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Dietary yeast culture supplementation enhances feed utilization in largemouth bass (*Micropterus salmoides*) via promotion of metabolic homeostasis and hepatointestinal health

Min Li [a,1], Ying Guan [a,1], Min Xue [a], Wenhao Zhou [b], Jie Wang [a], Hao Wang [a], Yaping Zhu [a], Xiaofang Liang [a,*]

[a] National Aquafeed Safety Assessment Center, Institute of Feed Research, Chinese Academy of Agricultural Sciences, Beijing 100081, China
[b] Beijing Enhalor Biotechnology Co., Ltd., Beijing 100081, China

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ABSTRACT

As a complex compound, yeast culture provides not only abundant proteins and amino acids, but also immunologically active components such as β-glucan, nucleotides, and mannose oligosaccharides. This study aimed to investigate the effects of dietary supplementation with yeast culture on the growth performance, metabolism, and hepatointestinal health of largemouth bass (*Micropterus salmoides*). Juvenile largemouth bass (initial body weight: 31.39 ± 0.05 g, n = 120) were randomly divided into two groups and reared for 65 days: a control group (Con) and supplemented with 3 % yeast culture on the basis of control group (YC). The results showed that although yeast culture supplementation did not significantly affect growth performance ($P > 0.05$), it significantly reduced the feed conversion ratio (FCR) and increased the productive protein value (PPV) ($P < 0.05$), indicating improved economic benefits. Fish fed YC diet enhanced the fasting glycolysis, gluconeogenesis, key lipolytic enzymes, and the basal energy metabolism ($P < 0.05$), which contributed to the protection of the liver from lipid accumulation. Additionally, addition of yeast culture reduced inflammatory infiltrated intestines and downregulated the expression of HIF1α and IL-10 ($P < 0.05$). It also promoted intestinal health by reducing the abundance of harmful bacteria and increasing beneficial microbes. In conclusion, yeast culture improves hepatointestinal health by modulating glucose and lipid metabolism, as well as optimizing the gut microbiota composition, leading to enhanced feed utilization and economic benefits.

1. Introduction

Yeast hydrolysates in aquaculture feed are commonly used in the form of yeast powder (a proteinaceous substance formed after yeast cell inactivation), without undergoing further processing such as cell wall disruption or enzymatic hydrolysis. This prevents the full release of the intracellular components of the yeast cells, limiting the functional efficacy of these substances. Yeast culture is microecological products fermented by yeast under specific conditions with a designated culture medium, containing yeast cells and their metabolic products, as well as denatured culture media (Lee et al., 2018; Upadhaya et al., 2019). The β-glucan and mannooligosaccharide (MOS) components in the yeast cell wall have immune-promoting effects (Miles and Bootwalla, 1991). Specifically, the β-glucan component can activate macrophages, leading to the release of interleukins, cytokines, and other immunoglobulins, which help aquatic animals resist various pathogens (Jayachandran et al., 2018). Richness in protein, amino acids, vitamins and organic acids (Pongpet et al., 2016; Ayiku et al., 2020), and characterized by high digestibility and ability to enhance the nutritional profile of feed (Wang et al., 2022), making yeast culture a potential additive to aquatic feed. By adjusting the structure of gastrointestinal flora, improving the intestinal morphology and promoting digestive enzyme activity, the digestion, absorption and utilization of dietary nutrients are promoted, thereby improving the growth performance of aquatic animals after yeast culture supplementation (Frankic et al., 2006; Torrecillas et al., 2013; Zhen et al., 2019). In addition to known nutritional components like vitamins, minerals, and amino acids, yeast culture also contains unidentified growth factors, including growth-promoting and

* Corresponding author.
E-mail address: liangxiaofang01@caas.cn (X. Liang).
[1] Authors with equal contribution.

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immune-enhancing factors (LeiandStahl, 2001). The potential advantages of yeast products in the fish farming industry are increasingly recognized, and using yeast products to improve fish growth and immune responses has become a research focus in recent years (Liu et al., 2018; Zhang et al., 2018; Bu et al., 2019).

Largemouth bass (*Micropterus salmoides*), colloquially referred to as California perch, is a North American carnivorous fish species that has gained prominence in China's commercial aquaculture sector due to its swift growth, palatable flesh, and substantial economic value (Gong et al., 2015). In 2024, China's largemouth bass production soared to 938, 509 tons. As a carnivore, this fish predominantly depends on fish meal for its protein needs (Huang et al., 2017). Research indicates that the limited utilization of carbohydrates in formulated diets can lead to liver glycogen accumulation, which may disrupt glucose and lipid metabolism, potentially causing metabolic liver disease (MLD) in largemouth bass, a significant issue in their intensive culture (Goodwin et al., 2002; Maher, 2016; Yu et al., 2018, 2019). Moreover, a diet high in plant protein can also induce MLD in carnivorous fish species, such as Amur sturgeon and Japanese seabass (Zhang et al., 2019; Wei et al., 2020). The "gut-liver axis", which encompasses the liver and intestine, is crucial in the development and progression of MLD, with intestinal microbes linking intestinal barrier integrity to liver and intestinal health (Akhter et al., 2015). Studies have demonstrated that an increase in beneficial gut microbiota can promote intestinal and liver health by optimizing nutrient metabolism and curbing inflammation (Kirpich and McClain, 2012; Hsu and Schnabl, 2023). Recent research suggests that yeast-derived protein sources can fulfill the nutritional demands of fish, boost growth, and enhance the health of aquatic species, including liver function (Feng et al., 2022). The study conducted by Xv et al. (2021) demonstrated that dietary supplementation with yeast culture can enhance the growth performance of largemouth bass fed high plant protein-based diets.

Although yeast culture has been examined in aquaculture, its effects in largemouth bass under diet-induced metabolic stress remain insufficiently characterized. Intensive bass culture faces MLD risks from poor carbohydrate utilization and high plant-protein diets. By framing yeast culture within the gut-liver axis, we jointly evaluate growth performance, feed efficiency, and hepatointestinal health alongside glucose/lipid metabolism and gut microbiota composition. Importantly, this study also incorporates an economic benefit analysis, linking feed cost-efficiency with biological performance, which has rarely been addressed in previous research. This integrated, mechanism- and profitability-oriented assessment addresses a practical gap in largemouth bass farming and is necessary for developing nutritional strategies that mitigate MLD while enhancing economic returns and supporting sustainable production.

2. Materials and methods

The Ethics Committee of the Institute of Feed Research at the Chinese Academy of Agriculture Sciences gave its approval to this study, ensuring full compliance with all pertinent ethical regulations (IFR-CAAS20220430). Throughout the duration of the experiment, the welfare of all fish was strictly adhered to in accordance with the Laboratory Animal Welfare Guidelines in China (General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China, Standardization Administration of China, GB/T 35892–2018).

2.1. Experimental diets

In this experiment, 30 % fish meal with 23.5 % cottonseed protein concentrate (CPC) were used as basic feed (Con). The experimental feed was supplemented with 3 % yeast culture to the control diet (YC). The yeast culture was provided by Beijing Enhalor Biotechnology Co., Ltd. The yeast culture is mainly made by high-density fermentation and concentration of brewing yeast (*Saccharomyces cerevisiae*), and is composed of yeast metabolites, yeast cells, and denatured culture medium. Its functional components include yeast cell wall polysaccharides, organic acids, nucleotides, polypeptides, amino acids, enzymes, alcohols, esters, B vitamins and so on. The content of its crude protein was 65 % and its mannose polysaccharides exceeds 1.5 %. Methionine, threonine and fish oil were added to the experimental diets to balance essential amino acids and fatty acids. Calcium dihydrogen phosphate was used to supplement available phosphorus. After superfine grinding and even mixing, the materials were extruded and expanded by twin-screw extruder to produce pellet feed. Once the feed was naturally dehydrated, it was preserved at a temperature of −20 °C. The formulation and nutritional content of the feed used in the experiment are detailed in Table 1.

2.2. Experimental fish

Largemouth bass were sourced from the Tianjin Yuqing aquatic science and technology development company (Tianjin, China). Our experiment was carried out in a circulating aquaculture system of the National Aquatic Feed Safety Assessment Base (Nankou, Beijing). Before the experiment began, fish were acclimatized to the system for two weeks provided with commercial feed. Healthy and uniform-sized largemouth bass with an average initial body weight of 31.39 ± 0.05 g were randomly selected and placed into conical culture tank with a volume of 0.26 m^3. Each group consisted of 3 tanks, and each tank contained 20 fish. The culture cycle lasted for 65 days. The fish were fed twice daily, at 8:00 and 17:00, with apparent satiation, and both dead fish and residual feed were recorded. Water quality parameters were monitored regularly to maintain the following conditions: dissolved oxygen (DO) concentration was above 7.0 mg/L, the concentration of total ammonia nitrogen was below 0.3 mg/L, pH between 7.5 and 8.5, and water temperature maintained between 24 and 27.5 ℃.

Table 1
Composition and nutrient levels of experimental diets (air-dry basis, %).

Items	Con	YC
Ingredients		
Fish meal	30.00	30.00
Yeast culture	0.00	3.00
Wheat flour	9.00	9.00
Tapioca flour	5.00	5.00
Single cell protein	4.00	4.00
Cottonseed protein concentrate	23.50	20.50
Wheat gluten	4.00	4.00
Soybean meal	3.50	3.50
Dried blood	4.00	4.00
Lecithin oil	2.00	2.00
Soybean oil	3.50	3.50
Fish oil	3.50	3.50
$Ca(H_2PO_4)_2$	1.70	1.70
α-cellulose	4.60	4.60
DL-Met	0.20	0.20
L-Thr	0.10	0.10
Premix*	1.40	1.40
Total	100.00	100.00
Nutrient levels		
Moisture	6.10	6.43
Crude protein	50.83	50.72
Crude lipid	12.10	12.17
Crude ash	10.73	10.85
Gross energy / (MJ / kg)	20.74	20.81
Price / (RMB / kg)	9.71	9.83

* The premix provided the following per kg of diets (mg·kg^{-1} diet): Vitamin premix: Vitamin A 20, Vitamin B_1 10, Vitamin B_2 15, Vitamin B_6, Vitamin B_{12} (1 %) 8, niacinamide 100, Vitamin C calcium phosphate (35 %) 1 000, calcium pantothenate 40, biotin (2 %) 2, folic acid 10, Vitamin E (50 %) 400, Vitamin K_3 20, Vitamin D_3 10, inositol 20, choline chloride 4000, corn gluten meal 150, $CuSO_4$·5 H_2O 1, $FeSO_4$·H_2O 300, $ZnSO_4$·H_2O 200, $MnSO_4$·H_2O 100, KI (10 %) 80, Na_2SeO_3 (10 % Se) 10, $CoCl_2$·6 H_2O (10 % Co) 5, NaCl 100, zeolite 4995, $MgSO_4$·5 H_2O 2000, TBHQ 200.

At the conclusion of the 65-day growth trial, the fish from each tank were weighed after a 24-hour fasting period. Food intake and survival numbers were recorded to calculate the growth index. From each treatment group, twelve fish (four from each tank) were randomly selected, euthanized using tricaine methanesulfonate (MS222) at a concentration of 200 mg/L, and then measured for body length, body weight, and the weights of internal organs such as the liver, visceral mass, and abdominal fat. Blood samples were collected, centrifuged at 1000 × g for 10 min at 4 °C to obtain serum. Liver and intestine tissue samples were taken for histological analysis, while the remaining liver and intestine samples were rapidly frozen for future analysis. All samples were stored at −80 °C.

2.3. Chemical analysis

Chemical analyses of the diets were conducted following the AOAC (2006) guidelines. The water content, crude protein, crude fat, crude ash content, and total energy of the raw materials, feed, and fish body were measured using the procedures outlined by Liang et al. (2019).

2.4. Histopathological examination of the liver and intestine

The liver (0.5 × 0.5 × 0.5 cm) was fixed in 4 % tissue fixation fluid and the distal intestine was fixed in the mixture of 60 % methanol and 10 % acetic acid for 24 h, and then dehydrated and embedded. Hematoxylin and eosin (H&E), alcian blue (A&B) and immunohistochemistry (IHC) staining were carried out. H&E staining was performed following the method described by Wei et al. (2020). As for A&B staining, after deparaffinizing by conventional methods, the intestine was stained with 1 % alcian blue solution for measuring inflammatory infiltration. As for IHC staining, the paraffin sections were blocked with endogenous peroxidase powerful blocking buffer (Beyotime, China) for 10 min. Hypoxia-inducible factor 1-alpha (HIF-1α) (Santa Cruz Biotechnology, SC-13515) polyclonal antibody (1:300) was then stained at 4 °C for one night. Following the washing step, the sections were incubated with biotin-labeled secondary antibody for 1 h. Multispectral panoramic tissue scanning microscope (Tissue Gnostics, Vienna, Austria) was used for scanning and analysis.

2.5. Biochemical analysis

Total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), total protein (TP), alkaline phosphatase (AKP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total antioxidant capacity (T-AOC) of serum, and hepatic TC, TG, glycogen (GLY) were quantified using assay kits (Nanjing Jiancheng Bioengineering Institute, China) in accordance with established protocols. The plasma glucose (GLU) contents were evaluated by assay kits (Shanghai Rongsheng Biotech Co. Ltd., China). Non-esterified fatty acid (NEFA) in plasma and liver were performed following standardized methodologies provided by Wako Pure Chemical Industries (Japan). The contents of cyclic-adenosine monophosphate (cAMP), the activities of glucokinase (GK), pyruvate kinase (PK), phosphoenolpyruvate carboxykinase (PEPCK), glucose-6-phosphatase (G6Pase), adipose triacylglyceride lipase (ATGL), hormone sensitive lipase (HSL) and monoacylglycerol lipase (MGL) in the liver were measured using ELISA kits (Jiangsu Meimian industrial Co., Ltd., China) followed the manufacturer' s instructions.

2.6. qPCR

Total RNA extraction, concentration determination, cDNA synthesis, and mRNA quantification were conducted following the methodological framework outlined in Yu et al. (2018). The expression of elongation factor 1-alpha (EF1α) was used as an endogenous reference gene. Primers were presented in Table 2.

Table 2
Primer sequences for real-time PCR.

Gene	Primer sequence (5′-3′)	Target size / bp	E-value / %	TM / ℃
TNFα	*F: CTTCGTCTACAGCCAGGCATCG *R: TTTGGCACACCGACCTCACC	161	106.0	63.0
IL1β	F: CGTGACTGACAGCAAAAAGAGG R: GATGCCCAGAGCCACAGTTC	166	101.3	59.4
TGFβ1	F: GCTCAAAGAGAGCGAGGATG R: TCCTCTACCATTCGCAATCC	118	104.0	59.0
IL10	F: CGGCACAGAAATCCCAGAGC R: CAGCAGGCTCACAAAATAAACATCT	119	113.6	62.1
GK	F: ACAGAGTGGTGGACGAGACC R: TCGTTCACCAGCTTCATCAG	115	102.6	60.0
PFK	F: ACAACGTCCCTGGAACAGAC R: ACCACAAACACTCGCCTCTT	118	98.3	60.0
PK	F: CCTATCGGAATTGCACTGGA R: TTCTTGTAGTCGAGCCAGAG	170	99.0	60.5
PEPCK	F: TGCTTGACTGGATGTTCAGG R: TTCCTCACCTCATCCACCTC	178	94.5	59.3
FBPase	F: CTTCACCTCCTGTGTGCTTG R: CAGCTGGCTCACCATCTGTA	182	95.9	59.3
G6Pase	F: GGGAGTCCAGGTGTGTGTCT R: CAGCGAAGGAGGTCAAGAAG	182	90.9	56.6
MGL	F: AAGGTTTTTCTGGCGAAGGT R: CGTGGAAGTTCAGCTCATCA	169	93.0	60.5
EF1α	F: TGCTGCTGGTGTTGGTGAGTT R: TTCTGGCTGTAAGGGGGCTC	147	102.8	60.4

* F: forward primer; R: reverse primer.

2.7. Intestinal microbiome analysis

The methods for DNA extraction, PCR amplification, and PCR product purification were outlined by Xie et al. (2022). Sequencing and bioinformatics analysis were conducted by Majorbio Bio-Pharm Technology Co. Ltd. (Shanghai, China). The purified products underwent equimolar and paired-end sequencing on the Illumina MiSeq PE300 and NovaSeq PE250 platforms (Illumina, San Diego, USA). Raw 16 s rRNA sequences were processed using fastp, FLASH, QIIME2, and the SILVA 16 s rRNA database (v13.8) to generate high-quality sequences, which were accessed via the Majorbio Website (cloud.majorbio.com).

2.8. Statistical analysis

The test data were expressed as Means ± SEM. All the data were analyzed by R (3.2.5) software. Before conducting statistical analyses, datasets were examined for normal distribution and equal variances. For normally distributed data, differences between two groups were assessed using two-tailed unpaired Student's *t*-tests. When normality was not met, the Kruskal-Wallis test followed by the Mann-Whitney *U* test was performed. Statistical significance was defined as $P < 0.05$.

3. Results

3.1. Effects of yeast culture on growth performance and morphometric indices

The effects of dietary yeast culture on the growth performance and morphometric indices of largemouth bass are summarized in Table 3. Dietary supplementation with yeast culture significantly reduced the FCR from 1.08 to 0.90 ($P < 0.05$), and markedly increased the PPV from 32.28 % to 37.37 % ($P < 0.05$). No notable disparities were detected in the remaining indices when comparing the two groups ($P > 0.05$). We did an economic analysis based on weight gain and feed costs. Although the unit price of feed in the YC group was slightly higher than that in the Con group (9.83 vs. 9.71 RMB/kg) (Table 1), the economic profit index (EPI) did not differ significantly between the two groups (Table 3). Notably, the YC group exhibited a significantly lower economic feed

Table 3
Effects of yeast culture on growth performance and body index of largemouth bass (Means ± S.E.M, n = 3).

Items[1]	Con	YC
SR (%)	92.50 ± 3.23	93.33 ± 3.33
FBW (g)	102.41 ± 1.59	109.67 ± 4.72
WGR (%)	213.91 ± 3.30	236.29 ± 17.88
SGR (% / d)	1.82 ± 0.03	1.92 ± 0.07
FCR	1.08 ± 0.01^{b}	0.97 ± 0.01^{a}
FR (%)	1.76 ± 0.03	1.64 ± 0.05
PPV (%)	32.28 ± 0.42^{a}	37.37 ± 0.76^{b}
CF (%)	2.57 ± 0.05	2.55 ± 0.03
VSI (%)	6.82 ± 0.16	6.96 ± 0.16
HSI (%)	1.55 ± 0.06	1.53 ± 0.09
VAI (%)	1.59 ± 0.13	1.74 ± 0.14
ECR (¥, kg·fish^{-1})	10.45 ± 0.11^{b}	9.49 ± 0.11^{a}
EPI (¥, kg·fish^{-1})	2.33 ± 0.03	2.55 ± 0.09

In the same row, values with different letter superscripts mean significant difference. [1]SR (survival rate, %) = 100 × final fish number / initial fish number;
FBW: final body weight (g);
WGR (weight gain rate, %) = (final weight (g) - initial weight (g) + dead fish weight (g)) / initial weight (g);
SGR (specific growth rate, % / d) = 100 × [ln (FBW / initial body weight)] / days;
FCR (feed conversion rate) = 100 × feed intake (g) / (final weight (g) - initial weight (g) + dead fish weight (g));
FR (feeding rate, % bw / d) = 100 × feed intake (g) / ((initial weight (g) + final weight (g) + dead fish weight (g)) / 2) / time (days);
PPV (produced protein value, %) = 100 × (final body weight (g) × C_t - initial body weight (g) × C_0 + W_d × C_0) / feed consumption), in which, C_t (%) is final nitrogen content in whole fish body, C_0 (%) is initial nitrogen content in whole fish body and W_d is total body weight of dead fish during experiment;
CF (condition factor, g/cm^3) = 100 × (body weight (g) / (body length^3 (cm^3));
VSI (viscerasomatic index, %) = 100 × (viscera weight (g) / body weight (g));
HSI (hepatosomatic index, %) = 100 × (liver weight (g) / body weight (g));
VAI (visceral adipose index, %) = 100 × (visceral adipose weight (g) / whole body weight (g));
ECR (economic feed conversion ratio, ¥, kg·fish^{-1}) = FCR × feed price (¥, kg^{-1});
EPI (economic profit index, ¥, fish^{-1}) = (FBW (kg) × fish market price (¥, kg^{-1})) - (ECR × WG (kg)).

conversion ratio (ECR) compared with the Con group, indicating improved feed utilization efficiency (Table 3).

3.2. Effects of yeast culture on whole body composition

Yeast culture supplementation had no significant impact on the whole-body composition of the fish, with parameters such as moisture, crude protein, crude lipid, crude ash, and liver lipid content comparable among the two dietary treatments ($P > 0.05$, Table 4).

3.3. Effects of yeast culture on liver health

The activity of ALT in plasma decreased significantly after adding yeast culture ($P < 0.05$, Table 5). No significant differences were seen in plasma AST, AKP, TP and T-AOC between the two groups ($P > 0.05$, Table 5).

In the Con group, mild pathological changes were observed in the liver. Among the 12 samples in this group, 10 exhibited no significant abnormalities, while 1 sample displayed a fatty liver phenotype and another exhibited a fibrosis phenotype. In contrast, no notable liver abnormalities were detected in the 12 samples from the YC group (Fig. 1A, B).

Table 4
Effects of yeast culture on body composition of largemouth bass (Means ± S.E.M, n = 3, %).

Items	Con	YC
Moisture	71.71 ± 0.26	71.30 ± 0.46
Crude protein	17.14 ± 0.04	17.33 ± 0.15
Crude lipid	6.98 ± 0.21	7.43 ± 0.26
Crude ash	3.65 ± 0.10	3.78 ± 0.12
Liver lipid	2.82 ± 0.21	2.98 ± 0.11

Table 5
Effects of yeast culture on liver function parameters and antioxidant responses in the plasma of largemouth bass (Means ± S.E.M, n = 8).

Items	Con	YC
AST (U / L)	5.49 ± 1.15	3.70 ± 1.24
ALT (U / L)	7.38 ± 0.89^{b}	4.73 ± 0.50^{a}
AKP (U / L)	36.20 ± 2.17	38.90 ± 2.70
TP (gprot / L)	20.87 ± 1.16	22.66 ± 0.78
TBA (umol / L)	2.99 ± 0.51	3.33 ± 0.15
T-AOC (mM)	0.26 ± 0.03	0.24 ± 0.04

3.4. Effects of yeast culture on glucose and lipid metabolism

Replacement CPC with yeast culture did not lead to a substantial disparity in fasting blood glucose levels or liver glycogen reserves ($P > 0.05$, Fig. 2A). However, the mRNA expression of *GK* and *G6Pase* in the YC group was higher compared to the Con group ($P < 0.05$, Fig. 2B). The transcriptional activity of key glycolytic and gluconeogenic enzymes *PFK*, *PK*, *PEPCK*, and *FBPase* showed comparable expression patterns across experimental groups, with no statistically detectable variations ($P > 0.05$, Fig. 2A). Moreover, yeast culture supplementation significantly upregulated the hepatic GK, PK, PEPCK, and G6Pase enzyme activities ($P < 0.05$, Fig. 2C), suggesting that yeast culture promotes the normal expression of key enzymes involved in glucose metabolism in largemouth bass.

Concerning lipid metabolism, the plasma TC, HDL-C, and hepatic TC concentrations remained comparable between the Con and YC groups ($P > 0.05$, Fig. 2D). However, a significant increase in NEFA levels was detected in both plasma and liver of yeast culture-fed fish ($P < 0.05$, Fig. 2E). In contrast, TG concentrations in plasma and liver exhibited no statistically significant variations between treatments ($P > 0.05$, Fig. 2E).

qPCR analysis indicated that yeast culture supplementation did not significantly affect the mRNA expression of key lipogenic and fatty acid oxidation regulators, including acetyl-CoA carboxylase 1 (*ACC1*), fatty acid synthase (*FASN*), peroxisome proliferator-activated receptor gamma (*PPARγ*), carnitine palmitoyltransferase 1 A (*CPT1A*), and *PPARα* ($P > 0.05$, Fig. 2F). In contrast, pronounced changes were observed in lipolytic gene expression: adipose triglyceride lipase (*ATGL*) was significantly downregulated ($P < 0.05$, Fig. 2F), whereas hormone-sensitive lipase (*HSL*) and monoglyceride lipase (*MGL*) were markedly upregulated ($P < 0.05$, Fig. 2F). Consistent with these transcriptional patterns, hepatic enzymatic activity assays revealed significant increases in ATGL, HSL, and MGL activities in the YC group ($P < 0.05$, Fig. 2G). Collectively, these results suggest that dietary yeast culture enhances hepatic lipolytic capacity while potentially suppressing lipid synthesis, thereby contributing to reduced hepatic lipid accumulation in largemouth bass.

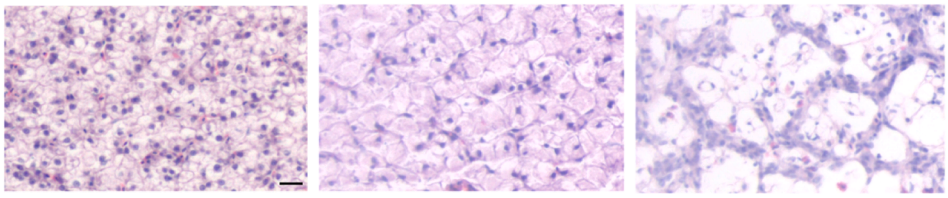
3.5. Effects of yeast culture on basal energy metabolism

The results revealed that yeast culture supplementation significantly elevated both hepatic cAMP concentrations and *CREB* mRNA expression ($P < 0.05$, Fig. 3).

3.6. Effects of yeast culture on intestine health

In the Con group, mild pathological alterations were observed in the intestines. Among the 12 specimens, 10 exhibited no apparent abnormalities, whereas 2 showed pronounced inflammatory infiltration (Fig. 4A-B). IHC staining further revealed elevated HIF-1α expression in

A



B

Items	Con	YC
No obvious abnormality	10	12
Fatty liver	1	0
Fibrotic liver	1	0
Total	12	12

Fig. 1. Effects of yeast culture on the health of liver in largemouth bass. (A) H&E staining of three liver phenotypes. Scale bars indicate 20 μm. (B) Statistical results of liver phenotypes (n = 12).

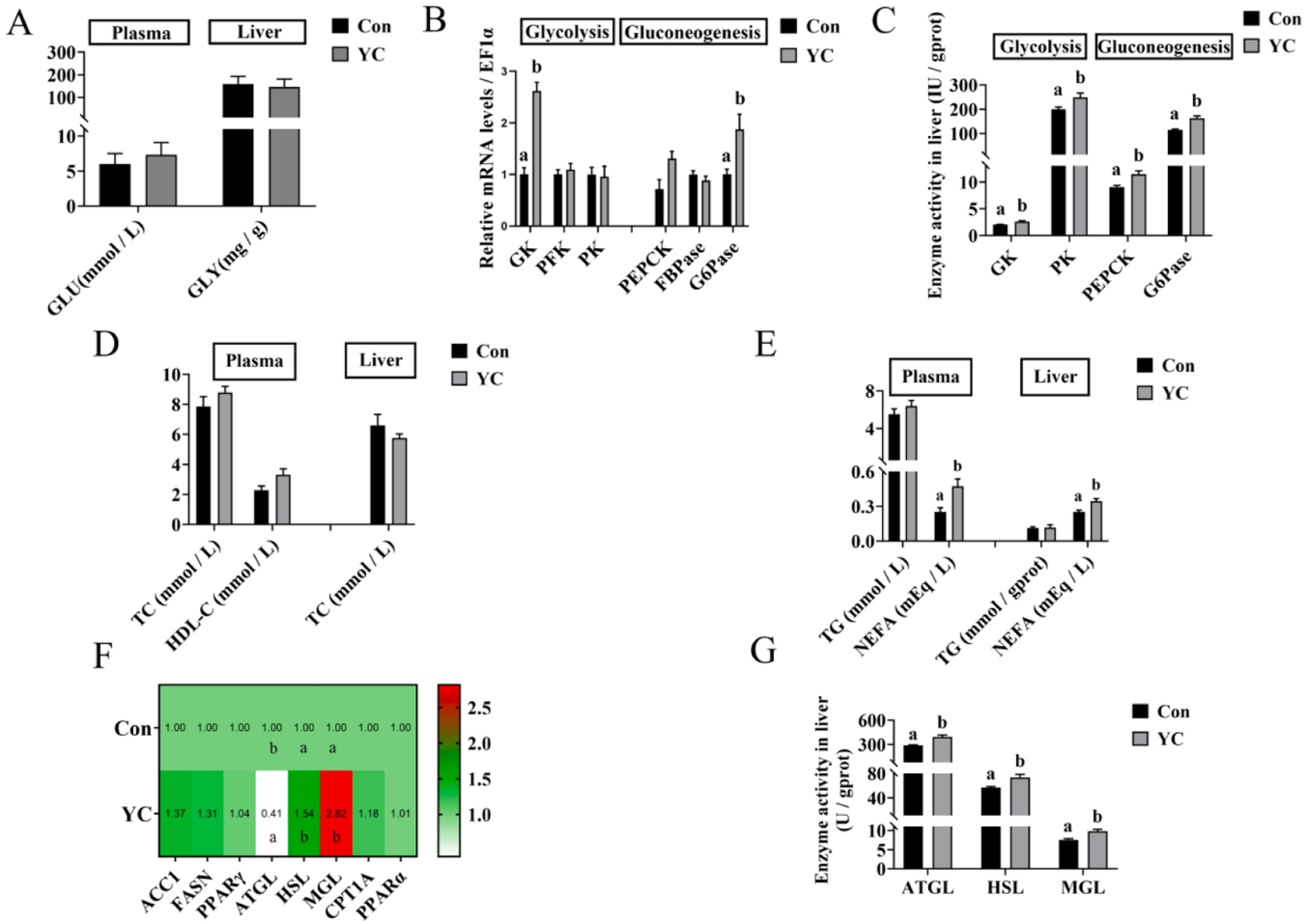


Fig. 2. Effects of yeast culture on glucose and lipid metabolism in largemouth bass. (A) Levels of glucose in the plasma and hepatic glycogen reserve. (B) Relative mRNA levels of genes related to glycolysis and gluconeogenesis. (C) Enzymatic activity of glycolysis and gluconeogenesis. (D) Levels of TC and HDL-C in the plasma and liver. (E) Levels of TG and NEFA in the plasma and liver. (F) Relative mRNA levels of genes related to lipid metabolism in the liver. (G) Enzymatic activity of lipid metabolism. Data are means ± SEM, n = 12. Bars with different letters represent significant differences between groups ($P < 0.05$).

the samples with inflammatory lesions. In contrast, histopathological examination demonstrated normal intestinal morphology in all 12 specimens from the YC group (Fig. 4A-B). Moreover, the expression of the anti-inflammatory cytokine *IL-10* was significantly reduced in the YC group ($P < 0.05$, Fig. 4C). Collectively, these findings suggest that dietary yeast culture supplementation confers intestinal anti-

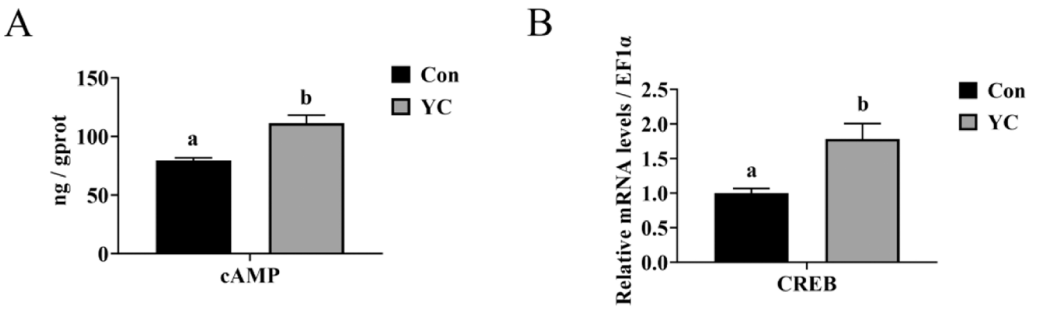


Fig. 3. Effects of yeast culture on the basal metabolism level in the liver of largemouth bass. (A) The content of cAMP. (B) Relative mRNA expression of *CREB*. Data are means ± SEM, n = 12. Bars with different letters represent significant differences between groups ($P < 0.05$).

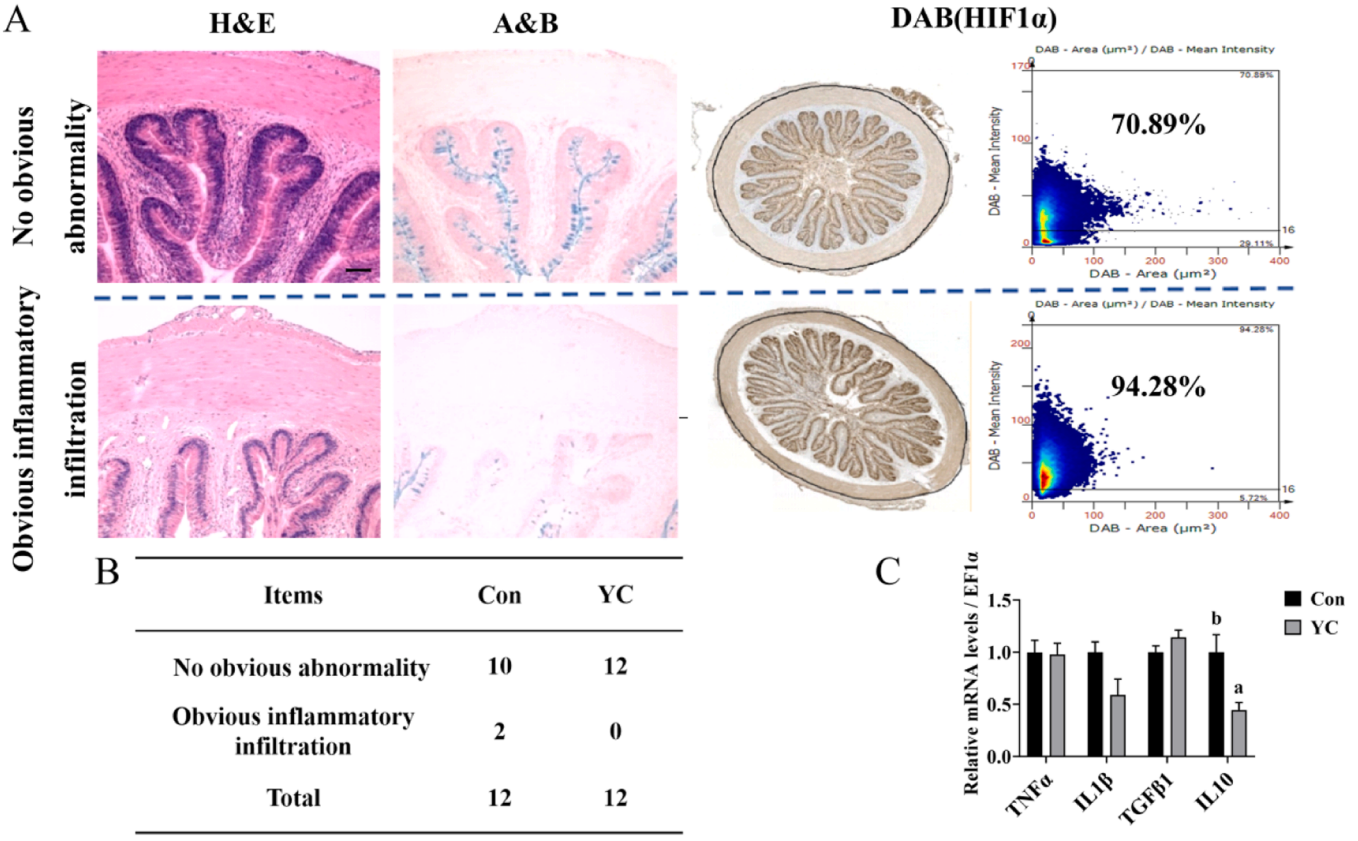


Fig. 4. Effects of yeast culture on the health of intestine in largemouth bass. (A) H&E and A&B staining of no obvious abnormality and obvious inflammatory infiltration intestine. Scale bars indicate 20 μm. (B) Statistical results of intestine phenotypes. (C) Relative mRNA levels of inflammatory factors. Data are means ± SEM, n = 12. Bars with different letters represent significant differences between groups ($P < 0.05$).

inflammatory effects, potentially by modulating the expression of key inflammatory cytokines.

Microbial community analysis revealed significant alterations in intestinal microbiota following yeast culture supplementation (Fig. 5). Yeast culture significantly reduced microbial Shannon diversity and richness ($P < 0.05$, Fig. 5A-B). We found that yeast culture treatment altered microbial community structure but not significantly (Fig. 5C). Taxonomic profiling at different phylogenetic levels showed distinct modulation patterns. At the genus level, yeast culture administration led to a notable reduction in the relative abundance of *Mycoplasma* compared to controls (Fig. 5D). Phylum-level analysis revealed an increased predominance of *Firmicutes* in YC group, whereas *Actinobacteria* showed higher abundance in Con group (Fig. 5E). Based on volcanic maps, *Mycoplasma* was significantly enriched in the control (Fig. 5F). These results demonstrate that dietary yeast culture supplementation selectively modulates the intestinal microbial ecosystem, potentially promoting beneficial bacterial populations while suppressing pathogenic microbiota.

4. Discussion

Yeast culture, derived from microbial fermentation, is a natural microecological product composed of denatured medium, small amounts of yeast cells, and extracellular metabolites (Lee et al., 2018; Upadhaya et al., 2019). As a new microecological agent, yeast culture exhibits a nutritionally diverse profile, containing substantial concentrations of amino acids, various vitamins, bioactive organic acids, and prebiotic oligosaccharides, along with other beneficial micronutrients (van der Peet-Schwering et al., 2007; Shen et al., 2009). It promotes the digestion and absorption of nutrients by stimulating food intake and

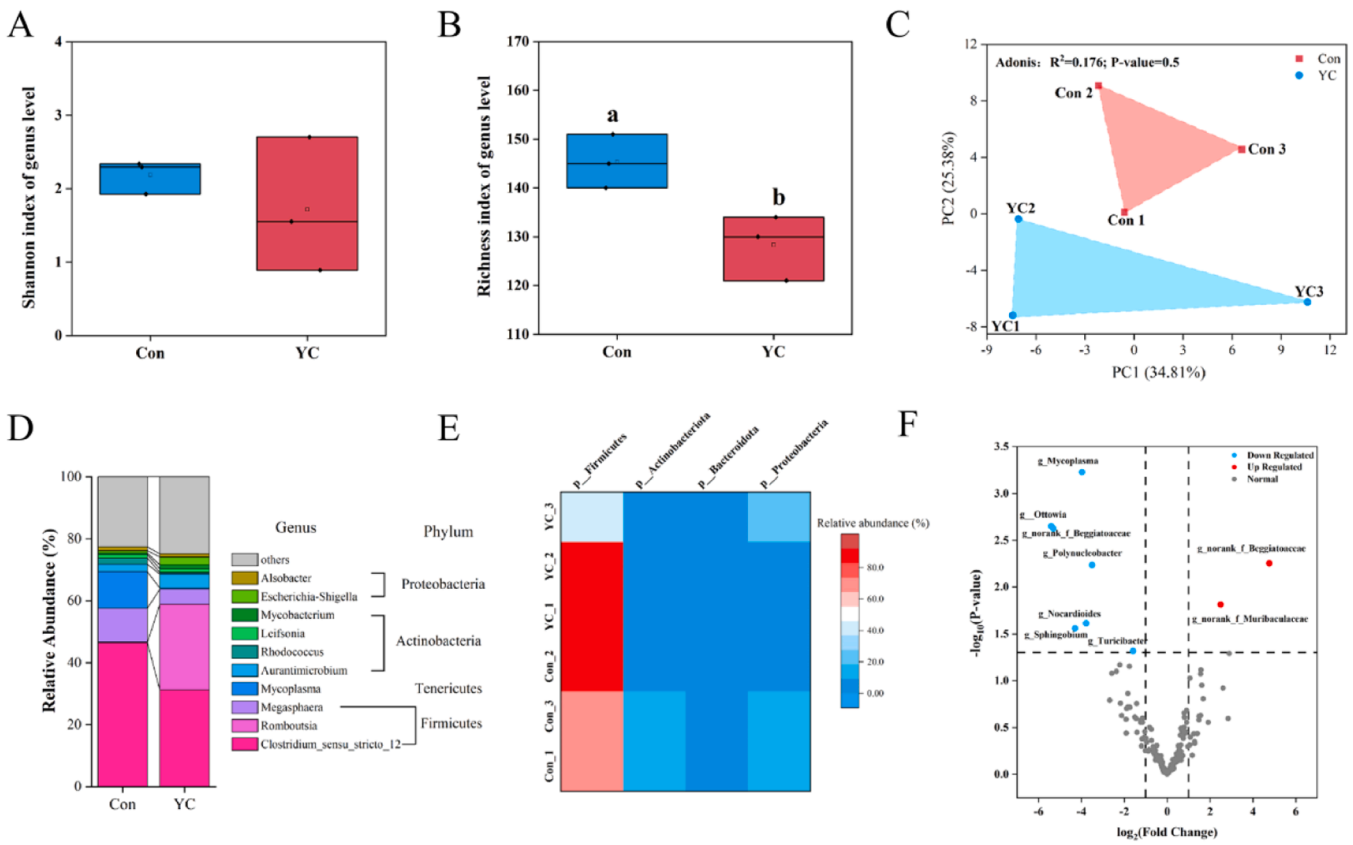


Fig. 5. Effects of yeast culture on intestinal microbiota in largemouth bass. (A) Shanno index. (B) Richness index. (C) Level of the intestinal microbiota. (D) The relative genus and phylum abundance of the microbiota. (E) Relative abundance of dominant phyla. (F) Differential flora. Data are means ± SEM, n = 3. Bars with different letters represent significant differences between groups ($P < 0.05$).

enhancing digestive enzyme activity, thereby improving the growth performance of aquatic animals (Essa et al., 2011; Berto et al., 2016). Studies on *Litopenaeus vannamei* and *Ctenopharyngodon idellus* have shown that the addition of yeast culture to the diet can notably enhance the growth performance of aquatic animals and reduce the FCR (Deng et al., 2013; Ayiku et al., 2020). Our results indicate that 3 % yeast culture supplementation significantly reduced FCR and hepatosomatic index (HSI), while increasing protein deposition, without affecting growth performance indicators such as FBW, WGR, and SGR. Yeast culture supplementation had no significant impact on the whole-body composition of largemouth bass, suggesting that yeast culture inclusion does not alter nutrient deposition or energy allocation and maintains overall body composition stability. These results could be attributed to the mechanisms of feeding attractants, organic acid acidification, and enzyme digestion-promoting of yeast culture. Additionally, the significantly increased liver cAMP levels suggest that yeast culture improved the basal energy metabolism level of largemouth bass. Therefore, it is recommended that the energy level in YC diets be appropriately increased. Furthermore, we found that although the YC diet was priced slightly higher than the Con diet, its markedly lower ECR reflected enhanced feed efficiency, effectively neutralizing the cost difference and delivering distinct economic advantages.

Compared to fish meal, plant proteins not only lack essential amino acids, essential fatty acids and available phosphorus, but also contain higher levels of carbohydrate (Zhang et al., 2020). As an obligate carnivore species, largemouth bass has a poor ability to utilize carbohydrates and cannot control the steady state of glucose metabolism, which predisposes it to MLD during aquaculture (Yu et al., 2019; Chen et al., 2023; Li et al., 2025). Biochemical indices in the blood provide crucial information about the nutritional status, metabolism, and the health of fish, serving as essential indicators for assessing the health of aquatic animals (Silveira-Coffigny et al., 2004). AST and ALT are key metabolic enzymes predominantly found in the heart and liver and are widely used as indicators of liver function. Elevated activity of these enzymes typically indicates liver damage and the extent of such damage (Nyblom et al., 2004; Kumar et al., 2011). Liver fibrosis arises from chronic liver damage of various etiologies and is typically reversible upon the cessation of the injurious stimuli (Hammel et al., 2001). Huang et al. (2025) reported that adding 10 g/kg of yeast culture to the diet resulted in higher intestinal lipase activity in largemouth bass compared with the control group, but their study did not focus on changes in glucose and lipid metabolism and liver health. In the present study, no significant differences were observed between the two groups of largemouth bass in hepatic lipid content or in plasma indices including AKP, TP, TBA, and T-AOC. However, yeast culture supplementation reduced plasma AST levels to some extent and significantly decreased plasma ALT levels. Moreover, histopathological analysis revealed that the liver of the Con group exhibited features of hepatic steatosis and fibrosis, indicative of liver injury, whereas no apparent abnormalities were observed in the YC group. Based on these results, dietary supplementation with 3 % yeast culture markedly improved hepatic health status in largemouth bass.

MLD in largemouth bass is intricately linked to the metabolism of glucose and lipids (Chen et al., 2023; Li et al., 2025). In our study, the addition of yeast culture to the feed significantly improved gluconeogenesis levels, which can be seen from the increased mRNA expression and enzyme activity of G6Pase and PEPCK. In order to effectively respond to upregulated gluconeogenesis, glycolysis levels were similarly promoted in the YC group, as shown by an increase in GK and PK levels. Adipose tissue exhibits significant anatomical distribution in teleost species, with adipocytes predominantly localized in visceral deposits, hepatic parenchyma, and intramuscular compartments (Tsuchiya et al.,

2014). The accumulation of liver fat in fish can lead to the disorder of nutrition metabolism, which leads to the decline of disease and stress resistance, making fish more susceptible to diseases outbreaks and even mortality under environmental stress (Hixson, 2014). Our results revealed that the levels of lipolysis related enzymes were upregulated after the addition of yeast culture, resulting in the significant down-regulation of liver TG content and the promotion of liver NEFA production. The increased NEFA levels improve energy supply efficiency, and this can be evidenced by the activation of the cAMP/CREB pathway. cAMP/CREB pathway can up regulate gene expression of lipolysis/β oxidation, improve the level of basic energy metabolism, so as to protect liver tissue from lipid accumulation (Kemp et al., 1999; Wahlang et al., 2018). In this study, the increased cAMP content in YC group protected the liver from lipid accumulation by upregulating the expression of *CREB* and lipolysis genes.

The intestinal mucosa serves as the primary defense against pathogenic invasion, with gut microbiota playing a crucial role in preserving its barrier function (Tlaskalova-Hogenova et al., 2004). Resident microbial communities contribute to various physiological processes, including immune modulation, nutrient assimilation, and maintenance of internal homeostasis (Hooper et al., 2002; Hooper and Macpherson, 2010; Cahenzli et al., 2013). However, pathogenic microorganisms can compromise mucosal integrity, leading to increased permeability that facilitates the translocation of both bacterial components and dietary macromolecules across the epithelial barrier (Ma et al., 2021). The alterations in dietary components had a notable impact on the composition and functionality of the intestinal microbiota in fish (Visschers et al., 2013). Earlier research has indicated that dietary yeast culture can significantly increase the number of *Firmicutes*, so as to contributes to the well - being of the intestinal mucosa and thus improve the immune response of channel catfish (Xia et al., 2022). Zhou et al. (2009) revealed that dietary yeast culture could encourage the growth of non - conventional beneficial bacteria in the intestines of tilapia. The above results are consistent with our research, we found that yeast culture significantly decreased the abundance of pathogenic bacteria (*Mycoplasma*) while promoting the proliferation of beneficial bacteria (*Firmicutes*). Similar to our study, Huang et al. (2025) reported that as the dietary yeast culture supplementation increased from 0 to 30 g/kg, the abundance of *Mycoplasma* in the intestinal microbiota of the control group was significantly higher than that in the YC10 and YC30 groups. However, unlike our findings, their study showed a significant decrease in the abundance of *Firmicutes* with increasing yeast culture supplementation. The discrepancies in intestinal microbiota composition may be attributed to differences in the source of the yeast culture. Combined with the pathological phenotype and gene expression of inflammatory factors, yeast culture can maintain the intestinal microflora homeostasis of largemouth bass, thus promote intestinal health and effectively alleviate intestinal inflammation.

5. Conclusions

The study reveals that supplementation with 3 % yeast culture to the diet can improve the liver health by enhancing glycolysis, gluconeogenesis, and lipolytic enzyme activity, protecting against lipid accumulation. It also reduced intestinal inflammation by modulating inflammatory markers like HIF1α and IL-10, while promoting a healthier intestinal microbiota by decreasing harmful bacteria and increasing beneficial microbes. These beneficial effects highlight the feasibility of using yeast cultured products as a nutritional strategy to improve the economic benefits of largemouth bass farming. However, the study is limited to a single species, and further research is needed to explore the applicability of yeast culture supplementation to other aquatic species. Additionally, the long-term effects of yeast culture supplementation on fish health, reproduction, and sustainability should be explored.

CRediT authorship contribution statement

Xiaofang Liang: Writing – review & editing, Visualization, Funding acquisition. **Ying Guan:** Writing – original draft, Investigation, Formal analysis, Data curation. **Min Xue:** Visualization, Conceptualization. **Min Li:** Writing – original draft, Methodology, Investigation, Formal analysis. **Hao Wang:** Visualization. **Yaping Zhu:** Writing – review & editing. **Wenhao Zhou:** Resources, Methodology. **Jie Wang:** Validation, Software.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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