Effects of dietary quercetin on growth performance, serum lipids level and body composition of tilapia (Oreochromis niloticus)

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Introduction

Quercetin is a safe and one of the major flavonoids, distributed widely in foods and beverages of plant origin, such as onions, apples, tea, cocoa, and red wine (Ross and Kasum, 2002). It has been demonstrated to possess a wide array of biological effects that are considered beneficial to health, including antioxidative, free radical scavenging, anticancer, and antiviral activities (Formica and Regelson, 1995; Ross and Kasum, 2002). Biological action of quercetin is considered to be scavenched with its antioxidant properties which are mainly due to its ability to scavenge free radicals and reactive oxygen species and to form complexes with metal ions, thus preventing oxidation of the metals with oxygen yielding reactive oxygen species (Prince and Sathiya, 2010).

In addition to the antioxidant properties of oral administration of quercetin, there is potential effect on lowering levels of lipid in mammal animals (Basararkers and Nathn 1983; Igarashi and Ohmura 1995; Ricardo et al., 2001; Kamada et al., 2006; de Boer et al., 2006; Krishnaveni et al., 2010; Kobori et al., 2011; Hu et al., 2012; Padma et al., 2012; Zhang et al., 2012) and porcine (Qureshi et al., 2011). However, there also seemed to be no remarkable influence on serum and hepatic lipid concentrations of rats (Rutts norvegicus) (Yugarani et al., 1992; Nakamura et al., 2000). Little information is available about effect of quercetin on blood lipid levels in aquatic animal. It is well known that increasing blood lipid levels is always considered to be signs of declining health condition of the cultured fish (Kikuchi et al., 2009). The high blood lipids levels might cause accumulation of hepatic triglyceride and cholesterol and form the fatty liver disease (Quesada et al., 2009). Fatty liver disease in freshwater fish and marine fish fed on artificial feeds was mainly responsible for the growth retardation, illness, and death (Jia et al., 2006). There is growing need in developing effective feed additives to lower blood lipids level and prevent fatty liver disease in cultivated fish.

Quercetin is not toxic to rainbow trout (Oncorhynchus mykiss) when fed for several months at high levels (Plakas et al., 1985). Recent researches in aquatic animals have been conducted to investigate the effect of quercetin on the reproductive system of female medaka (Oryzias latipes) (Weber et al., 2002), physiological characteristics and oxidative stress resistance in olive flounder (Paralichthys olivaceous) (Shin et al., 2010a, 2010b) and concentrations change of quercetin in tilapia (Oreochromis niloticus) plasma, liver and whole body homogenate (Park et al., 2009). The quercetin is absorbed quickly in tilapia and this flavonoid is deposited mainly in aglycone form in the body after absorption (Park et al., 2009). Consequently, the lipids lowering effects of quercetin might appear in tilapia, which is helpful to fish health. The increase in blood lipids parameters including triglyceride (TG), total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and the decrease of high-density lipoprotein cholesterol (HDL-C) implied that the fish might have had some disorder in lipid metabolism, leading to hyperlipidemia (Kritchevsky, 1995; Ye et al., 2011). The importance of tilapia as a component of global aquaculture has increased over the past several decades (Sarker et al., 2012), it can be a good trial animal to study the responses of dietary quercetin in fish. Therefore, the purpose of this study was conducted to investigate whether dietary quercetin exerts any beneficial effect on blood lipids parameters of tilapia (Oreochromis niloticus); the growth performance and whole body composition were also evaluated.
Materials and methods

Fish and rearing condition

Healthy male tilapia (Oreochromis niloticus), purchased in Chengyi Aquaculture Company of Xiamen (China), were acclimatized in two plastic tanks (200 cm x 90 cm x 100 cm), and during the adaptation period for 4 weeks. After adaptation to experimental condition, fish were kept in twenty circular aquariums (36 cm x 54 cm x 54 cm). Aerated water was supplied to the circular culture system with additional aeration provided by an air pump. The amount of the daily changing water was 50%. Fish were fed to satiation three times daily (at 8:00 h, 13:00 h and 18:00 h). Uneaten pellets were drawn out through a siphon. During the feeding trial, dissolved oxygen, pH, ammonia-N and nitrite-N were monitored twice weekly using multiparameter photometer (HI9804N, HANNA, Baranzate, MI, Italy). The values of these parameters ranged between 6 to 8 mg/L, 6.8 to 7.2, 0 to 2 mg/L and 0.5 to 0.5 mg/L, and the water temperature ranged from 22°C to 28°C.

Experimental design and diets

After adaptation to experimental condition, four hundred fish with the initial average body weight of 11.54±2.83 g were randomly divided into five treatment groups with four replicates in each group and 20 fish in each replicate. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks. Fish were fed the diets with the quercetin levels being 0 (control group), 200, 400, 800, and 1600 mg/kg, respectively; the trial lasted 7 weeks.

The basal diet consisted of 5% fish meal, 15% soybean meal, 20% rapeseed meal, 20% cotton seed meal, 15% high-gluten flour, 20% rice bran, 1% soybean oil, 1%monocalcium phosphate, 0.2% choline chloride, 0.2% vitamin premix and 0.6% mineral premix. Proximate analyses of the basal diet were as following: dry matter 92.2%, crude protein 30.4%, crude lipids 5.7%, ash 12.0% and digestible energy 12.8MJ/kg (calculated value).

The different levels of quercetin (content >98%, purchased from Nanjing Zelang Medical Technology Co., Ltd., Nanjing, China) were supplemented in the basal diet. All feed ingredients were mixed well and pelleted using a laboratory pellet machine without heating using a 2.5-mm diameter module. After processing, the diets were packed into small bags and stored at –20°C until they were given to the fish.

Sample collection and analysis

At the end of the trial, five fish were sampled from random from each replicate and anaesthetized by dipping in 50 mg/L of eugenol oil suspension in water for 30 s, and then the blood sample was collected from the caudal vein of each anaesthetized fish. After kept at 4°C for 30 min, the blood sample was centrifuged at 3500 g for 10 min at 4°C, and the supernatant serum was collected and stored at –20°C prior to analysis of serum lipids parameters. After collecting blood samples, the fish from each replicate were pooled, weighed, minced and then dried at 70°C. The crushed fish body were analyzed in plastic bags and stored at –20°C for subsequent analysis of whole-body composition.

The analyses of proximate composition on feed ingredients, experimental diets and whole fish body were performed using the standard methods of AOAC (1995). Moisture content was determined by the drying method using an oven at 105°C. Crude protein content was determined by the Kjeldahl method after an acid digestion using KjeltecTM 8400 Auto Sample Systems (Foss Tecator AB, H ganäs, Sweden) and crude protein was estimated by multiplying nitrogen content by 6.25. Crude lipid content was extracted by n-hexane using the Soxhlet method (Foss, SoxtecTM 2050, Foss Tecator AB, Denmark). Ash content was determined by the combustion method using a muffle furnace at 550°C for 6 h. The levels of TG, TC, HDL-C and LDL-C in serum were analyzed using an automatic biochemical analyzer (Hitachi 7020, Tokyo, Japan) with commercial clinical investigation kits (Nanjing Jiancheng Biotechnic Institute, China).

Data calculation

At the beginning and at the end of the trial, body weight and length were measured for the fish in each aquarium after 1 day of feed deprivation. The consumption of diet was recorded. The initial average body weight (IBW) and final average body weight (FBW) of fish, specific growth rate (SGR), feed conversion ratio (FCR), condition factor (CF) and survival rate (SR) were calculated as follows:

IBW (g/fish) = initial body weight of fish (g)/ initial number of fish.

FBW (g/fish) = final body weight of fish (g)/ final number of fish.

SGR (%) = 100× [ln final wet weight (g) - ln initial wet weight (g)]/Time (days).

FCR = feed intake (g)/weight gain (g).

CF =100×[body weight (g)/body length (cm)3].

SR (%) = 100× (final number of fish/initial number of fish).

Statistical analysis

Statistical analysis was performed with SPSS 11.5 statistical software (SPSS, Chicago, IL, USA). The results were presented as means ± SD (n=4). Data were subjected to one-way analysis of variance (ANOVA) followed by Duncan’s multiple range test for comparison of the means among different treatment groups; the significant effect was set at P<0.05. Data expressed as percentages or ratios were subjected to arcsine transformation prior to statistical analysis.

Results

The values of growth performance parameters are presented in Table 1. The FBW, SGR and CF in groups of fish fed quercetin were significantly higher than those of the control group (P<0.05), and their FCR were significantly lower than that of the control group (P<0.05). No significant differences in FBW, SGR, CF and FCR were found among the quercetin groups (P>0.05). There were no significant differences of SR among all the treatments (P>0.05).

Serum lipids concentration values are presented in Table 2; the serum TG concentrations of fish decreased with the increasing quercetin level, the TG concentration of quercetin groups were significantly lower than that of the control group (P<0.05). The differences of TC concentration were significant between control group and groups fed 200 mg/kg and 400 mg/kg quercetin groups (P<0.05), while no significant differences were found between control group and groups fed 800 mg/kg and 1600 mg/kg quercetin (P>0.05). The HDL-C concentration was found to differ significantly between the control group and quercetin supplementary groups (P<0.05), while no significant differences were found among the quercetin supplementary groups (P<0.05). The significant difference in LDL-C concentration was found only between the control group and group fed 1600 mg/kg quercetin (P<0.05), while there were no significant difference among the other groups (P>0.05).

The moisture content of the whole fish body was lowered (P<0.05) with the increasing quercetin levels, except in the case of the 200 mg/kg group of tilapia. Compared with the con-
In the present study, the growth performance of tilapia was significantly improved by supplementary quercetin in diets. This observation was consistent with the quercetin study on flounder conducted by Shin et al. (2010a, 2010b), who observed that the weight gain of flounder fed diet containing 0.25% or 0.50% quercetin, for 30 and 60 days was significantly higher than that of flounder fed diet which did not contain quercetin. It also indicated that high concentration of quercetin is more effective than low concentration in growth. Shin et al. (2010a) also found that feed efficiency ratio of flounder was improved by the administration of quercetin in diet. It was reported that other kinds of flavonoids also had the ability to enhance the animal growth performance. For example, the structural analogue of quercetin, dihydromyricetin, significantly increased the weight gain rate and SGR of tilapia by adding 2400 mg/kg to diet (Cai et al., 2010), and greatly promoted the SGR and FCR of broilers chicken with the level of 250 and 500 mg/kg (Han and Huang, 2006). Even though there were differences in species, feeding condition, nutrient need, and levels of dietary quercetin between our study and other reports, the differences in species, feeding condition, nutrient need, and levels of dietary quercetin between our study and other reports, the growth promotion effect of quercetin was confirmed. It was found that quercetin could be absorbed in tilapia and deposited mainly in aglycone form in the body after absorption, and the aglycone might be an advantageous form to exert its pharmacological effects (Park et al., 2009). At present, the mechanisms of quercetin promoting growth are not clear. From the results of previous researches it could be concluded, however, that the growth promoting effect of quercetin and its analogue might be due to the increase of digestive enzymes activity of intestine, immune ability and antioxidant ability in fish (Shin et al., 2010a, 2010b; Liu, 2012). Further study is needed to reveal the detail mechanisms of quercetin promoting growth.

Our results indicated that quercetin could decrease serum TG level and increase HDL-C level in tilapia, which might be helpful to avoid fatty liver pathological changes. Shin et al. (2010a) reported that TC levels in flounder fed diets containing 0.25% or 0.50% quercetin were significantly lower than that of flounder fed diet without quercetin. They also found

### Table 1. Effect of dietary quercetin level on growth parameters and survival rate of tilapia.

| Quercetin level, mg/kg | IBW, g/fish | FBW, g/fish | SGR, % | FCR | CF | SR, % |
|------------------------|------------|------------|--------|-----|----|------|
| 0                      | 11.51±0.04b | 62.39±3.53b | 3.28±0.20b | 1.41±0.10b | 3.48±0.42b | 93.75±1.25b |
| 200                    | 11.50±0.03b | 75.35±2.35b | 3.90±0.08b | 1.06±0.07b | 4.14±0.17b | 92.50±1.44b |
| 400                    | 11.54±0.08b | 70.08±4.94b | 3.79±0.13b | 1.20±0.05b | 4.05±0.02b | 92.50±1.25b |
| 800                    | 11.47±0.07b | 69.50±2.44b | 3.67±0.07b | 1.16±0.10b | 4.22±0.14b | 95.00±1.00b |
| 1600                   | 11.51±0.10b | 70.11±3.15b | 3.73±0.07b | 1.23±0.06b | 4.19±0.23b | 92.50±1.44b |

IBW, initial body weight; FBW, final body weight; SGR, specific growth rate; FCR, feed conversion ratio; CF, condition factor; SR, survival rate. a,bValues in the same column with different superscripts significantly differ (P<0.05).

### Table 2. Effects of dietary quercetin level on serum lipids concentration of tilapia.

| Quercetin level, mg/kg | TG, mmol/l | TC, mmol/l | HDL-C, mmol/l | LDL-C, mmol/l |
|------------------------|------------|------------|---------------|---------------|
| 0                      | 0.83±0.05b | 3.10±0.15b | 1.39±0.08b    | 1.78±0.08b    |
| 200                    | 0.66±0.03b | 3.57±0.14b | 2.06±0.14b    | 1.61±0.10b    |
| 400                    | 0.40±0.05b | 3.74±0.19b | 2.16±0.16b    | 1.67±0.02b    |
| 800                    | 0.43±0.05b | 3.18±0.15b | 1.90±0.13b    | 1.57±0.13b    |
| 1600                   | 0.38±0.03b | 3.09±0.19b | 1.87±0.17b    | 1.54±0.07b    |

TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol. a,bValues in the same column with different superscripts significantly differ (P<0.05).

### Table 3. Effects of dietary quercetin level on body composition of tilapia.

| Quercetin level, mg/kg | Moisture, % | Crude protein, % | Crude lipid, % | Ash, % |
|------------------------|-------------|------------------|----------------|--------|
| 0                      | 72.00±0.34b | 16.30±0.31b      | 8.43±0.23b     | 3.67±0.22b |
| 200                    | 71.99±0.44b | 17.06±0.14b      | 7.73±0.13b     | 3.89±0.16b |
| 400                    | 70.37±0.29b | 17.23±0.33b      | 8.17±0.34b     | 3.85±0.27b |
| 800                    | 71.16±0.36b | 17.33±0.25b      | 7.96±0.08b     | 3.90±0.20b |
| 1600                   | 70.88±0.12b | 17.50±0.29b      | 8.12±0.13b     | 3.82±0.26b |

a,bValues in the same column with different superscripts significantly differ (P<0.05).
that TC levels in flounder fed diets contained quercetin were significantly lower after 60 days compared with 30 days. Moreover, similar results about quercetin in the reduction of serum or hepatic lipids were previously reported in rats (Basarkar and Nath, 1983; Igarashi and Ohmura, 1995; Ricardo et al., 2001; de Boer et al., 2006; Krishnaveni et al., 2010; Hu et al., 2012; Padma et al., 2012), mice (Kobori et al., 2011; Zhang et al., 2012), chicken (Qureshi et al., 2011), rabbits (Kamada et al., 2005) and humans (Arai et al., 2000; Egert et al., 2010). Yugarani et al. (1992) found that quercetin did not cause any significant changes on the plasma TC, TG and liver fat at weeks 4, 7 and 10 in the rats fed high fat diet, and Nakamura et al. (2000) also indicated that oral quercetin (1.0g/kg) had no remarkable influence on lipid concentrations of serum and hepatic and fecal steroid excretion in rats. Those two reports are not consistent with the results in present study, it might be caused by the differences of animal species, dietary lipid level, dietary quercetin level, quercetin sources and trial period duration. Ricardo et al. (2001) concluded that quercetin showed potential activities in the reduction of cholesterol and triacylglycerol levels. Moon et al. (2012) found that up-regulation of LDL receptors by quercetin could effectively lower blood concentrations of LDL-cholesterol; their study demonstrates that quercetin strongly up-regulated LDL receptors gene expression by activating c-jun-N-terminal kinase and extracellular signal-regulated kinase signalling pathways and increasing nuclear sterol regulatory element binding protein2 levels, which might elicit hypolipemic effects by increasing the clearance of circulating LDL cholesterol levels from the blood.

The crude lipid level in fish body was lowered by the supplementation of quercetin in our study, which was consistent with the other reports on fat reduction in mice lung (de Boer et al., 2006), mice liver (Kobori et al., 2011; Jung et al., 2013) and rats kidney (Hu et al., 2012). Kobori et al. (2011) considered that the reason of chronic dietary intake of quercetin reducing liver fat accumulation might mainly be through decreasing oxidative stress and reducing peroxisome proliferator-activated receptor expression, and the subsequent reduced expression in the liver of genes related to steatosis. The study of Jung et al. (2013) also indicated that quercetin had a regulatory effect on lipid metabolism-related gene expression at the mRNA of liver in obese, and alterations in the expression of genes involved in lipid metabolism may account for decreased biosynthesis of hepatic fatty acids and triglycerides.

In addition, quercetin could up-regulate genes involved in fatty acid catabolism pathways in lungs (de Boer et al., 2006), and block the NOD-like receptor 3 inflammasome activation to improve the signaling impairments and reduce lipid accumulation in the kidney of rats (Hu et al., 2012). It might be concluded that quercetin could reduce or block some receptors genes expression involved in lipid metabolism of fish body, which should be conformed by the further study.

Conclusions

This study demonstrated that supplementary quercetin in tilapia diet increased the growth performance, and confirmed the reduction of the lipid levels in blood observed by other authors in other species.

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