute, Ningbo University, China.

**Consent to participate** Not applicable.
Consent for publication  All authors review and approve the manuscript for publication.

Conflict of interest  The authors declare no competing interests.

References

Anvith P, Sankar R (2015) The comprehensive review on fat soluble vitamins. IOSR J Pharm 5(11):12–28
AOAC (Association of Official Analytical Chemists) (2006) Official Methods of Analysis. 18th Edition, Washington DC, 1018
Benítez-Dorta V, Caballero MJ, Izquierdo M, Manchado M, Infante C, Zamorano MJ, Montero D (2013) Total substitution of fish oil by vegetable oils in Senegalese sole (Solea senegalensis) diets: effects on fish performance, biochemical composition, and expression of some glucocorticoid receptor-related genes. Fish Physiol Biochem 39:335–349
Bergh G (1991) The Role of the Liver in Metabolic Homeostasis: Implications for Inborn Errors of Metabolism. In: Harkness RA, Pollitt RJ, Addison GM (eds) J Inherited Metab Dis Springer, Dordrecht 407–420
Boone L, Meyer D, Cusick P, Ennulat D, Bolliger AP, Everds N, Meador V, Elliott G, Honor D, Bounous D, Jordan H (2005) Selection and interpretation of clinical pathology indicators of hepatic injury in preclinical studies. Vet Clin Pathol 34:182–188
Boujad T (2004) Regulation of feed intake, growth, nutrient and energy utilisation in European sea bass (Dicentrarchus labrax) fed high fat diets. Aquaculture 231:529–545
Cantó C, Auwerx J (2009) PGC-1alpha, SIRT1 and AMPK, an energy sensing network that controls energy expenditure. Curr Opin Lipidol 20(2):98
Cao XF, Dai YJ, Liu MY, Yuan XY, Wang CC, Huang YY, Liu WB, Jiang GZ (2019) High-fat diet induces aberrant hepatic lipid secretion in blunt snout bream by activating endoplasmic reticulum stress-associated IRE1α/XBP1 pathway. Biochim. Biophys. Acta. Mol Cell Biol Lipids 1864:213–223
Cao XF, Liu WB, Zheng XC, Yuan XY, Wang CC, Jiang GZ (2019) Effects of high-fat diets on growth performance, endoplasmic reticulum stress and mitochondrial damage in blunt snout bream Megalobrama amblycephala. Aquacult Nutr 25:97–109
Chen D, Bruno J, Easton E, Lin SJ, Cheng HL, Alt FW, Guarente L (2008) Tissue-specific regulation of SIRT1 by calorie restriction. Genes Dev 22(13):1753–1757
Davis RJ (2000) Signal transduction by the JNK group of MAP kinases. Cell 103:239–252
Dhanasekaran DN, Reddy EP (2008) JNK signaling in apoptosis. Oncogene 27(48):6245–6251
Din JN, Newby DE, Flapan AD (2004) Omega 3 fatty acids and cardiovascular disease e fishing for a natural treatment. Br Med J 328(7430):30e35
Du ZY, Clouet P, Huang LM, Degrace P, Zheng WH, He JG, Tian LX, Liu YJ (2008) Utilization of different dietary lipid sources at high level in herbivorous grass carp (Ctenopharyngodon idella): mechanism related to hepatic fatty acid oxidation: dietary lipid sources and levels in grass carp. Aquacult Nutr 14:77–92
Fang W, Chen Q, Li J, Liu Y, Zhao Z, Shen Y, Mai K, Ai Q (2021) Endoplasmic reticulum stress disturbs lipid homeostasis and augments inflammation in the intestine and isolated intestinal cells of large yellow croaker (Larimichthys crocea). Front Immunol 12:738143
Francis GA, Fayard E, Picard F, Auwerx J (2003) Nuclear receptors and the control of metabolism. Annu Rev Physiol 65(1):261–311
Fu S, Yang L, Li P, Hofmann O, Dicker L, Hide W, Lin X, Watkins SM, Ivanov AR, Hotamisligil GS (2011) Aberrant lipid metabolism disrupts calcium homeostasis causing liver endoplasmic reticulum stress in obesity. Nature 473:528–531
González-Félix ML, Maldonado-Othón CA, Perez-Velazquez M (2016) Effect of dietary lipid level and replacement of fish oil by soybean oil in compound feeds for the shortfin corvina (Cynoscion parvipinmis). Aquaculture 454:21–228
Gou N, Ji H, Zhong M, Chang Z, Deng W (2021) Effects of dietary fish oil replacements with three vegetable oils on growth, fatty acid composition, antioxidant capacity, serum parameters and expression of lipid metabolism related genes in juvenile Onychostoma macrolepis. Aquacult Nutr 27:163–175
Guo J, Zhou Y, Zhao H, Chen WY, Chen YJ, Lin SM (2019) Effect of dietary lipid level on growth, lipid metabolism and oxidative status of largemouth bass, Micropterus salmoides. Aquaculture 506:394–400
Hu P, Han Z, Couvillon AD, Kaufman RJ, Exton JH (2006) Autocrine tumor necrosis factor α links endoplasmic reticulum stress to the membrane death receptor pathway through IRE1α-mediated NF-κB activation and down-regulation of TRAF2 expression. Mol Cell Biol 26:3071–3084
Huang Y, Wen X, Li S, Li W, Zhu D (2016) Effects of dietary fish oil replacement with palm oil on the growth, feed utilization, biochemical composition, and antioxidative status of juvenile Chu’s croaker,Nibea Coibor. J World Aquacult Soc 47:786–797
Ji R, Xiang X, Li X, Mai K, Ai Q (2021) Effects of dietary curcumin on growth, antioxidant capacity, fatty acid composition and expression of lipid metabolism-related genes of large yellow croaker fed a high-fat diet. Br J Nutr 126:345–354
Jia R, Cao LP, Du JL, He Q, Gu ZY, Jeney G, Xu P, Yin GJ (2020) Effects of high-fat diet on antioxidative status, apoptosis and inflammation in liver of tilapia (Oreochromis niloticus) via Nrf2, TLRs and JNK pathways. Fish Shellfish Immunol 104:391–401
Jiao B, Huang X, Chan CB, Zhang L, Wang D, Cheng CH (2006) The co-existence of two growth hormone receptors in teleost fish and their differential signal transduction, tissue distribution and hormonal regulation of expression in seabeam. J Mol Endocrinol 36(1):23–40
Jin M, Yuan Y, Lu Y, Ma H, Sun P, Li Y, Qiu H, Ding L, Zhou Q (2017) Regulation of growth, tissue fatty acid composition, biochemical parameters and lipid related genes expression by different dietary lipid sources in juvenile...
black seabream, Acanthopagrus schlegelii. Aquaculture 479:25–37

Jin M, Pan T, Cheng X, Zhu TT, Sun P, Zhou F, Ding X, Zhou Q (2019) Effects of supplemental dietary l-carnitine and bile acids on growth performance, antioxidant and immune ability, histopathological changes and inflammatory response in juvenile black seabream (Acanthopagrus schlegelii) fed high-fat diet. Aquaculture 504:199–209

Jin M, Pan T, Tocher DR, Betancor MB, Monroig Ō, Shen Y, Zhu T, Sun P, Jiao L, Zhou Q (2019) Dietary choline supplementation attenuated high-fat diet-induced inflammation through regulation of lipid metabolism and suppression of NFκB activation in juvenile black seabream (Acanthopagrus schlegelii). J Nutr Sci 8:e38

Jin M, Zhu T, Tocher DR, Luo J, Shen Y, Li X, Pan T, Yuan Y, Betancor MB, Jiao L, Sun P, Zhou Q (2020) Dietary fenofibrate attenuated high-fat diet-induced lipid accumulation and inflammation response partly through regulation of pparα and sirt1 in juvenile black seabream (Acanthopagrus schlegelii). Dev Comp Immunol 109:103691

Jin M, Shen Y, Pan T, Zhu T, Li X, Xu F, Betancor MB, Jiao L, Tocher DR, Zhou Q (2021) Dietary betaine mitigates hepatic steatosis and inflammation induced by a high-fat diet by modulating the Sirt1/Srebpl/Pparα pathway in juvenile black seabream (Acanthopagrus schlegelii). Front Immunol 12:694720

Kikuchi K, Furuta T, Iwata N, Onuki K, Noguchi T (2009) Effect of dietary lipid levels on the growth, feed utilization, body composition and blood characteristics of tiger puffer Takifugu rubripes. Aquaculture 298:111–117

Larbi Ayisi C, Zhao J, Wu JW (2018) Replacement of fish oil with palm oil: effects on growth performance, innate immune response, antioxidant capacity and disease resistance in Nile tilapia (Oreochromis niloticus). PLoS ONE 13(4):e0196100

Levin SG, Godukhin OV (2011) Anti-inflammatory cytokines, TGF-β1 and IL-10, exert anti-hypoxic action and abolish posthypoxic hyperexcitability in hippocampal slice neurons: Comparative aspects. Exp Neurol 232(2):329–332

Li Y, Liang X, Zhang Y, Gao J (2016) Effects of different dietary soybean oil levels on growth, lipid deposition, tissues fatty acid composition and hepatic lipid metabolism related gene expressions in blunt snout bream (Megalobrama ambycephala) juvenile. Aquaculture 451:16–23

Li Y, Jia Z, Liang X, Matulic D, Hussein M, Gao J (2018) Growth performance, fatty-acid composition, lipid deposition and hepatic-lipid-metabolism-related gene expression in juvenile pond loach Misgurnus anguillicaudatus fed diets with different dietary soybean oil levels: effect of soybean oil on m. anguillicaudatus. J Fish Biol 92:17–33

Li X, Ji R, Cui K, Qiuchi C, Qiang C, Fang W, Mai K, Zhang Y, Xu W, Ai Q (2019) High percentage of dietary palm oil suppressed growth and antioxidant capacity and induced the inflammation by activation of TLR-NF-κB signaling pathway in large yellow croaker (Larimichthys crocea). Fish Shellfish Immunol 87:600–608

Li X, Shen Y, Bao Y, Wu Z, Yang B, Jiao L, Zhang C, Tocher DR, Zhou Q, Jin M (2022) Physiological responses and adaptive strategies to acute low-salinity environmental stress of the euryhaline marine fish black seabream (Acanthopagrus schlegelii). Aquaculture 554:738117

Lin YH, Shiau SY (2007) Effects of dietary blend of fish oil with corn oil on growth and non-specific immune responses of grouper, Epinephelus malabaricus. Aquac Nutr 13:137–144

Liu T, Zhang L, Joo D, Sun SC (2017) NF-κB signaling in inflammation. Sig Transduct Target Ther 2:17023

Lomb DJ, Laurent G (1804) Haigis MC (2010) Sirtuins regulate key aspects of lipid metabolism. Biochim Biophys Acta, Proteins Proteomics 8:1652–1657

Lu KL, Xu WN, Liu WB, Wang LN, Zhang CN, Li XF (2014) Association of mitochondrial dysfunction with oxidative stress and immune suppression in blunt snout bream Megalobrama ambycephala fed a high-fat diet. J Aquat Anim Health 26:100–112

Lu KL, Wang LN, Zhang DD, Liu WB, Xu WN (2017) Berberine attenuates oxidative stress and hepatocytes apoptosis via protecting mitochondria in blunt snout bream Megalobrama ambycephala fed high-fat diets. Fish Physiol Biochem 43:65–76

Metón I, Mediavilla D, Caseras A, Cantó E, Fernández F, Baanante IV (1999) Effect of diet composition and ration size on key enzyme activities of glycolysis-glucoseconogenesis, the pentose phosphate pathway and amino acid metabolism in liver of gilthead sea bream (Sparus aurata). Br J Nutr 82:223–232

Milián-Sorribes MC, Martínez-Llorens S, Cruz-Castellon C, Jover-Cerdá M, Tomás-Vidal A (2021) Effect of fish oil replacement and probiotic addition on growth, body composition and histological parameters of yellowtail (Seriola dumerili). Aquacult Nutr 27:3–16

Miranda-Díaz AG, García-Sánchez A, Cardona-Muñoz EG (2020) Foods with potential prooxidant and antioxidant effects involved in Parkinson’s disease. Oxid Med Cell Longevity 2020:1–17

Mourente G, Good JE, Thompson KD, Bell JG (2007) Effects of partial substitution of dietary fish oil with blends of vegetable oils, on blood leucocyte fatty acid compositions, immune function and histology in European sea bass (Dicentrarchus labrax L.). Br J Nutr 98:770–779

Mu H, Shen H, Liu J, Xie F, Zhang W, Mai K (2018) High level of dietary soybean oil depresses the growth and anti-oxidative capacity and induces inflammatory response in large yellow croaker Larimichthys crocea. Fish Shellfish Immunol 77:465–473

Mu H, Wei C, Zhang Y, Zhou H, Pan Y, Chen J, Zhang W, Mai K (2020) Impacts of replacement of dietary fish oil by vegetable oils on growth performance, anti-oxidative capacity, and inflammatory response in large yellow croaker Larimichthys crocea. Fish Physiol Biochem 46:231–245

Nasopoulou C, Zabetakis I (2012) Benefits of fish oil replacement by plant originated oils in compounded fish feeds. A Review LWT 47(2):217–224

National Research Council (NRC) (2011) Nutrient requirements of fish and shrimp. National Academies Press, Washington, DC, pp 102–125

Naylor RL, Hardy RW, Buschmann AH, Bush SR, Cao L, Klinger DH, Little DC, Lubchenco J, Shumway SE, Troell M (2021) A 20-year retrospective review of global aquaculture. Nature 591:551–563
Turchini GM, Hermon KM, Francis DS (2018) Fatty acids and beyond: fillet nutritional characterisation of rainbow trout (Oncorhynchus mykiss) fed different dietary oil sources. Aquaculture 491:391–397

Wang X, Li Y, Hou C, Gao Y, Wang Y (2015) Physiological and molecular changes in large yellow croaker (Pseudosciaena crocea R.) with high-fat diet-induced fatty liver disease. Aquac Res 46:272–282

Wang Y, Branicky R, Noë A, Hekimi S (2018) SIRT1 regulates hepatosteatosis and fatty liver disease via controlling hepatic lipids metabolism and metabolic dysfunction in skeletal muscle in mice. PLoS ONE 10(2):e0117494

Wang X, Li Y, Hou C, Gao Y, Wang Y (2015) Physiological and molecular changes in large yellow croaker (Pseudosciaena crocea R.) with high-fat diet-induced fatty liver disease. Aquac Res 46:272–282

Wang Y, Branicky R, Noë A, Hekimi S (2018) SIRT1 regulates hepatosteatosis and fatty liver disease via controlling hepatic lipids metabolism and metabolic dysfunction in skeletal muscle in mice. PLoS ONE 10(2):e0117494

Yilmaz E (2017) Endoplasmic reticulum stress and obesity. Obes Lipotoxicity 261–276

Yoshida H (2007) ER stress and diseases: ER stress and diseases. FEBS J 274:630–658

Yuan F, Wang H, Tian Y, Li Q, He L, Li N, Liu Z (2016) Fish oil alleviated high-fat diet–induced non-alcoholic fatty liver disease via regulating hepatic lipids metabolism and metaflammation: a transcriptomic study. Lipids Health Dis 15:20

Yuan F, Wang H, Jin M, Sun P, Zhou Q (2019) Influence of different lipid sources on growth performance, oxidation resistance and fatty acid profiles of juvenile swimming crab, Portunus trituberculatus. Aquaculture 508:147–158

Zhang K, Kaufman RJ (2008) From endoplasmic-reticulum stress to the inflammatory response. Nature 454:455–462

Zhou F, Xiao JX, Hua Y, Ngandzali BO, Shao QJ (2011) Dietary l-methionine requirement of black sea bream (Acanthopagrus schlegeli). Aquaculture 513:734397

Xie S, Lin Y, Wu T, Tian L, Liang J, Tan B (2021) Dietary lipid levels affected growth performance, lipid accumulation, inflammatory response and apoptosis of Japanese seabass (Lateolabrax japonicus). Aquacult Nutr 27:807–816

Yao X, Liu R, Li X, Li Y, Zhang Z, Huang S, Ge Y, Chen X, Yang X (2021) Zinc, selenium and chromium co-supplementation improves insulin resistance by preventing hepatic endoplasmic reticulum stress in diet-induced gestational diabetes rats. J Nutr Biochem 96:108810

Yildiz M, Oforí-Mensah S, Arslan M, Ekici A, Yamaner G, Baltaci MA, Tacer S, Korkmaz F (2020) Effects of different dietary oils on egg quality and reproductive performance in rainbow trout Oncorhynchus mykiss. Anim Reprod Sci 221:106545

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