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Bile acids in aquaculture nutrition: Enhancing growth, nutrient utilization, and sustainability

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Abstract
Ensuring food and nutritional security is top for global food-producing sectors among projections of a 60% increase in food consumption by 2050 due to population growth. To address this challenge sustainably, the food and feed industry must conserve resources while feeding a growing population. Mechanically stable farming practices are recommended by the FAO to meet this demand. Intensive aquaculture, crucial for meeting nutritional needs, relies on cost-effective and nutritionally balanced fish feed. Bile acids (BAs) is complex physiological particles which aiding lipid absorption and digestion and play a vital role in aquaculture nutrition. BAs enhance growth, nutrient assimilation, and regulate gut microbiota in aquatic species. However, plant-based feed lacks necessary components for optimal BA production, affecting lipid utilization and growth in fish. Supplementation of plant-based feeds with BAs shows promise in improving fish growth and nutrient utilization, although with varying effects on different species. Additionally, BAs influence lipid metabolism, biochemical composition, and body indices in aquatic organisms, impacting growth and lipid levels. Furthermore, BAs influence gut microbiota composition and organ histomorphology, with implications for overall health and disease resistance in fish. Understanding the role of BAs in aquaculture nutrition is critical for developing sustainable feeding systems that may meet rising food demand while reducing resource use and environmental impact.

Keywords: Aquaculture nutrition, enhancing growth, nutrient utilization, sustainability

Introduction

Food and nutritional security is a top priority for food-producing sectors throughout the globe. Food consumption is anticipated to rise by 60% by 2050 as the world's population rises from its current estimated 7.7 billion to 9.7 billion. As a result, it is imperative for the whole food and feed industry to save resources and feed the world's population sustainably. FAO suggests that farming and related industries be mechanically stable to meet this issue. In light of its impact on growth, good health, and manufacturing costs, intensive aquaculture depends on the development of cost-effective nutritionally balanced fish feed. Aquaculture uses the high energy (high fat) diet to boost growth, reduce nitrogen waste, and follow "protein-sparing effects." However, fish whose diets are too high in dietary lipids experience metabolic stress and accumulate fat, stunting their growth. The intestine's ability to absorb and digest fat or fat-soluble compounds is enhanced by the emulsifying effects of bile acids, which make the lipids more accessible to the pancreatic lipases. Bile acids (BAs) are complex physiological particles that solubilize, absorb, and transport dietary lipids Within the gastrointestinal system (Zhou *et al.*, 2018) [30] and help to reduce stress and use nutrients (Ding *et al.*, 2020) [3]. Bile acids decrease the accumulation of lipids in the liver. (El-Shenawy *et al.*, 2020) [5], assimilating nutrients, absorbing lipid and fat-soluble vitamins, and controlling fish gut microbes (Jiang *et al.*, 2018) [12]. BA reduces FCR and boosts aquatic animal growth (Ding *et al.* 2020) [3]. Cholic acid and chenodeoxycholic acid are necessary BAs. Intestinal bacteria transfer several important bile acids. Bile acids combine to form bile salts, which are produced in the liver from cholesterol and stored in the gallbladder. Bile salts are Sodium Glycocholate (from Glycine) and Sodium Taurocholate (from Taurine). It helps emulsify by forming smaller lipid particles. Bile salts improve pancreatic lipase function. Cholesterol and taurine or glycine are the building blocks of bile acids, which are produced in the liver and then released from the hepatocyte.

(Hofmann, 1999) [10]. Bile acids help to transport cholesterol from the hepatocyte into the intestinal lumen as bile. (Hofmann, 1999) [10]. BAs receptors minimize liver damage and accelerate liver recovery (Fan *et al.*, 2015) [6].

Study of nutraceutical requirement

Due to high cost of fish meals and limited availability, aquaculture production requires cheaper protein sources like plant protein. Because of their high carbohydrate content, especially in the form of non-starch polysaccharides and various anti-nutritional elements, plant-based components have a reduced nutrient digestibility. Nutrient malabsorption and improper digestion reduce growth, immunity, wound healing, and more. Since there is little evidence that vaccinations actually work, and because anti-antibiotics cause problems like bioaccumulation and resistant genes, neither is an ideal solution. Nutraceuticals can help with this innovative strategy.

Influence of bile acid levels on growth, nutrient utilization, and survival

Bile acids act as emulsifiers and play a role in activating pancreatic lipases to break down lipids, enhancing the absorption of fats and fat-soluble nutrients in the intestine. (Maldonado-Valderrama *et al.*, 2011) [16]. When it comes to the formation of bile acid or bile form, plant materials are deficient in taurine and cholesterol. Thus, fish fed plant-based feed may have low lipid utilization and poor growth due to poor BAs or bile salt synthesis. BAs or bile salts improved rainbow trout and turbot growth on plant protein-based diets, as expected (Gu *et al.*, 2017) [8]. Cholytaurine (BAs) supplementation with a plant-based diet increased rainbow trout bile salt level. If it's cost-effective for the feed companies, supplementing plant-based feed with BAs may improve the growth of fish. Evidence suggests that certain bile salts are advantageous to fish, such as inflammation reduction. (Jin *et al*., 2019) [13], while other bile salts may cause harm (Kortner *et al*., 2016) [14]. Ding *et al.* (2020) [3] found that big yellow croaker fish were affected by the adverse effects of a high-fat diet on growth, *Larimichthys crocea*, may be reduced by increasing the amounts of bile acids from 0.015% to 0.045%. In rainbow trout (*O. mykiss*) fed a diet predominantly consisted of fishmeal, the addition of cholic acid at 0.5% or 1% resulted in higher lipid digestibility and lipase activity, however it did not influence growth or feed efficiency. (Jin *et al.*, 2019) [13].

Bile Acids: Key Role in Lipid Metabolism, Biochemical Composition, and Body Indices

Bile acid/salts can improve lipids digestibility coming from plant proteins (Iwashita *et al.* 2010; Gu *et al.* 2017) [11, 8], However, this was not observed in S. salar that were given taurocholate (cholyltaurine) or bovine bile salts (1.8%) on a diet primarily on plant protein. (Kortner *et al.* 2016) [14]. Hepato-somatic index (HIS) and viscera-somatic index (VSI) vary despite the fact that dietary bile salts/acids do not affect lipid digestion. Fish size/ growth tends to increase body lipid (Shearer 1994) [21], Nevertheless, additional variables might potentially play a role in this relationship in fish that are given dietary bile acids or salts. Dietary bile improved growth and whole-body crude lipid content in *S. maximus*, but it also increased lipid digestibility, intestinal lipase activity, and serum cholesterol (Gu *et al.*, 2017) [8]. However, introducing dietary bile acids resulted in a significant decrease in body/muscle fat in *Oreochromis niloticus*, with growth being either increased or decreased depending on the concentration. (Jiang *et al.* 2018) [12]. Feeding dietary bile acids to *C. idella* enhanced growth while decreasing body/liver lipid content. (Zhou *et al.*, 2018) [30]. The result was probably due to the increased expression of genes involved in lipid breakdown, such as pancreatic triglyceride lipase and hormone-sensitive lipase, as well as in fatty acid burning, including hepatic, muscle, and adipose tissue PPAR-alpha. Sun *et al.* (2014) [22] was observed that include bile acids in the diets of turbot, S. maximus, with lipid levels of 10% or 18% resulted in a substantial drop in muscle polyunsaturated fatty acids (PUFA) while increasing levels of monounsaturated and saturated fatty acids. Dietary bile acids were found to increase the expression of CPT-1 and fatty acid synthase (FAS), enzymes involved in long-chain fatty acid oxidation as well as de novo lipogenesis of saturated or monounsaturated fatty acids (Zhou *et al.*, 2018) [30].

Bile Acid Levels: Influence on Gut Microbiota Composition and Organ Histomorphology

The intestinal microbiota is the varied and dynamic community of microorganisms that inhabit in the intestines. Dietary choices have a substantial impact on this microbiota, which affects numerous aspects of fish health, including disease resistance and nutrition metabolism. Advanced techniques such as metagenomics and high-throughput sequencing have provided useful genetic information, allowing for a better understanding of how diet effects the complicated interplay between the microbiome and human metabolism. Bile salts, in addition to producing secondary bile acids, which have been shown to have both antibacterial and beneficial effects on different intestinal microbes in mammals, bile salts play a crucial role in shaping the structure of the intestinal microbiota. This shows that dietary factors may influence the microbiome's composition and function, ultimately impacting the overall health and well-being of the host organism. (Begley *et al.* 2005; Urdaneta and Casadesus 2017) [1, 24]. Bile acids directly suppress bile-sensitive gut microbiota by disrupting their cell membranes, destroying their DNA, and affecting the structure of proteins within the bacteria. Bile acids can promote the growth of other microbes that can utilize bile acids for their own growth and survival (Ridlon *et al*. 2014; Urdaneta and Casadesus 2017) [17, 24]. Studies on mice have shown the impact of bile acids on the composition of the gut microbiota. (Devkota and Chang 2015; Zheng *et al*. 2017) [2, 29]. Bile acids might potentially influence the composition of gut bacteria, hence impacting bile acid profiles. (Yokota *et al*., 2012) [27]. Indeed, there is continuous data suggesting that bile salts can also impact the gut microbes. Current study in this field mostly focuses on *C. idella*, with fairly varied results. (Xiong *et al*. 2018; Zhou *et al*. 2018) [25, 30].

Study indicates that consuming high amounts of dietary bile acids might result in negative consequences. The dose-response investigation found that liver abnormalities were caused in *Oreochromis niloticus* at the highest concentration studied, which ranged from 0% to 0.135%. The abnormalities observed were nuclear migration and hepatocyte vacuolization. No harm was detected. (Jiang *et al*. 2018) [12]. Despite the presence of higher serum aspartate aminotransferase (AST) and alanine aminotransferase

(ALT), which are frequently used as indications of liver injury based on the notion that raised serum levels are caused by lysed hepatocytes, no major liver damage was seen. (Ebrahimi *et al*. 2017) [4]. Jiang *et al*. (2018) [12] suggested that a surplus of bile acids results in a taurine deficit, as more taurine is required to produce bile acids and perhaps increases the possibility of bile acids binding with glycine. The final concept was based on observing that the gallbladder is more fragile and more susceptible to rupture under the most concentrated bile acid treatment. This is due to the formation of insoluble salts from glycine-derived bile salts, which results in the calcification of the gallbladder. (Jiang *et al*. 2018) [12]. According to the current research, bile acids in fish are not synthesized with glycine, as mentioned in the section on Bile acid production and circulation. Elevated serum AST and ALT levels might be exacerbated by heightened susceptibility to hemocyte lysis caused by taurine deficiency. (Takagi *et al*. 2010) [23]. Increasing dietary supplementation of unconjugated bile acids may enhance interest in taurine compared to using taurocholate (cholyltaurine), which is cholic acid combined with taurine. Initially, it was believed that taurine deficits produced biliary obstructions, resulting in the buildup of bile salt and the development of "green liver syndrome" in *P. major*. (Goto *et al*. 2001) [7]. The scientists eventually determined that the increased presence of bile pigments, such as biliverdin and bilirubin, was due to severe hemolysis caused by the osmotically weak hemocyte membranes resulting from a taurine shortage. (Takagi *et al*. 2010) [23]. Research shown that dietary taurine can prevent "green liver syndrome" in Se. quinqueradiata as reported in Reviews in Aquaculture, 1–26. Copyright 2019 Wiley Publishing Asia Pty Ltd 19 Effects of diet on bile acid metabolism in fish (Takagi *et al*. 2010) [23] and totoaba, Totoaba macdonaldi (Satriyo *et al*. 2017) [20]. In T. carolinus, hepatocyte hemolysis, hematocrit, or increased bilirubin were not indicative of a taurine deficiency. Instead, liver vacuolization decreased cytochrome C oxidase and certain amino acids in the muscle (Salze *et al*. 2016) [19]. Although Salze and Davis (2015) [18], have thoroughly examined the significance of dietary taurine. The last section will briefly examine the potential effect of dietary taurine on bile acid levels, focusing on recent studies. Table 1 provides the levels of bile acid supplementation in high-fat diets for different species.

Table 1: Requirement of Bile acid of different species at the different sizes

Species	Body weight. (g)	Dose (g per kg of feed)	Condition	Duration Experiment (Days)	References
Nile tilapia	20.14	0.5	Fed with high lipid diet + bile acid	56	El-Shenawy *et al.*, 2020 [5]
Larimichthys crocea	12.25	0.3 – 0.45	Fed with high-lipid (18%) diets + bile acid	70	Ding *et al.* (2020) [3]
Micropterus salmoides	23.69	0.35	Fed with high-starch diet + bile acid	56	Guo *et al.*, 2020 [9]
Micropterus salmoides	6.17	0.3	Fed with high starch diet + bile acid	70	Yu *et al.*, 2019 [28]
Ctenopharyngodon idella	69.91	0.06	Fed with bile acid supplemented high lipid diet	56	Zhou *et al.*, 2018 [30]
Oreochromis niloticus	8.27	0.15	Fed with plant-based diets + bile acid	63	Jiang *et al.*, 2018 [12]

Conclusion

The role of bile acids (BAs) in the field of aquaculture nutrition cannot be overemphasized in addressing the challenges toward food and nutritional security in the face of the growing global population. Food consumption has been forecasted to increase significantly by 2050, meaning that sustainable feeding is of the essence within the food and feed industry. Bile acids are one of a complex milieu of physiological particles that participate in the growth and regulation of gut microbiota in aquatic species and with the processes of assimilation of nutrients. In aquaculture, however, reliance on plant-based feeds is problematic because such dietary components often lack these required components to stimulate optimal BA production, which, in turn, causes limited lipid utilization and poor fish growth. Although plant-based feeds when supplemented with BAs possess potential for improving fish growth and nutrient utilization, such effects are variable between species.

Second, BAs can have an effect on lipid metabolism, biochemical composition, and indices in aquatic organisms that have their influence on growth and lipid levels. Finally, BAs have a major effect on gut microbiota composition, in parallel with organ histomorphology, with the implication that it affects the overall health and resistance against disease in fish. Though the BAs supplementation process is beneficial in all ways in aquaculture, there are both advantages and disadvantages, and care needs to be taken in this process because it may have several adverse effects, in dosage, on fish health. More research and understanding in such areas regarding the complex relationship among BAs, diet and fish physiology should be realized for sustainable feeding programs that can address increasing food demands with least resource utilization and environmental pressures within the aquaculture industry.

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