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Short communication

Resveratrol attenuates oxidative stress and inflammatory response in turbot fed with soybean meal based diet

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ABSTRACT

Adding immunopotentiators to plant protein based diets has been a feasible way to improve fish growth performance and healthy status. In this study, an 8-week trial was carried out to explore the effects of resveratrol, a natural polyphenolic compound, on growth performance, anti-oxidative capacity and immune responses in turbot fed soybean meal based diet. As the results showed, replacement 45% fish meal with soybean meal (SBM) significantly depressed the fish growth, feed utilization and the heights of villi and microvilli in distal intestine. The mRNA levels of hepatic antioxidant enzymes, including *superoxide dismutase* (*sod*), *glutathione peroxidase* (*gsh-px*) and *peroxiredoxin 6* (*prx 6*), were highly inhibited in SBM group. The inflammation related genes in intestine were also responsive to soybean meal. Supplying resveratrol showed no effects on fish growth performance but significantly restored the intestinal morphology and improved the mRNA levels of hepatic antioxidant enzymes as well as the activity of SOD. Meanwhile, resveratrol significantly improved the mRNA levels of anti-inflammatory cytokine *transforming growth factor-β* and inhibited the expression of pro-inflammatory cytokines *tumor necrosis factor-α* (*tnf-α*), *interleukin-1β* (*il-1β*) and *interleukin-8* (*il-8*). The results indicate that resveratrol could attenuate the oxidative stress and inflammatory response induced by soybean meal in turbot. This study shows resveratrol is an effective immunopotentiator to carnivorous fishes fed plant protein sources.

1. Introduction

Due to the well balanced amino acid profile and highly palatability, fish meal (FM) is the major protein source in the diet for carnivorous species. However, limited supply of FM has been inadequate to the demands of aquaculture [1]. In the past decades, numerous studies were carried out to replace fish meal with other protein sources [2–4]. Among the alternative ingredients, soybean meal (SBM) showed a promising performance because of its high content of protein, reasonable amino acid profile and stable supply [4–6]. However, the replacement level of SBM should be limited to be lower than 30% for carnivorous species [6–9]. Oversubstitution always led to inferior growth performance and poor disease resistance. Negative effects of oxidant-stressed status and inflammatory response induced by SBM were widely observed in turbot [10], Atlantic salmon [11] and rainbow trout [12].

Previous studies showed high levels of SBM disturbed the oxidative homoeostasis of fish [13]. The imbalance between reactive oxygen species (ROS) generation and elimination would induce oxidative stress. Exceeded ROS production might damage proteins, lipids and DNA in organisms [14,15]. The antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT) and glutathione-related enzymes, play critical roles in eliminating the free radicals [16].

The immunity of fish gut was also highly affected by the diet [17]. The hind gut was sensitive to protein sources and achieved strong immune responses when fed high levels of SBM [18]. Soybean meal induced enteritis (SBMIE) has been widely referred in Atlantic salmon, grass carp and turbot [10,17–19]. It has been indicated as a lymphocyte-mediated and lymphokine-driven inflammation [20]. An induction of inflammatory-related cytokines, such as nuclear factor-κB (NF-κB) and tumor necrosis factor-α (TNF-α), were observed in the progress of SBMIE [21,22].

In order to improve the healthy status of aquaculture species and reduce the usage of chemical drugs, adding immunopotentiators to the diets has been a feasible way to improve fish antioxidant capacity, immunity and growth performance [23]. Supplying immunopotentiators could enhance the nonspecific defense mechanisms or the specific immune response of animals [24]. To date, various

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immunopotentiators have been used in aquaculture, including probiotics, chitosan and extract preparations from plants [25–27]. However, the immunopotentiators might reduce the feed palatability and affect the growth performance of fish [25].

Resveratrol (*trans*-3,4,5-Trihydroxystilbene) is a natural polyphenol consisted in numerous plants, such as grapes, peanuts, and other groundnuts [28]. It exhibits a variety of functions, including anti-oxidant, anti-inflammatory, anti-aging and anti-tumorigenic [28,29]. Resveratrol protects the body from oxidative damage through removing ROS directly and activating the antioxidant enzyme system [30]. Meanwhile, a strong anti-inflammatory effect of resveratrol was exhibited [31]. In mammals, resveratrol could inhibit the expression of pro-inflammatory cytokines and promoting the expression of anti-inflammatory cytokines [32,33]. Previous studies have reported that resveratrol could modulate the innate and inflammatory responses in turbot leucocytes [34] and improve lipid and glucose metabolism in blunt snout bream [35]. However, little is known about its effects on the oxidative homoeostasis and immune responses induced by high plant protein sources diets.

In the present study, a feeding trial was conducted to investigate the effects of resveratrol in turbot, which was sensitive to the plant protein diets [36]. The growth performance, antioxidant capacity and intestinal immune responses were determined to assess the application of resveratrol in aquaculture.

2. Materials and methods

2.1. Experimental diets

Three isonitrogenous (52% crude protein) and isoenergetic (20.0 kJ/g diet of gross energy) diets were formulated as described previously [36]. As shown in Table 1, fish meal, soybean meal and wheat gluten meal were used as the main protein sources. Fish oil and soy lecithin were used as the dietary lipid sources. A fish meal based diet (FM diet) was formulated with 60% fish meal. The soybean meal based diet (SBM diet) was formulated with 45% FM replaced by SBM. Resveratrol (98% purity) was obtained from Tongze Biological Technology (Xi'an, China). 500 mg resveratrol was added to pre kg SBM diet (referred as RSV diet), which showed a growth enhancement effect in other animals [35,37]. All the ingredients were mashed to through 178 μm mesh, mixed and blended with oil and water. The diets were produced using a granulating machine and dried in a ventilated oven at 45 °C for 12 h. The diets were stored in −20 °C until further used.

2.2. Feeding trial

All procedures performed in present study were in strict accordance with the recommendations in the Guide for the Use of Experimental Animals of Ocean University of China. Juvenile turbots were obtained from a commercial farm in Qingdao, China. The feeding trial was carried out in Yihaifeng Aquatic Product Co. Ltd (Qingdao, China). Prior to the experiment, fish were acclimatized for 2 weeks with a commercial diet (Great seven Bio-Tech Co. Ltd, Qingdao, China). After fasting for 24 h, fish (initial body weight: 7.50 ± 0.01 g) were randomly assigned to 9 tanks in a recycling seawater system (300 L, 35 fish per tank). Fish were fed to apparent satiety twice a day (08:00 and 18:00) for 8 weeks. During the experimental period, water temperature ranged from 18 to 22 °C, salinity was 29‰–32‰, and dissolved oxygen was above 6 mg/L. Both the concentration of ammonia-nitrogen and nitrite were less than 0.1 mg/L.

2.3. Sample collection

At the end of the trial, fish were fasted for 24 h and group weighed after anesthetized with eugenol (1:10,000). Five fish from each tank were sampled for whole body composition analysis and stored frozen at −20 °C. Tissues samples (liver and distal intestine) for gene expression analysis and enzyme assay were sampled, frozen in liquid nitrogen and stored at −80 °C until further analysis. For histological analysis, the distal intestine was collected and fixed by Bonn's solution and transferred to the 70% alcohol solution after 24 h.

Table 1
Formulation and proximate coposition of the experimental diets (% dry matter)[1].

	Diets (% dry diet)		
	FM	SBM	RSV
Ingredients			
Fish meal[a]	60.00	33.00	33.00
Soybean meal[a]	0.00	35.10	35.10
Wheat meal[a]	20.00	4.40	4.40
Wheat gluten meal[a]	7.50	10.50	10.50
Fish oil	4.50	6.50	6.50
Soy lecithin	2.00	2.00	2.00
Vitamin premix[b]	2.00	2.00	2.00
Mineral premix[c]	1.00	1.00	1.00
Others[d]	3.00	3.00	3.00
Resveratrol[e]	0.00	0.00	0.05
Microcrystalline cellulose	0.00	2.50	2.45
Proximate composition (dry matter basis)			
Crude protein	52.74	52.02	52.31
Crude lipid	11.57	12.02	12.25
Gross energy	19.61	19.89	19.94

[1] FM, Fish meal diet; SBM, replacement 45% fish meal with soybean meal; RSV, supplementing 0.05% resveratrol to the SBM diet.

[a] Supplied by Great seven Bio-Tech (Qingdao, China); Fish meal, crude protein 68.67% dry matter, crude lipid 7.66% dry matter; Soybean meal, crude protein 52.97% dry matter, crude lipid 2.12% dry matter; Wheat meal, crude protein 15.26% dry matter, crude lipid 1.79% dry matter; Wheat gluten meal, crude protein 79.62% dry matter, crude lipid 1.60% dry matter.

[b] Vitamin premix (mg/kg diet): retinyl acetate, 32; cholecalciferol, 5; α-tocopheryl acetate, 240; menadione sodium bisulphite, 10; ascorbic acid, 120; cyanocobalamin, 10; biotin, 60; choline dihydrogen citrate, 7000; folic acid, 20; inositol, 800; niacin, 200; D-calcium pantothenate, 60; pyridoxine HCl, 20; riboflavin, 45; thiamine HCl, 25; microcrystalline cellulose, 16,473.

[c] Mineral premix (mg/kg diet): $MgSO_4{\cdot}7H_2O$, 1200; $CuSO_4{\cdot}5H_2O$, 10; $FeSO_4{\cdot}7H_2O$, 80; $ZnSO_4{\cdot}H_2O$, 50; $MnSO_4{\cdot}H_2O$, 45; $CoCl_2$, 50; Na_2SeO_3, 20; calcium iodine, 60; zeolite powder, 8485.

[d] Others: choline chloride, 0.30; $Ca(H_2PO_4)_2$, 1.00; Calcium propionic acid, 0.05; Ethoxyquinoline, 0.05; Yttrium oxide, 0.10; Sodium alginate, 0.50; Attractants (betaine: DMPT: threonine: glycine: inosine-5-diphosphate trisodium salt = 4:2:2:1:1), 1.00.

[e] Resveratrol: Tongze Biological Technology (Xi'an, China) Co., LTD.

2.4. Chemical analysis

Proximate composition of ingredients, diets and fish samples were performed by AOAC method. Moisture content was analyzed by drying the samples to constant weight at 105 °C for 24 h. Crude protein content was analyzed according to the Kjeldahl method (KjeltecTM8400, FOSS, Sweden). Crude lipid content was measured by diethyl ether extraction using Soxhlet method (Buchi 36680, Switzerland). Ash was examined after combustion in a muffle furnace at 550 °C for 16 h.

2.5. Intestinal histology

After fixation, the distal intestines were dehydrated in a series of alcohol solutions, equilibrated in xylene and embedded in paraffin. The tissues were sliced into 5-μm sections and stained with haematoxylin and eosin (H&E). Histological observation was performed with an imaging microscope (Olympus). All micrographs were analyzed using Image Pro Plus 6.0 software. The heights of villi and microvilli were determined which indicated the absorptive capacity and healthy status of intestine. The ratio (R) between the villi height (VH) or microvilli

height (MVH) and the lumen diameter (LD) of the distal intestines (R_1 = VH/LD, R_2 = MVH/LD) were determined as described previously [38]. At least six images from each group were analyzed.

2.6. Enzyme assay

The activities of superoxide dismutase (SOD), catalase (CAT) and the content of malondialdehyde (MDA) were measured using commercial kits by enzymatic colorimetric methods (Jiancheng, Nanjing, China). Briefly, the tissues were homogenized in phosphate buffer (50 mM, pH6.8). The homogenates were centrifuged at 2500 g for 10 min at 4 °C and the supernatant was used for enzyme assays. Protein concentration was measured by a Bradford protein assay kit (Jiancheng, Nanjing, China). The results of enzymes activities and MDA content were expressed as U per mg protein and nmol per mg protein.

2.7. Quantitative real-time PCR analysis

Total RNA from liver and intestine were extracted using Trizol reagent following the manufacturer's instructions (Invitrogen, USA). The quality and quantity of RNA were tested by 1.2% agarose gel and NanoDrop 2000 spectrophotometer (Thermo, USA). cDNA was synthesized using the PrimeScript™ RT reagent Kit (Takara, Japan). The mRNA expression of *sod*, *glutathione peroxidase* (*gsh-px*), *peroxiredoxin* 6 (*prx6*) in liver and *transforming growth factor-β* (*tgf-β*), *tumor necrosis factor-α* (*tnf-α*), *interleukin-1β* (*il-1β*), *interleukin-8* (*il-8*) expression levels in intestine were determined by qRT-PCR. RNA *polymerase II subunit D* (*rpsd*) was selected as the reference gene for sample normalization due to its stably expression among treatments. The sequences of primers used in this study were showed in Table 2.

The qRT-PCR assay was carried out with a thermal cycler Mastercycler ep realplex (Eppendorf, Germany). The reaction system was performed as described previously [39]. The melting curve was performed to confirm the specificity of reaction production. The expression levels of target genes were calculated using the $2^{-(\Delta\Delta Ct)}$ method.

2.8. Calculations and statistical methods

Growth parameters and body condition indexes were calculated as follows:

Survival rate (SR, %) = 100 × final fish number / initial fish number

Weight gain rate (WGR, %) = (final body weight - initial body weight) / initial body weight × 100

Specific growth rate (SGR, %/d) = (Ln final body weight - Ln initial body weight) × 100 / days

Feed efficiency (FE) = wet weight gain (g) / dry feed intake (g)

Table 2
Primer sequences used for quantitative real-time PCR.[a].

Genes	Forward primer (5′-3′)	Reverse primer (5′-3′)
sod	AAACAATCTGCCAAACCTCTG	CAGGAGAACAGTAAAGCATGG
gsh-px	CCCTGATGACTGACCCAAAG	GCACAAGGCTGAGGAGTTTC
prx6	TCAGAGAGCGAGGGAATGAC	CCGATGAGATAGACAAGGATGG
tgf-β	ACAAGCCGACGGGCTACCATG	CAGCAGGGCTGGGCAGAGG
tnf-α	GGGTGGATGTGGAAGGTGAT	GGCCTCTGTTTGGCTTGACT
il-1β	GAGAGCATCGTGGAAGAACA	GTTTCGGACCAGAACGAAGT
il-8	GGCAGACCCCTTGAAGAATA	TGGTGAACCCTTCCCATTAT
rpsd	CTGCTGTTCCCTAAAGAGTTCG	GAGCCGTGTAGTTCAGGGTCT

[a] *sod, superoxide dismutase; gsh-px, glutathione peroxidase; prx6, peroxiredoxin 6; tgf-β, transforming growth factor-β; tnf-α, tumor necrosis factor-α; il-1β, interleukin-1β; il-8, interleukin-8; rpsd, rna polymerase ii subunit d.*

Table 3
Effects of resveratrol supplementation on growth performance and feed utilization in turbot.[a].

	FM	SBM	RSV
IBW[b] (g)	7.50 ± 0.01	7.50 ± 0.01	7.50 ± 0.01
FBW[c] (g)	39.31 ± 0.44[b]	33.12 ± 0.16[a]	32.42 ± 0.74[a]
SR[d] (%)	98.89 ± 1.11	100.00 ± 0.00	100.00 ± 0.00
WGR[e] (%)	424.11 ± 5.92[b]	341.54 ± 2.07[a]	332.68 ± 9.56[a]
SGR[f] (%/d)	2.96 ± 0.02[b]	2.65 ± 0.08[a]	2.61 ± 0.04[a]
FE[g]	1.44 ± 0.01[b]	1.28 ± 0.03[a]	1.22 ± 0.04[a]
PER[h]	2.88 ± 0.02[b]	2.56 ± 0.05[a]	2.44 ± 0.08[a]

[a] Values expressed as mean ± standard error, n = 3; values in the same row with different superscripts mean significant difference ($p < 0.05$).
[b] IBW: initial body weight.
[c] FBW: final body weight.
[d] SR: survival rate = 100 × final fish number/initial fish number.
[e] WGR: weight gain rate = (final body weight - initial body weight)/initial body weight × 100%.
[f] SGR: specific growth rate = (Ln final body weight - Ln initial body weight) × 100/days.
[g] FE: feed efficiency = wet weight gain (g)/dry feed intake (g).
[h] PER: protein efficiency ratio = wet weight gain (g)/protein ingested (g).

Protein efficiency ratio (PER) = wet weight gain (g) / protein ingested (g)

All data were subjected to a one-way analysis of variance (ANOVA) by the software SPSS 17.0. Differences between the values were tested by Tukey's multiple range tests and $P < 0.05$ was considered to be statistically significant. Data were expressed as means ± standard error.

3. Results

3.1. Growth performance, feed utilization and body composition

As shown in Table 3, after the 8-week feeding trial, the final body weight (FBW), weight gain rate (WGR), specific growth rate (SGR), feed efficiency (FE) and protein efficiency ratio (PER) in SBM group were significantly lower than those in the FM group ($P < 0.05$). Supplying resveratrol to the diet showed no effects on the growth performance and feed utilization in turbot.

For the body composition, both the SBM group and RSV group showed a lower content of crude protein and crude lipid than those in FM group ($P < 0.05$). However, the moisture in SBM group and RSV group were higher than that in FM group ($P < 0.05$) (Table 4).

3.2. Intestinal morphology

As shown in Fig. 1, the heights of villi and microvilli in SBM group were significantly lower than those in the FM group. Supplying resveratrol could partly rescue the adverse performance induced by SBM. The height of villi in RSV group showed no significant difference compared with the FM group ($P > 0.05$). Adding resveratrol to the plant-based diet significantly improve the height of microvilli

Table 4
Effects of resveratrol supplementation on the whole-body composition in turbot.[a].

	FM	SBM	RSV
Moisture	77.32 ± 0.16[a]	78.10 ± 0.17[b]	78.11 ± 0.10[b]
Crude protein	15.65 ± 0.09[b]	14.98 ± 0.12[a]	14.84 ± 0.13[a]
Crude lipid	4.07 ± 0.06[b]	3.27 ± 0.11[a]	3.58 ± 0.03[a]

[a] Values expressed as mean ± standard error, n = 6; values in the same row with different superscripts mean significant difference ($p < 0.05$).

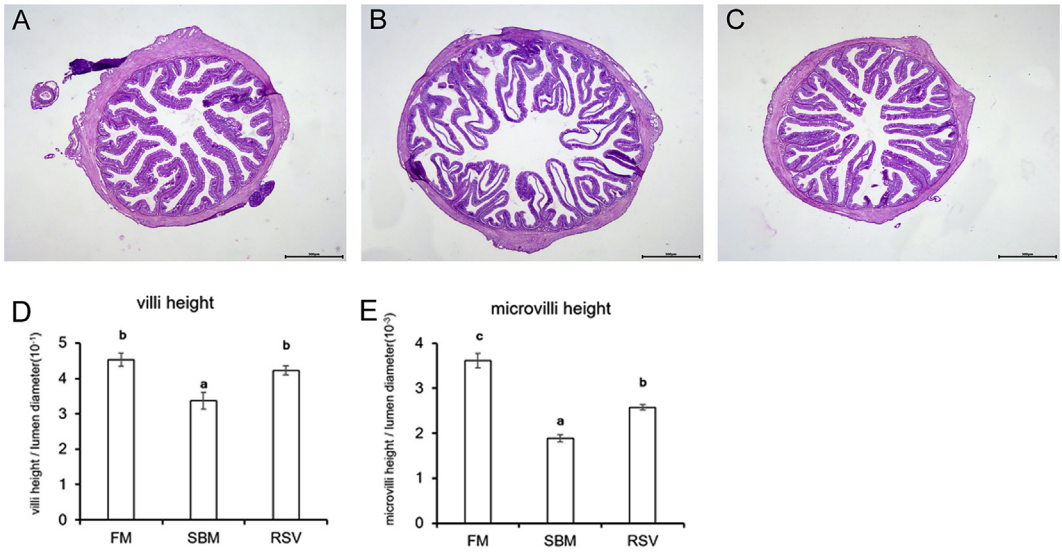

Fig. 1. Effects of resveratrol supplementation on distal intestinal histology indexes of turbot. Intestine sections were stained by haematoxylin and eosin. A-C were sections from fish fed diet FM, CON and RSV, respectively. Scale bars are presented as 500 μm. D-E showed the heights of villi and microvilli. Values expressed as mean ± standard error, n = 6; values in the same row with different superscripts mean significant difference ($P < 0.05$).

($P < 0.05$) although it was still lower than that in FM group.

3.3. Hepatic antioxidant responses

As the results shown in Fig. 2, FM group showed a significantly higher gene expression of *sod* (~6.1 fold), *gsh-px* (~5.7 fold) and *prx6* (~3.7 fold) when compared with SBM group. Dietary resveratrol improved the expression levels of *sod* (~5.0 fold), *gsh-px* (~3.4 fold) and *prx6* (~5.4 fold) compared with SBM group ($P < 0.05$). Moreover, the expression of *sod* and *prx6* expression in FM group and RSV group showed no significant difference ($P > 0.05$) while *gsh-px* expression in RSV group was still lower than that in FM group (Fig. 2A). A significant lower activity of SOD was observed in the SBM group compared with both the FM group and RSV group ($P < 0.05$). The content of MDA in FM group and RSV group were also significant lower than that in SBM group, accounting for about 0.52 and 0.55 fold respectively. No difference of CAT activities was observed among all the treatments (Fig. 2B).

3.4. Immune responses

In order to explore the effects of RSV on immune responses in turbot, the expression of *tgf-β*,*tnf-a*,*il-1β* and *il-8* were determined. As shown in Fig. 3, replacement FM with SBM significantly reduced the expression of anti-inflammatory cytokine *tgf-β* (decreased to ~54%) and increased the expression of pro-inflammatory cytokines like *tnf-a* (~2.0 fold), *il-1β* (~1.3 fold) and *il-8* (~1.8 fold) levels ($P < 0.05$). Supplying resveratrol to the SBM diet significantly reduced the levels of

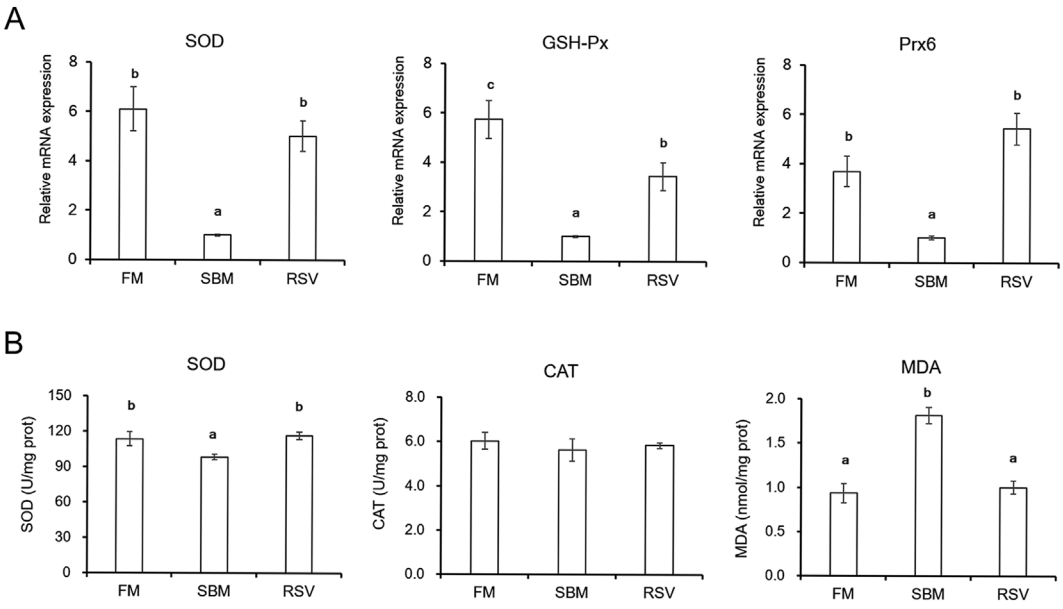

Fig. 2. Hepatic antioxidant responses. The relative mRNA expression levels of *sod, gsh-px, prx6* were measured by quantitative real-time PCR (qRT-PCR) and normalized by *rpsd* (A). The value of SBM group was normalized to 1.0 and the rest groups were expressed as relative expression values to the SBM group. Enzyme activities of SOD, CAT and content of MDA were showed in B. All the data are expressed as means ± S.E.M. (n = 6). Different letters above the bars denote significant differences between groups at the $P < 0.05$ level.

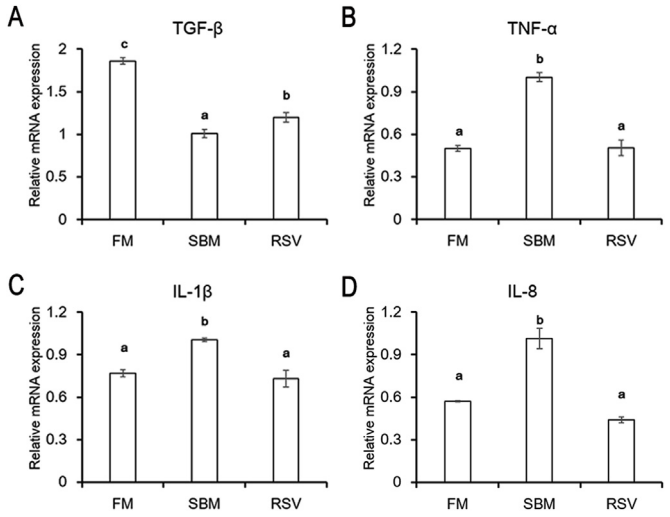

Fig. 3. Relative mRNA levels of inflammation related genes in intestine. The relative mRNA expression levels of *tgf-β*,*tnf-α*,*il-1β* and *il*-8 mRNA levels were measured by quantitative real-time PCR (qRT-PCR) and normalized by *rpsd*. The value of SBM group was normalized to 1.0 and the rest groups were expressed as relative expression values to the SBM group. The data are expressed as means ± S.E.M. (n = 6). Different letters above the bars denote significant differences between groups at the $P < 0.05$ level.

tnf-α,*il-1β* and *il-8* to the comparable expressions in FM group. A moderate enhancement of *tgf-β* expression (~1.2 fold) was also observed induced by resveratrol while it was also lower than that in FM group.

4. Discussion

Resveratrol exhibits wide biological activities in mammals, including anti-oxidant, anti-inflammatory, anti-aging and anti-tumorigenic effects [28,30]. In the present study, the effects of resveratrol were examined in turbot fed with SBM based diet. Consistent with the previous studies, replacement of 45% FM with SBM resulted in serious growth retardation and feed utilization reduction of turbot [6,36]. Supplying resveratrol to the diet (600 mg per kg diet) stimulated the growth of southern flounder [37]. The growth enhancement was attributed to the depression of protein oxidative damage and ubiquitinylation [37]. However, no significant difference was observed in the present study which might be due to the duration of the feeding trial. The stimulation in southern flounder was intensified during 9–16 weeks while the feeding trial in this study lasted 8 weeks. Besides, a growth depression effect was observed in blunt snout bream by dietary 1.08% resveratrol [35]. The growth inhibition of excess resveratrol might be related to the appetites of animals. Resveratrol depressed the expression of neuropeptide Y (NPY) and resulted in a decrease in food intake [40]. Meanwhile, resveratrol showed an inhibitory effect on amino acid-stimulated the mechanistic target of rapamycin (mTOR) signaling [41], which is one of the key master regulators in cell growth and proliferation [42]. Previous studies in turbot reported that mTOR played critical roles in fish growth and nutrient sensing [43]. The effects of resveratrol on growth in fish might also be related to the mTOR signaling pathway. The exact mechanisms need to be further studied.

Reactive oxygen species (ROS) homeostasis was critical for preventing oxidative injury. The effect of plant protein sources on fish antioxidant status was complicated. On one hand, some antioxidants in plants, such as flavonoids, phenolic compounds, might be involved in ROS homeostasis and improved the antioxidantive capacity [44,45]. On the other hand, some anti-nutritional factors in plant protein sources might decrease the antioxidantive enzyme activities in fish [46]. A severe depression of *sod*, *gsh-px*, *prx6* mRNA levels as well as the SOD activity was observed in SBM group. It is assumed that these antioxidant enzymes were consumed during the defense against the oxidation caused by anti-nutritional factors in SBM. Numerous studies reported resveratrol was one of the most potent antioxidants against oxidative stress. Resveratrol could decrease the mitochondrial ROS generation and enhance the activities of GSH-Px and SOD2 through AMPK-PGC-1α-ERRα-Sirt3 signaling pathway [47]. In the present study, resveratrol enhanced the mRNA expression of *sod*, *gsh-px* and *prx6* and the activity of SOD significantly. The attenuation of oxidative damage and enhancement of the antioxidant enzyme activities were also reported in southern flounder [37] and Annual Fish *Nothobranchius guentheri* [48]. The antioxidative effect of resveratrol makes it an important functional supplement for aquafeed.

Fish intestine, the major organ for digestion and absorption, was susceptible to the protein sources [36,49]. Destruction of intestinal villi and acute intestinal inflammation were widely observed in fishes fed with plant meal based diet [18,49]. In the present study, replacement of FM with SBM reduced the heights of villi and microvilli and induced intestinal inflammation, through promoting the expression of the pro-inflammatory cytokines *tnf-α*, *il-1β*, *il-8* and inhibiting the expression anti-inflammatory cytokine *tgf-β*. An improvement was observed in the individuals with the supplement of resveratrol. Similarly, resveratrol showed effects of improving intestinal morphology and decreasing apoptosis of crypt cells in mice [50]. The protective effects on intestine might include the inhibition of TNF-α expression via Sirt1 and wide anti-inflammation properties [51]. In contrast, high dose of resveratrol led to intestine deformation in tilapia *Oreochromis niloticus* [50]. The exact mechanisms of resveratrol involved in intestinal homeostasis are unclear so far.

In summary, we have demonstrated that dietary resveratrol supplementation improved the hepatic antioxidant capacity and ameliorated distal intestinal inflammation in turbot. Resveratrol might be an effective immunopotentiator to improve the utilization of plant protein sources in carnivorous fishes.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgment

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