Metabolomic Insights into Fish Oil Replacement with Other Alternatives: A Mini Review

Syed Izhar Ullah Shah[1], Ching Fui Fui[1], Yoong Soon Yong[2,3], Chuan Chee Hoe[1], and Muhammad Dawood Shah[1]*

[1]Higher Institution Centre of Excellence (HICoE), Institut Marin Borneo, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia.

[2]China-ASEAN College of Marine Sciences, Xiamen University Malaysia, 43900 Sepang, Selangor, Malaysia

[3]R&D Quality Department, Osmosis Nutrition Sdn Bhd, Bandar Nilai Utama, 71800 Nilai, Negeri Sembilan, Malaysia

Corresponding author: dawoodshah@ums.edu.my

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Abstract

The rapid growth in the aquaculture sector has resulted in the need to find alternative sources of fish oil (FO), which is rich in LC-PUFAs. Most alternative lipid sources can promote normal growth of fish; however, conventional evaluation methods emphasize performance rather than considering the overall metabolic impact on fish health and product quality. This mini review highlights the use of metabolomics to understand the biological effects of FO replacement in aquafeeds. Metabolomics enables detailed analysis of the effects of dietary lipid substitution on key physiological processes by examining low-molecular-weight metabolites. Major metabolic pathways of β -oxidation, glycolysis, and the oxidative stress-related pathway are altered during lipid substitution. Recent research indicates that the oxidative stress reactions, immune response, and lipid metabolic pathways are species-specific and are changed after FO replacement. This review summarizes metabolomic data on key alternative lipid sources, including vegetable oils, animal fats, microalgal oils, and crude palm oil (CPO). CPO is a promising alternative due to its low cost and bioactive compounds. In addition to being used as substitutes for FO, these substitutes can also modify the fatty acid composition of fillet, antioxidant activity, and immune response differently. However, critical gaps remain, particularly in the application of untargeted metabolomics across species and life stages. Integrating metabolomics with other omics approaches will be essential to develop sustainable aquafeeds and identify biomarkers for long-term fish health.

Keywords: Aquaculture nutrition, Metabolomics; Fish oil (FO) replacement, Alternative lipid sources, Crude palm oil (CPO)

Introduction

Aquaculture has emerged as the most rapidly spreading animal food production industry and has assumed a vital role in addressing the demands of the world in terms of high-quality aquatic protein. At the heart of this development is aquaculture nutrition, which has always considered FO as a primary lipid source because of its richness in LC-PUFAs, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), all essential to fish development, well-being, and product quality (Wong et al., 2025). However, the sustainability of FO is becoming a controversial topic since it is mainly sourced through limited wild fish species, which means it is susceptible to overexploitation, fluctuation, and environmental limitations (Demets & Foubert, 2021).

To overcome these issues, many studies have been conducted to find alternatives to FO by using vegetable lipids (e.g., soybean, rapeseed, palm, sunflower, linseed), animal lipids (e.g., lard, poultry fat, beef tallow), microbial lipids (e.g., microalgae oils such as *Schizochytrium sp.*), and other agro-industrial (Oliva-Teles et al., 2022). The traditional techniques for the evaluation grounded in growth and proximate composition are not adequate to entirely reflect these metabolic changes, and complex analytical tools are required (Roques, Deborde, Richard, et al., 2020). Among these alternatives, microalgal oils are especially important given that they offer a direct and sustainable source of EPA and DHA to supplement the functional value provided by alternative lipid sources, including CPO. The technique of metabolomics has gained momentum in aquaculture nutritional studies to systematically analyse the low-molecular-weight metabolites, indicating physiological and biochemical conditions. It offers insights into key metabolic and physiological processes, going beyond the conventional performance metrics (Cao et al., 2022). It is important to note that strategies of lipid substitution also systematically adjust metabolic pathways of relevance to most energy balance systems, namely β-oxidation, glycolysis, and oxidative stress-associated pathways, along with associated physiological adjustments. Recent metabolomic analysis of FO nutrition has indicated that amino acid metabolism, core energy, and redox pathways are some of the major pathways that dietary lipid substitution can notably alter (Liu et al., 2024; Salaro et al., 2022). In the case of glucose, lactate, and certain amino acid changes, metabolic adaptation and energy consumption changes can be observed. Moreover, changes in antioxidant-related metabolites indicate a change in the oxidative stress response, which should not be ignored when it comes to the choice of lipid sources that could enable the pharmacological balance in physiology. This method is especially useful when subtle metabolic changes due to FO substitution plans are to be evaluated, which cannot be determined by traditional analyses. For example, Nuclear magnetic resonance (NMR) based metabolomics can give high sensitivity in identifying key metabolites, including key metabolic intermediates, whereas Liquid chromatography mass spectrometry (LC-MS) techniques can give high-sensitivity profiles of lipid-derived metabolites, including acylcarnitines and oxidized fatty acids, which are directly related to the β-oxidation pathway and oxidative.

CPO, a major product of the palm oil industry, has received prominence as a potential alternative source of lipids, given that CPO is cheap, is abundantly available in large quantities, and is also full of bioactive compounds, including tocopherols, tocotrienols, and carotenoids. On the production side, palm oil is currently one of the most available vegetable oils, producing more than 70 million tonnes every year, which further challenges the notion that it can be used as an alternative to FO due to its potential in sustainability. However, in contrast to the microbial oils like *Schizochytrium sp*., which more directly provide the essential LC-PUFAs (EPA and DHA), CPO mainly provides energy and antioxidant properties. Thus, lipid sources complement each other in the nutritional intake of fish, making it important to select or combine them wisely. Recent research indicates that under dietary conditions of CPO substituting FO in part or entirely, CPO has the potential to increase fish resistance to diseases, optimize lipid metabolism, and boost antioxidant capacity (Samsi & Asthutiirundu, 2022). Other variations like soybean oil, microalgae oil, and several animal fats are also examined as functional substitutes of lipids in similar studies. Both these sources contain unique fatty acids and have varied effects on metabolism (Davis et al., 2021; Liu et al., 2024). But we still know little about the metabolic processes involved, and in particular, their effects on a larger, systemic scale in fish.

This mini review will summarize the existing metabolomic findings concerning the topic of FO substitution in aquaculture feeds with a wide range of alternative lipid sources. To give context, we initially describe in a structured manner an overview of the key alternative lipid categories and their properties. Subsequently, by combining the results of metabolomics-based research, this review aims to clarify the key changes in metabolic pathways caused by lipid substitution and to outline knowledge gaps to inform future studies towards more sustainable and nutritionally efficient aquafeeds.

Materials and Methods

This mini review was a narrative review performed through a search of the scientific literature. The combinations of such keywords in such databases as Scopus and Google Scholar were queried: metabolomics, aquaculture nutrition, FO replacement, alternative lipids, CPO, soybean oil, microalgae oil, animal fats, and vegetable oils. Peer-reviewed articles, reviews, and conference proceedings published till 2026 were deemed relevant. Results were tabulated to give a logical review of the present metabolomic studies on the topic, with special emphasis on the formation of universal metabolic reactions, and CPO was used as an example.

Results

Importance of FO

The role of FO in the physiology of aquatic animals, including omega-3 PUFAs like EPA and DHA, varies in importance, with a positive effect on membrane structure, neural development, immune response, and reproductive performance. Such fatty acids play a vital role in the fluidity of cell membranes, the control of inflammatory responses, larval development, and survival in most fish species. In aquaculture, FO is very significant in the optimal growth, as anything that causes stress or diseases (Mansour, 2023). These physiological roles contribute to FO being an important ingredient in aquafeeds because most fish species have a limited capacity to produce LC-PUFAs de novo. Consequently, EPA and DHA are required in the diet to ensure that normal metabolic and physiological functions are maintained, especially in marine organisms (Emery et al., 2016).

FO contains a lot of the benefits of omega-3 PUFAs of EPA and DHA, and has many health benefits. It is especially useful in the prevention of cardiovascular diseases as it decreases triglycerides and decreases blood pressure in addition to enhancing the functioning of endothelial cells (Liao et al., 2022). The functions of the omega-3 fatty acids in the development of the brain, retinas, and sperm also have a very important role (Politano & López-Berroa, 2020). Also, FO has anti-inflammatory effects, which are useful in such ailments as rheumatoid arthritis and other autoimmune disorders (Balachandar et al., 2023). Although FO supplements offer numerous advantages, they contain varying amounts of EPA and DHA, and this may have an impact on their effectiveness (Hilton et al., 2024). Additionally, there have been the raising of concerns over the existence of heavy metals and environmental toxins in FO, although advantages usually supersede the dangers (Wong et al., 2025). The effects of FO on reproductive health also stand out, as it has inconsistent impacts on the formation of prostaglandins, the production of oocyte and sperm motility (Trop-Steinberg et al., 2024). In general, FO can be successfully used as a supplement in a variety of health conditions, although it should be taken in the right dosages and sources (Tewari et al., 2022).

Alternative Lipid Sources for FO Replacement in Aquaculture Nutrition

The short supply of wild fish stocks, coupled with increasing demand for FO in the aquaculture industry due to its desirable omega-3 fatty acids, has prompted efforts to find alternative sources of sustainable aquaculture feed. There is a broad assortment of alternative lipid ingredients that have been tested as an alternative to FO. Among them, there are vegetable oils which include soybean, rapeseed (canola), sunflower, and linseed oil; animal fats like beef tallow, pork lard, poultry fat, and fish offal oil; and microbial oils which are sourced by microalgae, including the *Schizochytrium* sp. Microalgae, including *Schizochytrium* sp., have demonstrated high potential, as they are less harmful to the environment with fewer negative impacts on biotic resources and global warming potential than conventional FO (Davis et al., 2021; McKuin et al., 2022).

Every lipid source has a unique fatty acid content, and this is critical in the determination of its metabolic effects in fish. An example is that CPO is rich in palmitic (C16:0) and oleic acid (C18:1), it is mainly composed of palmitic acid (C16:0, ~40–45%) and oleic acid (C18:1); soybean oil is very rich in linoleic acid C18:2, as compared to rapeseed (canola) oil, which has a high content of oleic acids (~ 55-65 %), sunflower oil is dominated by linoleic acid (5070 percent). Saturated and monounsaturated fatty acids commonly constitute the animal-based fats, and occasionally LC-PUFAs, such as docosahexaenoic acid (DHA are common components of microalgal oils, in high proportions depending on the species (e.g., *Schizochytrium* sp.) (Delavarian et al., 2025). Such compositional variations constitute the major source of variability in metabolic and physiological processes in fish, which affects the lipid metabolism, energy expenditure, and general health conditions.

One of the most available and cheap vegetable oils is CPO. In addition to providing essential fatty acids, CPO contains a significant number of bioactive compounds, including tocopherols and carotenoids, and provides better antioxidant potential and oxidative stability to fish diets. On the same note, linoleic and α- linolenic acids, the precursors in the manufacture of LC-PUFA in fish, are rich in other vegetable oils like soybean and linseed oil (Salaro et al., 2022). Animal fats provide a good source of energy and can also be used to substitute FO, as far as growth performance is concerned. Nevertheless, they tend to distort the fatty acid profile of fish fillets, with the trend generally being towards higher amounts of saturated and monounsaturated fatty acids (Liu et al., 2024). This is because the fatty acid composition of fish tissues is largely dependent on the lipid profile of diet fat sources, be it vegetable or animal-based (Bordignon et al., 2020). Experimental research, both summarized in Table 1 and practical studies, shows that CPO could be used to substitute FO in other species like largemouth bass without negative effects on growth performance when it is fresh and not oxidized (Jiang et al., 2023; Yun et al., 2013). Furthermore, tropical species like Asian seabass (*Lates calcarifer*) and groupers have also shown promising responses to alternative lipid sources, and this shows the wider applicability of FO replacement efforts to a variety of aquaculture systems. Evidence on these species suggests that the alternative lipids (such as CPO and other vegetable oils) could sustain growth performance and affect metabolic and physiological responses in a way similar to temperate species (Safiin et al., 2022; Samsi & Asthutiirundu, 2022). Such outcomes can be extrapolated to other substitutes, i.e., rapeseed and soybean oils have been successfully used as the hybrid sturgeon and gilthead seabream, respectively (Yu et al., 2020). To promote not only the sustainability of aquaculture but also address ethical and environmental issues related to the traditional use of FO, the incorporation of these alternative ingredients is also essential (Matias et al., 2024; Tignani et al., 2024). Moreover, CPO utilization is also correlated with the principles of the circular economy, which aims to instead of relying on marine resources to secure a favorable effect on metabolic health as well as to valorize an existing agro-industrial product (Li et al., 2025). Otherwise, when one develops sustainable columns in the aquafeed, a strategy must be developed to integrate the various replacing lipids depending on their presence, price, and their impacts on metabolism.

An extensive variety of lipid substitutes have been considered to substitute for fish oil in aquaculture feeds. The vegetable oils, animal-based fats, and microbial or algal oils are all equally broad categories of these substitutes, each having different nutritional and sustainability impacts (Figure 1). These alternatives are briefly summarized below, and crude palm oil is later discussed.

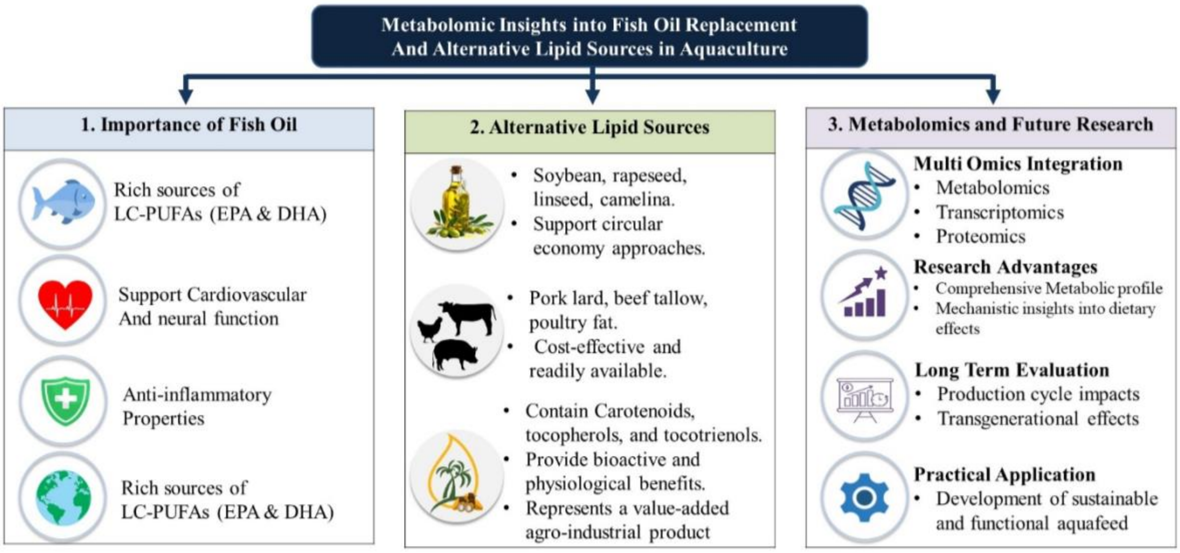

Figure 1. Overview of FO importance, sustainability challenges, alternative lipid sources, and the role of metabolomics in evaluating dietary lipid replacement in aquaculture.

Overview of Fish Oil (FO) Replacement Strategies

The motivation behind various initiatives to substitute FO with aquafeeds is a combination of the realities of exhaustible marine resources, the high prices of FO, and the necessity to create a more environmentally sustainable aquaculture. To find the appropriate alternatives, one has to compare them to some important criteria. These are a good fatty acid composition, high digestibility and energy efficiency, good effects on fish health and growth, low adverse effects on fillet quality (particularly its nutritional benefits to the consumer), and sustainability and cost-effectiveness, in general. The primary types of substitutes under consideration are vegetable oils, animal fats, microbial and algal oils, and mixed lipid approaches.

Vegetable Oil Sources

The most commonly studied and utilized alternatives to FO are vegetable oils, as they are available globally and are cheaper. Alternatives to FO in aquafeeds, such as vegetable oils, have been well-investigated, and each has a unique fatty acid profile that has both impacts on fish performance and ultimate fillet quality. Soybean oil, which contains a lot of linoleic acid (18: 2 n-6), is the most common and is a good growth promoter, but its intake usually decreases the levels of EPA and DHA in fillets, making it incumbent to use it as a partial replacement strategy (Yu et al., 2020). By comparison, rapeseed or canola oil has a well-balanced profile of monounsaturated and polyunsaturated fatty acids that are easily digestible and has been effectively utilized in fish such as gilthead seabream, salmonids, and sturgeon, although large proportions in the diet may require a finishing grain with a FO to replenish LC-PUFA (Izquierdo et al., 2003; Yu et al., 2020). Linseed oil contains the highest levels of the richest source of 18:3n-3, 18:3n-3 or alpha-linolenic acid (ALA) as the precursor to endogenous synthesis of EPA and DHA, although its conversion efficiency is low, especially in marine fish, and is widely used in combination with other lipid sources to provide a balanced fatty acid composition (Salaro et al., 2022). In the meantime, oils such as sunflower oil, high in linoleic acid, are often combined to assist in energy intake but, just like the soybean oil, are deficient in omega-3 fatty acids and need to be supplemented with other sources to maintain fillet nutritional quality (Mozanzadeh et al., 2016). CPO is one of the suggested options, and its popularity is supported by the availability, affordability, and the availability of bioactive compounds that can be effectively utilized.

Crude Palm Oil (CPO) as a Functional Feed Ingredient

CPO is gaining acceptance as a viable functional feed in marine aquaculture with both nutritional and significant environmental and economic properties. CPO is a good source of saturated and monounsaturated fatty acids, especially palmitic and oleic acids, in addition to being a low-cost alternative energy source instead of FO. Reports point to the ability of CPO to partially or completely substitute FO without having an adverse impact on the growth performance and survival of such species as Asian seabass and barramundi (Safiin et al., 2022; Samsi & Asthutiirundu, 2022). CPO is also a source of natural antioxidants, especially tocopherols and tocotrienols that improve immune performance and alleviate oxidative stress in fish (Reda et al., 2020). Nevertheless, having it in diets may be linked to lower concentrations of LC-PUFAs, e.g., EPA and DHA, in fish flesh (Safiin et al., 2022; Samsi & Asthutiirundu, 2022). CPO production can be more eco-friendly than FO, but issues of deforestation and loss of biodiversity persist, which demonstrates the need to consider responsible sourcing and certification (Purnama et al., 2025). CPO tends to be more cost-effective than FO and most other vegetable oils due to its extensive distribution, low price, and large energy content, thus making it an attractive choice when creating aquafeed (Fan et al., 2024).

Animal-Derived Lipid Sources

Another possible substitute is the lipids of terrestrial animals. Common ones are fat of poultry, beef tallow, pork lard, as well as fish processing by-products (oils). These fats boast of high energy content and are easily digestible, thus they are economical with regard to supporting the basic energy needs of fish. Nevertheless, they tend to raise the proportion of saturated (SFA) and monounsaturated fatty acids (MUFA) in the fish fillet while lowering the concentration of the omega-3 LC-PUFA (Liu et al., 2025; Mozanzadeh et al., 2016). This increase of SFA and MUFA can be observed using metabolomic methods, as a change in β-oxidation intermediates, lipid peroxidation indicators, as well as energy metabolism indicators (e.g., TCA cycle metabolites) are indicative of changes in energy use and oxidative state in fish. So, they are optimal in partial replacement plans. Environmentally speaking, the use of animal by-products will contribute to the principles of the circular economy by demonstrating the value of waste products of other food production industries.

Microbial and Algal Oils

The microbial and microalgae-based oils, including those of *Schizochytrium sp*. and *Nannochloropsis sp*are a promising future alternative source of lipids. Their main strength is that they are both excellent sources of DHA and EPA, which are very long-chain PUFAs, the signature of FO. These oils are the result of fermentation in laboratory settings and provide a sustainable and scalable substitution that is not based on the availability of wild fish. Although currently constrained by their high cost of production, they have enormous potential to completely replace FOs and especially (within) the finfish niche to enrich the LC-PUFA content of farmed fish fillets prior to harvest (Davis et al., 2021; McKuin et al., 2022).

Blended Lipid Strategies

Since there is no single available alternative to FO that fully matches the lipid profile and functional characteristics of FO, integrated lipid policies are usually most effective in commercial feeds. Formulators have a chance to balance the cost, growth outcomes, and the end fillet quality by incorporating various sources of lipids, including a vegetable oil to provide energy and affordability, an animal fat to provide energy, and an algal oil to provide essential omega-3s. Such a strategy enables a greater customization of the diet lipid profile to the needs of the cultured species and may be combined with a finishing diet strategy to complete the nutritional benefit of the final product.

Sustainability and Future Perspectives

The shift towards alternative lipids is integral to building a more sustainable aquaculture industry. This does not just imply the replacement of FO, but also becomes the application of the principles of the circular economy through the use of the by-products of agriculture and food processing. In the future, biotechnology might result in the creation of specially designed engineered oils that have fatty acid profiles. Finally, precision nutrition is the vision: developing species-specific, stage-specific diets that are optimal in terms of promoting fish health and productivity with minimum harm to the environment.

Metabolomic Applications in Aquaculture Nutrition

The above descriptions have outlined the available options of alternative lipid sources that can replace FO. Although these options have been mostly justified by growth performance and feed efficiency, there is an urgent need to know the physiological and metabolic impacts of these options on the fish. It is at this point that metabolomics comes in as a necessary instrument that will enable us to assess the minor yet important metabolic modifications to lipid substitution in the diet. The use of metabolomics in aquaculture nutrition, despite these achievements, is relatively under-explored as opposed to other omics techniques. Most of the current literature is based mainly on targeted studies or has investigated only a small number of metabolites, and these may not be the most extensive metabolic responses to a dietary lipid substitution. This weakness limits us to comprehending intricate connections between lipid metabolism and energy utilization, oxidative stress, and immune reactions at a global scale. Thus, it will be necessary to increase the application of untargeted methods in metabolomics technology, using larger datasets and comparisons across species to discover new metabolic processes and biomarkers. Moreover, the application of metabolomics in conjunction with other technologies (transcriptomics and proteomics) might give an entirely different insight into, at a systems level, the effect of the use of other sources of lipid on fish physiology. The future of sustainability in aquafeed nutrition will require such progress to build it in terms of precise nutritional strategies and enhanced sustainable formulations of aquafeed.

Rationale for Using Metabolomics in Fish-Oil Replacement Studies

The main justification for using metabolomics to achieve this is the human difference in the fatty acid composition between FO and its substitutes. Replacing FO with, say, a vegetable oil or an animal fat implies a different ratio of fatty acids that may have significant implications on major physiological functions. These are energy metabolism routes (e.g., glycolysis, 2 oxidations, TCA cycle), immune activity (by altering the synthesis of signaling molecules such as eicosanoids), response to oxidative stress (because of varying levels of pro- and antioxidants), and nutrient utilization efficiency in general. Metabolomics is one method that offers a holistic picture of these processes in a manner that the dietary intervention is directly related to the metabolic condition and overall health status of the fish.

Overview of Metabolomics

Metabolite analysis in biological samples is becoming a common practice in the field of aquaculture to improve the efficiency of the process and health, as well as the sustainability of fish. Metabolomics can be instrumental in the identification of biomarkers that signify physiological changes in response to environmental or culture conditions and which can be used to manage hatchery production (Roques, Deborde, Richard, et al., 2020). It can give insights into how various feeds influence fish metabolism, which can be used to optimize diets. As an example, fish have been shown to grow better and regularly fed on plant-oriented diets were supplemented with insect protein extracts (Roques, Deborde, Guimas, et al., 2020; Yadav et al., 2025). Also, other feeds can be evaluated with regard to their effects on fish nutrition and health using metabolomics (Kumari et al., 2022; Yadav et al., 2025). Nutritional and disease-related metabolic disorders can be diagnosed using metabolomics, which can be used to manage health in aquaculture (Aru et al., 2021; Sahoo et al., 2022). It can detect how stress changes or disease changes (or immune responses) impact metabolism, which can inform interventions (Alfaro et al., 2022). As a particular example in assessing alternative lipids, metabolomics could identify the impact of various dietary oils on these pathways and provide a mechanistic insight into their effects on fish.

Analytical Platforms

NMR spectroscopy is the most common analytical platform in metabolomics, even though it is less sensitive than mass spectrometry (MS) (Emwas et al., 2019; Nagana Gowda & Raftery, 2022). The high reproducibility of NMR, the lack of destruction, and the possibility to identify the unknowns and determine absolute concentrations make NMR useful in long-term clinical studies, as well as in the analysis of complex mixtures (Emwas et al., 2019; Nagana Gowda & Raftery, 2021, 2022). Innovations in technology, including

CryoFlowProbes™, hyperpolarization methodologies, and technologies, have enhanced the detection limit and sensitivity of NMR (Pawar et al., 2025). Integration of NMR with MS advances metabolite brokering, taking advantage of structural elucidation of NMR and high sensitivity of MS (Borges & Teixeira, 2024; Gathungu et al., 2020). Combined methods such as LC-MS-NMR and smart tags are also used to optimize the detection and identification of metabolites even more (Gathungu et al., 2020). There is a wide range of applications of NMR, including drug discovery, disease management, and environmental research, which proves its universal applicability and relevance in metabolomics research (Nagana Gowda & Raftery, 2021; Pawar et al., 2025; Yu et al., 2024).

Advantages in Fish Nutrition Research

The metabolomics offers a detailed study of the metabolites, whose researchers were able to learn about the physiological and biochemical processes that underlie nutritional interventions in fish. This methodology can be used to explain the impact of various nutrients and feed ingredients on fish metabolism and health in general (Roques, Deborde, Richard, et al., 2020; Zhang et al., 2025). A vital use of metabolomics is the identification of dietary biomarkers. These biomarkers have the ability to effectively quantify diets and nutritional status objectively, surpassing shortcomings of the conventional self-reporting techniques. Metabolomics play a major role in the identification of new biomarkers that are reflective of the consumption of specific nutrients and nutrition-eating habits and could be utilized to track and enhance fish nutrition (Kortesniemi et al., 2023). Metabolomics enables the assessment of functional ingredients in fish diets through the metabolic responses to the various components of the feed. The method can be used in evaluating the efficacy and effects of other options of feeds, like plant-based resources, on fish development, well-being, and metabolism. Metabolomics can be used to design more sustainable and efficient aquaculture feeds by offering valuable information about the metabolic modifications associated with different dietary interventions (Roques, Deborde, Richard, et al., 2020; Yadav et al., 2025). Metabolomics promotes nutritional research in fish by providing deeper insights into underlying nutritional mechanisms, identifying biomarkers that can be trusted, and assessing the effects of nutritional ingredients, thus supporting more accurate and efficient nutritional interventions in aquaculture.

Application to Alternative Lipid Sources

The idea of metabolomics perfectly answers the question of why a more comprehensive analysis of FO alternatives is essential and should be used to define the metabolic effects that they provoke. Research has used these methods to characterize the impact of many lipid classes, in which species-specific alterations in metabolism were found. To provide an example, vegetable oils may change the hepatic lipid metabolism and raise the level of glucose (Yu et al., 2020), and animal fats can promote higher lipid peroxidation in a specific situation (Silva-Brito et al., 2019). To be more precise, has been indicated that the substitution of FO with animal fat in tiger puffer has caused a drastic shift in the metabolites related to lipid oxidation and antioxidant defenses, i.e., their effect on controlling glutathione-related circuits, demonstrating better oxidative balance. Similarly, (Salaro et al., 2022) also found that fed linseed oil increased the intermediates of fatty acid elongation and desaturated pathways within fish, and they showed improved endogenous production of long-chain polyunsaturated fatty acids. In another study, indicated that glucose and lactate were higher in fish fed vegetable oil-based diets, implying a metabolic changeover to the use of glycolytic energy. Microalgal oils, a direct source of LC-PUFAs, are supposed to be able to yield metabolic profiles closer to FO, but it still remains a subject of study. In the example of CPO, the metabolomics technique can be applied in order to match bioactive compounds of CPO, like tocopherols and carotenoids, to the observed changes in antioxidant capacity and immune responses by tracing the changes in related metabolites. Altogether, these investigations prove that metabolomics is able to trace the effects of lipid replacement on fatty acid metabolism, antioxidant systems, immune processes, and energy expenditure in fish.

Although these studies offer broad information about metabolic changes, a specific response at the level of metabolites may be gained better through analysing particular responses. To enhance the metabolomic explanation of lipid substitution further, a variety of studies have also depicted unique changes in metabolites at specific levels with distinct physiological meanings. Indicatively, fish fed with vegetable oil-based diets tend to exhibit augmented quantities of glucose and lactate, signifying a metabolic alteration of higher glycolysis and diminished dependence on lipid β-oxidation to generate energy (Yu et al., 2020). This implies that reduced supply of LC-PUFAs in these diets could limit fatty acid oxidation in the mitochondria, thus promoting the use of carbohydrates as an alternative energy source.

Moreover, changes in the acylcarnitine profiles, which are significant intermediates in the processes of fatty acid transport in the mitochondrion, have been detected in the case of the replacement of FO with a saturated or monounsaturated lipid source (Liu et al., 2024). Modifications in the levels of acylcarnitine can be manifestations of disturbances or adjustments of β-oxidation routes and could represent energy metabolism bottlenecks.

The dietary lipid composition is also important in relation to oxidative stress-related metabolites. As an example, the alterations in glutathione metabolism of fish fed alternative lipids, especially a change in reduced-oxidized glutathione ratio (GSH/GSSG), have been reported, indicating alterations in redox balance and antioxidant activity in the cellular environment (Liu et al., 2024). On the other hand, high concentrations of lipid peroxidation-related products like malondialdehyde (MDA) indicate oxidative damage caused by low-quality or oxidized food lipid (Jiang et al., 2023).

Furthermore, α-linolenic acid (ALA)-enriched diets (linseed oil) have been found to raise intermediates in fatty acid elongation and desaturation processes, an indication of endogenous synthesis of the LC-PUFAs(Salaro et al., 2022). This is a compensatory metabolic effect in species able to catabolize C18 fatty acids as longer-chain fatty acids like EPA and DHA, but this ability is restricted in many marine species.

Together with these findings of metabolomics, it can be observed that FO alternative induces coordinated variations in energy metabolism, regulation of oxidative stress, and lipid bioconversion processes. The implications of these changes on fish health, stress response, and fillet nutritional value have direct implications on the selection of lipid sources when aimed at promoting metabolic stability in conjunction with growth performance.

Metabolic Responses

Along with the search for suitable substitutes, recent research has been more focused on understanding the impact of various sources of lipids on the metabolic and physiological performance of fish. Metabolomic analysis can offer a potent means to analyze these effects through identifying biochemical alterations linked to various dietary lipids. These studies have started to define the individual metabolite profiles of various categories of alternative lipids with an insight into nutrient assimilation, health conditions, and feed efficiency broadly. This summary of these metabolomic responses is presented in Table 1. The fatty acid profile of the experimental diets is the composition of fatty acids of the experimental diets, depending on the source of lipid applied. Metabolomic responses are metabolic products and biochemical routes that were characterized with the help of NMR and LC-MS analysis. In this table, only the data of the metabolomics derived data appear; the growth performance and physiological outcomes are reported separately in the main text.

Sustainability and Practical Implications

The results of metabolic research studies of alternative lipids directly relate to sustainable feed formulation. CPO, an agro-industrial by-product of high relevance, can be utilized to make aquafeeds in a sustainable manner that promotes the concepts of the circular economy. By making use of other by-products of producing microalgae, like animal fats and oils, this serves to save on resources, too. In addition to financial advantage, CPO has been shown by a metabolomic study to enhance stress-tolerance and antioxidant potential of farmed fish. Other options, such as microalgae oils, have been studied since they may directly improve the nutritional value of fish fillets by adding LC-PUFAs. This would potentially result in better health of stocks and reduced reliance on artificial diet antioxidants, which would be beneficial to the environment and sustainable economic performance. CPO is also useful in alleviating the pressure on wild fish populations and maintaining the efficiency of production through the replacement of readily available terrestrial lipids by marine-obtained lipids, which are limited in quantity. Finally, the potential implications of these results relate to dynamic, integrated lipid approaches that integrate alternative sources that have been selected depending on local availability, costs, and the metabolic requirements of the fish itself to create robust and sustainable aquaculture systems.

Table 1. Replacement of fish oil (FO) as an alternative lipid source in aquaculture species using metabolomics to detect its effects.

Fish Species	Scientific Name	Lipid Source	Replacement Level (%)	Dietary Fatty Acid Profile (Experimental Diet)	Metabolomic Responses (NMR/LC–MS Identified Metabolites & Pathways)	References
Gilthead seabream	*Sparus aurata*	Soybean, rapeseed, linseed oils	Up to 60	High C18 PUFA (linoleic, α-linolenic acids); reduced LC-PUFA	↑ Desaturase-related metabolites (Δ5, Δ6 activity); modulation of lipid metabolism pathways	(Izquierdo et al., 2003)
European seabass	*Dicentrarchus labrax*	Animal fats	Up to 100	High SFA and MUFA; low n-3 LC-PUFA	↑ Lipid peroxidation metabolites; altered oxidative stress pathways; changes in hepatic lipid metabolism pathways	(Silva-Brito et al., 2019)
Japanese seabass	*Lateolabrax japonicus*	Mixed lipids (lard, tallow, poultry fat, soybean oil)	50	Reflects dietary FA profile (higher SFA/MUFA)	Altered amino acid metabolites; shifts in energy metabolism pathways (e.g., TCA cycle intermediates)	(Xue et al., 2006)
Hybrid sturgeon	*Acipenser baeri × A. schrencki*i	Vegetable oils (soybean, corn, canola, sunflower)	Up to 100	High C18 fatty acids; variable n-3/n-6 ratios	↑ Glucose and lactate; enhanced glycolysis; altered hepatic lipid metabolism pathways	(Yu et al., 2020)
Silvery-black	*Sparidentex hasta*	Canola oil,	50–100	High MUFA (canola); high SFA	↓ Immune-related metabolites;	(Mozanzadeh et al., 2016)

Fish Species	Scientific Name	Lipid Source	Replacement Level (%)	Dietary Fatty Acid Profile (Experimental Diet)	Metabolomic Responses (NMR/LC–MS Identified Metabolites & Pathways)	References
porgy		sunflower oil, tallow		(tallow)	alterations in lipid metabolism pathways	
Largemouth bass	*Micropterus salmoides*	Soybean oil, poultry fat, palm oil	100	Diet-dependent FA composition; high SFA/MUFA in some treatments	↑ Oxidative stress-related metabolites (e.g., malondialdehyde, MDA); alterations in lipid metabolism pathways under oxidized lipid conditions	(Jiang et al., 2023; Yun et al., 2013)
Giant trahira	*Hoplias lacerdae*	Linseed, soybean, canola oils	100	High ALA (linseed); high linoleic acid (soybean)	↑ Intermediates of LC-PUFA biosynthesis: enhanced elongation and desaturation pathways	(Salaro et al., 2022)
Tiger puffer	*Takifugu rubripes*	Lard, fish offal oil	Up to 100	High SFA and MUFA; low LC-PUFA	↑ Glutathione-related metabolites (GSH/GSSG); modulation of oxidative stress pathways	(Liu et al., 2024)
Asian seabass	*Lates calcarifer*	Palm oil-based diet (CPO)	Partial–complete	High SFA and MUFA (palmitic and oleic acids)	↑ Antioxidant-related metabolites; enhanced oxidative stress response pathways	(Safiin et al., 2022)

Research Gaps

The extent of metabolomic analysis of aquaculture nutrition is poor despite the fact that there have been more studies on the efficacy of FO substitutes. The available body of research is focused on a small number of metabolites or is based on the targeted methodology and their ability to capture metabolic system adaptations. Consequently, the fundamental signaling pathways interacting with energy metabolism, lipid remodeling, oxidative stress, and immune regulation are often not detailed to the full extent.

Also, the studies are not consistent in their approaches to the selection of species, the experiment and analysis (e.g., NMR vs LC MU), and so on, which cannot be traced to each other. To demonstrate this, when other studies reveal positive alterations of glycolytic activity (e.g., elevated glucose and lactate levels) with vegetable oil diets, the other studies reveal their alterations with lipid oxidation and antioxidant pathways with the use of animal fats or diets containing saturated lipids. Such inconsistencies reveal that standard metabolomic frameworks might be required not only to permit cross-study comparisons but also to make more robust inferences.

The other restriction is that in the metabolomic research, the tropical and commercially important aquaculture species are poorly represented. Although an increasing number of species, such as the Asian seabass and groupers, are receiving research attention, most metabolomic basis information is about the temperate species, limiting the generalization of findings. Moreover, there is little research on long-term fed metabolically and life-stage specific effects or transgenerational impact, primarily on short-term feeding experiments.

Interestingly, a combined method of metabolomics with other omics has not been elaborated. There is a paucity of research incorporating metabolomic analyses alongside transcriptomic, proteomic, or microbiome analyses to provide a systems understanding of the influence of dietary lipids. Without such integration, one cannot possibly describe in all detail the mechanisms of regulation of the relationships between dietary input and metabolic output and physiological performance.

Future Research Direction

The next steps in dealing with these shortcomings include taking metabolite profiling beyond descriptive analyses to integrative and comparative analyses that characterize particular metabolic signatures with respect to physiology across brains. To enhance reproducibility and facilitate meaningful cross-study comparisons, standardization of experimental designs, such as dietary formulations, sampling strategies, and platforms used in analytical processes, will be necessary. Specifically, by applying untargeted metabolomics methods on a larger scale, the discovery of new biomarkers related to lipid metabolism, oxidative stress, and immune performance in response to dietary lipid replacement will be possible. The focus of future research must be on determining and confirming particular metabolite-based biomarkers, such as acylcarnitine (lipid oxidation), glutathione-related metabolites (oxidative stress), and eicosanoids (immune response), especially in connection with sustainable lipid sources like CPO.

To achieve a complete perspective of the impacts of CPO and other alternative lipids on fish physiology, future studies employing a multi-omics approach that integrates metabolomics with transcriptomics, proteomics, and microbiome analysis are suggested. Specifically, the untargeted metabolomics methods will be vital in capturing new and hitherto unknown lipid-derived metabolites and metabolic rearrangements that targeted assays can fail to capture. These integrated strategies will give a systems-based perspective of how dietary lipids can affect molecular pathways, including gene expression and metabolic flux. The species within aquaculture should be considered as a more diverse species, and studies should be done on metabolic reactions during the critically important stages in the life cycle, from larvae to broodstock.

The long-term feeding studies to assess the growth, health, and progeny performance of diets containing different alternative lipids after long-term feeding will need long-term feeding studies including transgenerational effects. Such studies are needed to ensure that a short-term growth performance is converted to long-term health and multi-generational-level reproductive success. Linking particular bioactive substances, alternatives like CPO (tocopherols and carotenoids) or microalgae oils (specific carotenoids and PUFAs) to reported metabolic and health consequences would be made easier with their identification and quantification. The comprehension of these structure-function associations will allow the creation of functional feeds that are not just able to support growth.

The optimization of lipid blends, which may entail a combination of substitutes like CPO and microalgae oils or certain vegetable oils, may result in better fatty acid balance and an improvement in the nutritional value of the fillets without having an adverse impact on costs. To enable real-time monitoring and accurate feeding of fish in aquaculture systems, future studies should focus on the validation of metabolite-based biomarkers that relate to lipid metabolism, oxidative stress, and immune functioning. Finally, the quest to come up with workable metabolic biomarkers of nutritional condition, oxidative stress, and immune functionality will assist in real-time monitoring and automated feed regulation in commercial aquaculture to plug the gap between science and practice. These biomarkers may be used to predict the early warning of nutritional deficiency or metabolic disequilibrium to make appropriate changes in diets.

Conclusion

In this mini review, the potential of metabolomics in stimulating sustainable aquaculture nutrition, particularly in the evaluation of FO alternatives such as CPO, and other vegetable oils, animal fats, and microalgae oils, is emphasized. The organized discussion of alternative sources of lipids, as shown herein, indicates that each source, including animal fats, microbial oils, and vegetable oils, has different nutritional content and metabolic effects. CPO provides functional properties beyond maintaining growth performance through its bioactive constituents. There is also the alternative of certain vegetable oils, which enhance endogenous LC-PUFA production, and microalgae oils, which address deficiencies of the essential fatty acids: each supplying a unique contribution. There is no perfect substitute for FO, underscoring the significance of integrated approaches with respect to species and objectives of production. Nevertheless, metabolomics detects sensitive, species-specific alterations in the metabolism pathways associated with oxidative stress, immune action, and lipid metabolites that can be missed by traditional methods. The metabolomic knowledge is essential in taking beyond the simple measures of growth to a broader perspective on fish health and welfare.

CPO has been proven to be an advantageous and sustainable lipid source, and an assortment of alternatives offers the flexibility needed to formulate sustainable feeds. As discussed in this review, metabolomic studies have demonstrated that FO replacement consistently affects core metabolic pathways such as β-oxidation, glycolysis, and oxidative stress, and these responses are often species-specific and related to the specific fatty acid composition and bioactive compounds of the FO replacement. The application of metabolomics in other lipid studies has shown that not all species or types of lipid respond the same way to the metabolic response, and thus optimization to different species is essential.

However, the existing literature lacks in-depth untargeted metabolomic studies that are effectively able to capture their systemic and long-term impact. Closing this gap by way of properly designed, long-term research based on advanced mathematical analysis platforms will be the key to the future of aquaculture nutrition. Through integration of metabolomics into future research, aquaculture nutrition can now make feeds that can promote metabolic health, metabolic resilience, and metabolic sustainability without having to compromise on fish welfare or the quality of the product, but with a true optimization in nutritional optimality.

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