frontiers | Frontiers in Marine Science

TYPE Review
PUBLISHED 16 May 2024
DOI 10.3389/fmars.2024.1368436

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OPEN ACCESS

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RECEIVED 15 January 2024
ACCEPTED 24 April 2024
PUBLISHED 16 May 2024

CITATION
Amenyogbe E, Droepenu EK, Ayisi CL, Boamah GA, Duker RQ, Abarike ED and Huang J-s (2024) Impact of probiotics, prebiotics, and synbiotics on digestive enzymes, oxidative stress, and antioxidant defense in fish farming: current insights and future perspectives.
Front. Mar. Sci. 11:1368436.
doi: 10.3389/fmars.2024.1368436

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Impact of probiotics, prebiotics, and synbiotics on digestive enzymes, oxidative stress, and antioxidant defense in fish farming: current insights and future perspectives

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There has been a surge of research in the aquaculture industry investigating probiotic, prebiotic, and synbiotic interventions on the physiological mechanisms of fish, specifically digestive enzymes, oxidative stress, and antioxidant defense. In fish, probiotics have been shown to improve nutrient utilization and growth performance by stimulating digestive enzymes. Meanwhile, probiotics, prebiotics and synbiotics have also been studied for their ability to modulate oxidative stress and antioxidant defense mechanisms in fish, highlighting their multifaceted health benefits. This review identified current trends, research gaps, and future considerations in this evolving field. Although promising findings have been made, a significant research gap exists in understanding the specific role of probiotics prebiotics, and synbiotics in modulating digestive enzymes, oxidative stress, and antioxidant defense systems in a variety of fish species. As this study investigate into the existing body of literature, it becomes evident that while certain aspects of these interactions have been elucidated, a nuanced and comprehensive understanding still needs to be discovered. The variations in experimental design, species-specific responses, and the lack of standardized methodologies contribute to the complexity of the field. Digestive physiology and antioxidant defense mechanisms vary among different fish species, so future research should focus on species-specific responses to probiotic, prebiotic, and synbiotic formulations. It will also be possible to establish robust correlations between dietary interventions and observed effects through a systematic experimental design and methodology approach. Accordingly, further research is needed to understand the interactions between probiotics, prebiotics, and synbiotics in fish and digestive enzymes, oxidative stress, and antioxidant defense. Identifying research gaps and adopting standardized methodologies can help develop tailored strategies to optimize aquaculture fish health and growth performance.

KEYWORDS

oxidative damage, antioxidant systems, digestive health, nutritional supplements, synbiotic effects, aquaculture

1 Introduction

In the ever-evolving landscape of aquaculture, the delicate balance between maximizing fish production and ensuring the health and well-being of aquatic organisms remains a paramount concern (Ribas and Piferrer, 2014; Ibrahem, 2015; Dawood and Koshio, 2016; Mukherjee et al., 2019). One of the pivotal aspects in achieving this equilibrium lies in comprehending the complex interaction between digestive enzymes, oxidative stress, and antioxidant defense mechanisms in fish (Hoseinifar et al., 2015a; Hoseinifar et al., 2015b; Hoseinifar et al., 2021). Over the years, significant strides have been made in elucidating the multifaceted relationship between these physiological processes (Schieber and Chande, 2014; Hoseinifar et al., 2021). Nonetheless, a conspicuous research gap persists, necessitating a comprehensive review to synthesize existing knowledge, identify current limitations, and chart the course for future investigations.

The digestive system of fish is a complex network of enzymatic reactions that orchestrate the breakdown and assimilation of nutrients essential for growth, development, and overall physiological function (Mata-Sotres et al., 2016; Assan et al., 2022; Amenyogbe et al., 2022a; Amenyogbe et al., 2022b; Amenyogbe et al., 2022c). In tandem with these digestive processes, oxidative stress and antioxidant defense mechanisms play a pivotal role in maintaining cellular homeostasis (Hoseinifar et al., 2021). Recent studies have underscored the potential modulatory effects of probiotics, prebiotics, and synbiotics on these crucial physiological pathways in fish (Olmos-Soto, 2014; Wang C. et al., 2019; Wang et al., 2021; Assan et al., 2022). Probiotics, live microorganisms with documented health benefits, prebiotics, non-digestible compounds that selectively stimulate the growth and activity of beneficial microorganisms, and synbiotics, combinations of probiotics and prebiotics, have emerged as promising candidates for enhancing the digestive efficiency and oxidative stress resilience of fish (FAO/WHO, 2001; Beck et al., 2014; Olmos-Soto, 2014; Dawood et al., 2016a, b; Van Doan et al., 2016; Xia et al., 2018; Hoseinifar et al., 2019; Wang C. et al., 2019; Zuo et al., 2019; Wang et al., 2021).

While individual studies have investigated the influence of probiotics, prebiotics, and synbiotics on either digestive enzymes or oxidative stress in fish (Table 1), there exists a discernible gap in the literature that systematically integrates these disparate aspects into a unified framework (Olmos-Soto, 2014; Hoseinifar et al., 2015a, b; Wang Y. et al., 2019; Wang et al., 2021; Assan et al., 2022). This review aims to bridge this gap by comprehensively synthesizing current research findings, highlighting interactions, and identifying areas that require further exploration. By doing so, the study aspire to offer a holistic understanding of how probiotics, prebiotics, and synbiotics collectively impact fish's digestive enzymes and oxidative stress responses.

As this study probe into the existing body of literature, it becomes evident that while certain aspects of these interactions have been elucidated, a nuanced and comprehensive understanding still needs to be discovered. The variations in experimental design, species-specific responses, and the lack of standardized methodologies contribute to the complexity of the field. Consequently, this review will critically evaluate the methodologies employed in existing studies and propose standardized approaches to facilitate cross-study comparisons and data extrapolation. Looking ahead, it is imperative to outline a roadmap for future investigations. Identifying specific strains, doses, and application methods of probiotics, prebiotics, and synbiotics that yield optimal outcomes in different fish species represents a critical avenue for further exploration. Moreover, the molecular mechanisms underlying the observed effects still need to be more understood and warrant in-depth investigation. By addressing these research gaps, the study aim to contribute to the sustainable advancement of aquaculture practices, fostering a balance between increased production efficiency and preserving fish health and welfare.

2 Data availability, materials and methods

Following the methods used by Amenyogbe (2023), in brief, detecting or identifying papers was conducted using Web of Science, Google Scholar, and subscribed journals as Core Collections. In order to retrieve papers published up to 2023, several keywords were initially used as hunt criteria. According to the preliminary search results, studies related to fish probiotics, prebiotics, and synbiotics were distinguished. A total of 233 publications describing aquaculture probiotics, prebiotics, and synbiotics have been obtained in full text.

TABLE 1 An overview of the application of probiotics in regulating digestive enzymes in cultured fish.

Probiotic	Source	Recommended dosage	Duration	Route of admin.	Stimulated enzyme	Fish species	Reference
Bacillus subtilis	commercial	3.5×10^{11} CFU	56 days	Diet	A,L,P ↑	*P. hypophthalus*	Abdel-Latif et al., 2023
Enterococcus faecium	commercial	2.0×10^{11} CFU	56 days	Diet	A,L,P ↑	*P. hypophthalus*	Abdel-Latif et al., 2023
Lactobacillus plantarum	commercial	2.0×10^{11} CFU	56 days	Diet	A,L,P ↑	*P. hypophthalus*	Abdel-Latif et al., 2023
lactic acid bacteria 119	Native	1×10^{8} CFU/g	56 days.	Diet	A,L,P ↑	*Channa argus*	Kong et al., 2021
Saccharomyces cerevisiae	commercial	1.0×10^{10} CFU		Diet	A,L,P ↑	*P. hypophthalus*	Abdel-Latif et al., 2023
Enterococcus faecalis W24	Native	1×10^{8} CFU/g	56 days.	Diet	A,L,P ↑	*Channa argus*	Kong et al., 2021
Pantoea agglomerans RCS2	Native	1×10^{12} CFU/mL^{-1} and 1×10^{10} CFU/mL^{-1}	10 weeks	Diet	A,C,L,P ↑, T	cobia *(Rachycentron canadum)*	Amenyogbe et al., 2022a
Lactobacillus casei	commercial	5×10^{7} CFU L. casei kg–^{1}	75 days		A, L, P ↑, T	*Cyprinus carpio*	Mohammadian et al., 2019
Bacillus sp. *RCS1 and Bacillus cereus RCS3*	Native	1×10^{10} and 1×10^{12} CFU/mL^{-1}	10 weeks	Diet	A,C,L,P ↑, T	cobia *(Rachycentron canadum)*	Amenyogbe et al., 2022b
Bacillus sp. *RCS1, Pantoea agglomerans RCS2, and Bacillus cereus RCS3 mixture*	Native	1×10^{12} CFU mL^{-1}	10 weeks	Diet	A,C,L,P ↑, T	cobia *(Rachycentron canadum)*	Amenyogbe et al., 2022c
Bacillus licheniformis	Commercial	1×10^{6} cfu g^{-1}	8 weeks	Diet	P, L, A ↑	*Lates calcarifer*	(Adorian et al., 2018)
Bacillus subtilis	Commercial	1×10^{6} cfu g^{-1}	8 weeks	Diet	P, L, A ↑	*Lates calcarifer*	(Adorian et al., 2018)
Lactobacillus sp.	*Cyprinus carpio*	2.0 X 10^{7} cfu g^{-1}	60 days	Diet	P, L, A ↑	*Cyprinus carpio*	(Yanbo et al., 2006)
Micrococcus MCCB 104	Commercial	10^{3} cfu animal^{-1} day^{-1}	28 days	Diet	A, L ↑	*Etroplus suratensis Oreochromis mossambicus*	(Sankar et al., 2017)
Bacillus MCCB 101	Commercial	10^{3} cfu animal^{-1} day^{-1}	28 days	Diet	A, L ↑	*Etroplus suratensis Oreochromis mossambicus*	(Sankar et al., 2017)
PrimaLac®	Commercial	1%	45 days	Diet	P, L, A ↑	*Rutilus frisii kutum*	(Mirghaed et al., 2018)
Bacillus subtilis NIOFSD017	*Oreochromis niloticus*	10^{7} cfu g^{-1}	60 days	Diet	P, L, A ↑	*Oreochromis niloticus*	(Essa et al., 2010)
Lactobacillus plantarum NIOFSD018	*Oreochromis niloticus*	10^{7} cfu g^{-1}	60 days	Diet	P, L, A ↑	*Oreochromis niloticus*	(Essa et al., 2010)
Saccharomyces cerevisiae NIOFSD019	*Oreochromis niloticus*	10^{4} cfu g^{-1}	60 days	Diet	A ↑	*Oreochromis niloticus*	(Essa et al., 2010)
B. subtilis	*Cyprinus carpio*	5 g kg^{-1}	28 days	Diet	P, L, A ↑, C	*Penaeus vannamei*	(Wang, 2007)
Bacillus coagulans, palustris	*Cyprinus carpio*	10^{6} cfu g^{-1}	60 days	Diet	P, A, C ↑	*Ctenopharyngodon idella*	(Wang, 2011)
Rhodopseudomonas	*Cyprinus carpio*	10^{6} cfu g^{-1}	60 days	Diet	P, A, C ↑	*Ctenopharyngodon idella*	(Wang, 2011)

(Continued)

TABLE 1 Continued

Probiotic	Source	Recommended dosage	Duration	Route of admin.	Stimulated enzyme	Fish species	Reference
Lactobacillus acidophilus	*Ctenopharyngodon idella*	10^6 cfu g^{-1}	60 days	Diet	P, A, C ↑	*Ctenopharyngodon idella*	(Wang, 2011)
Clostridium butyricum	*M. rosenbergii*	2×10^9 cfu g^{-1}	60 days	Diet	P, A ↑	*Macrobrachium rosenbergii*	(Sumon et al., 2018)
Bacillus megaterium PTB 1.4	*Clarias sp*	10^{10} cfu mL^{-1}	30 days	Diet	P, A ↑	*Clarias sp*	(Afrilasari and Meryandini, 2016)
B. coagulans SC8168	Pond sediment	5.0×10^5 cfu ml^{-1}	ND	Diet	P, L, A ↑	*Penaeus vannamei*	(Zhou et al., 2009)
Bacillus subtilis	Fermented pickles	10^8 cfu g^{-1}	8 weeks	Diet	P, A ↑	*Litopenaeus vannamei*	(Zokaeifar et al., 2012)
Bacillus sp.	Pond	1 g kg^{-1}	60 days	Diet	P, L, A ↑	*Cyprinus carpio*	(Yanbo et al., 2006)
Debaryomyces hansenii CBS 8339	Rainbow trout	10^6 cfu g^{-1}	37 days	Diet	L, A, T ↑	*Dicentrarchus labrax*	(Tovar-Ramírez et al., 2004)
Lactobacillus spp.	Commercial	ND	ND	Diet and water	L, A, T ↑	*Sparus aurata, L.*	(Suzer et al., 2008)
Bacillus subtilis Ch9	Grass carp	3×10^9 cfu kg^{-1}	56 days	Diet	P, L, A ↑	*Ctenopharyngodon idella*	(Wu et al., 2012)
B. cereus	*C. gariepinus*	1×10^{10} cfu kg^{-1}	60 days	Diet	P, L, A ↑	*Clarias gariepinus*	(Reda et al., 2018)
B. amyloliquefaciens	*C. gariepinus*	1×10^{10} cfu kg^{-1}	60 days	Diet	P, L, A ↑	*Clarias gariepinus*	(Reda et al., 2018)
B. subtilis	*C. gariepinus*	1×10^{10} cfu kg^{-1}	60 days	Diet	P, L, A ↑	*Clarias gariepinus*	(Reda et al., 2018)
Bacillus subtilis HAINUP40	Pond water	10^8 cfu g^{-1}	8 weeks	Diet	P, A ↑	*Oreochromis niloticus*	(Liu H. et al., 2017)
Pseudoalteromonas sp. strain C4	Haliotis midae	2.4×10^{10} cfu g^{-1}	15 months	Diet	Alginase ↑	*Haliotis midae*	(ten Doeschate and Coyne, 2008)
Rhodotorula benthica D30	Mud	10^6 cfu g^{-1} and 10^7 cfu g^{-1}	30 days	Diet	A, C, alg↓inase	*Apostichopus japonicus*	(Wang et al., 2015)

A, amylase; C, Cellulose; P, Pepsin; T, Trypsin; P, Protease; L, Lipase; ND, Not defined; Bent-Up Arrow indicates "increase in assessment to the control": Down Arrow indicate "decrease in assessment to the control.

3 Overview of the importance of digestive health and the role of oxidative stress and antioxidant defense in fish health

A group of enzymes present in the digestive tracts of animals are known as digestive enzymes, a, play a crucial role in breaking down macromolecules into their tiniest sizes for efficient absorption via the body, energy metabolism, and overall health (Watling, 2015; Mata-Sotres et al., 2016; Xiong et al., 2019; Assan et al., 2022; Gao et al., 2022; Amenyogbe et al., 2022a; Amenyogbe et al., 2022b; Amenyogbe et al., 2022c). Understanding the complexities of fish digestive physiology is essential for optimizing aquaculture practices, preserving wild populations, and ensuring sustainable fisheries (Xiong et al., 2019). While data from fish indicates qualitative similarities with digestive enzymes in other vertebrates, the understanding of fish digestive processes lags behind that of mammals. This disparity arises from different methodologies used in analyzing data, particularly in the collection of digestive tract secretions from other vertebrates (Assan et al., 2022). Examining the presence and activity levels of digestive enzymes provides valuable insights into food acceptance, the rate of fish larvae development, digestive efficiency, and ultimately, survival rates (Suzer et al., 2008). Research, such as that undertaken by Solovyev et al. (2014), demonstrates that analyzing the activity of digestive enzymes in fish offers valuable understanding of their role in ecosystems and feeding habits under natural conditions. Mata-Sotres et al. (2016) noted that impressive growth rates in larval fish result from effective food processing facilitated by high ingestion rates and the presence of highly active digestive enzymes. Fish need proteases to break down proteins from their diet into amino acids (Huang et al., 2021). Amino acids are essential for various physiological functions, including growth, tissue repair, and the synthesis of enzymes and hormones. Lipases help in the digestion of lipids (fats) (Calado et al., 2007; Rivera-Pérez et al., 2010; Gao et al., 2022). Fatty acids derived from lipid digestion are crucial for energy production, cell membrane formation, and the synthesis of hormones and signaling molecules. Carbohydrases are responsible for breaking down complex carbohydrates into simple sugars. These sugars serve as a direct energy source for fish and are essential for maintaining metabolic processes. The efficiency of digestion directly impacts the fish's growth, development, and overall health.

In literature, the participation of cellulolytic, lipolytic, proteolytic, and amylolytic, enzymes in breaking down carbohydrates, proteins, lipids, and cellulose during fish digestion is emphasized (Falc´on-Hidalgo et al., 2011; Ray et al., 2012; Nedaei et al., 2019; Gao et al., 2022). These enzymes play a crucial role in stimulating the development and growth of aquaculture fish species (Kavitha et al., 2018). The rate of digestion in fish is established to impact nutrient uptake, consequently influencing the overall growth and development of the organism (Pittman et al., 2013). In aquaculture, the growth and production costs of fish are heavily influenced by the digestibility of their feed, which can be improved through the augmentation of digestive enzyme activityThe presence of intestinal bacteria aids in food digestion, while the introduction of probiotic bacteria enhances nutrient absorption and promotes more efficient food digestion (Afrilasari and Meryandini, 2016). Probiotic bacteria have been shown to increase digestive enzyme activities, leading to enhanced growth in various species, including white shrimp *Litopenaeus vannamei*, Indian white shrimp *Fenneropenaeus indicus*, abalone *Haliotis asinina*, and humpback grouper *Cromileptes altivelis* (Takami et al., 2006; Zokaeifar et al., 2012; Marlida et al., 2014; Faturrahman et al., 2015). Probiotics, as beneficial microbes, are recognized for improving the overall health and nutrition of host organisms (Assan et al., 2022). Research has shown that probiotics enhance the activity of digestive enzymes in fish by producing their own enzymes. These enzymes are released into the intestinal tract, increasing the overall pool of enzymes. As a result, they break down food nutrients, making them more accessible to the host fish through the resulting metabolites they secrete (Wang, 2007; Suzer et al., 2008; Zhou et al., 2009). Research on fish digestive health has substantially contributed to understanding nutrient digestion, absorption, and utilization (Table 1) (Burns et al., 2016; Yan et al., 2016; Nie et al., 2017; Smith et al., 2017). Studies have elucidated the enzymatic processes involved in breaking down complex nutrients, such as proteins, lipids, and carbohydrates. Moreover, advancements in molecular biology have allowed researchers to explore the microbiota residing in the fish gut, shedding light on its role in nutrient metabolism and host immunity (Liu H. et al., 2017; Nie et al., 2017).

Elevated levels of reactive oxygen species (ROS) within cells, associated with oxidative stress, can lead to detrimental effects on lipids, proteins, and DNA (Schieber and Chande, 2014; Hoseinifar et al., 2021). Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the ability of the fish's antioxidant defense system to neutralize them. The imbalance between ROS production and antioxidant defense, termed oxidative stress, can result in DNA hydroxylation, protein denaturation, lipid peroxidation, apoptosis, and ultimately cell damage (Hoseinifar et al., 2021). Hydroxyl radicals and hydrogen peroxides are key oxygen radicals contributing to ROS. To counteract the negative impacts of naturally occurring ROS, living organisms have developed an antioxidant defense system, comprising enzymatic antioxidants (e.g., superoxide dismutase, glutathione peroxidase, glutathione reductase, and catalase) and non-enzyme antioxidants (e.g., glutathione, thioredoxin, vitamin C, and vitamin E) (Hoseinifar et al., 2021). ROS, such as superoxide radicals and hydrogen peroxide, can cause damage to lipids, proteins, and DNA within the fish's cells (Schieber and Chande, 2014; Hoseinifar et al., 2021). This antioxidant defense system maintains the balance between ROS production and removal under normal physiological conditions (Li et al., 2016; Dong et al., 2017), playing a crucial role in preserving homeostasis and preventing oxidative stress-related damage (Li et al., 2016; Dong et al., 2017). Fish produce ROS as byproducts during normal metabolic processes. Factors like pollution, temperature changes, and poor water quality can increase ROS production (Cadenas, 1995; Schieber and Chande, 2014; Halliwell and Gutteridge, 2015). Infections and diseases can trigger ROS production as part of the fish's immune response. ROS can damage cell membranes, proteins, and DNA, leading to impaired cellular function (Halliwell and Gutteridge, 2015; Li et al., 2016; Dong et al., 2017). Fish experiencing oxidative stress are more susceptible to diseases (Jena, 2012; Birnie-Gauvin et al., 2017; Prego-Faraldo et al., 2017; Biller and Takahashi, 2018; Ji et al., 2018; Hematyar et al., 2019). Oxidative stress can hinder growth rates in fish.

The physiological status of an organism is closely linked to its antioxidant defense, with increased efficiency and levels of antioxidant defense providing various benefits to the host (Halliwell and Gutteridge, 2015; Li et al., 2016; Yang et al., 2018). Consequently, there has been considerable research focused on enhancing the activities of antioxidant enzymes in fish and shellfish. While synthetic antioxidants such as butylated hydroxyanisole and butylated hydroxytoluene have been traditionally employed to boost antioxidant defense and inhibit lipid peroxidation, their use is becoming restricted due to environmental and health concerns, including liver damage and cancer (Halliwell and Gutteridge, 2015; Li et al., 2016; Yang et al., 2018). In recent years, efforts have been directed toward identifying novel and safe natural antioxidants as alternatives to synthetic compounds (Hoseinifar et al., 2021).

Fish have evolved elaborate antioxidant defense mechanisms to counteract oxidative stress and maintain cellular homeostasis (Halliwell and Gutteridge, 2015; Li et al., 2016; Yang et al., 2018; Hoseinifar et al., 2021). These defense mechanisms include enzymatic and non-enzymatic antioxidants. Converts superoxide radicals into hydrogen peroxide. Converts hydrogen peroxide into water and oxygen (Yang et al., 2018; Gao et al., 2022). Neutralizes hydrogen peroxide and lipid peroxides. Non-enzymatic Antioxidants: Vitamins C and E Act as scavengers of free radicals. Glutathione acts as a crucial cellular antioxidant. Carotenoids have antioxidant properties and contribute to fish coloration (Malhotra and Kaufman, 2007; Birnie-Gauvin et al., 2017; Xie et al., 2019). In the context of aquaculture, where oxidative stress is particularly relevant, especially in intensive and stressful modern culture systems, researchers are exploring the potential of enhancing the antioxidant defense of cultured organisms using beneficial microbes. Previous studies in aquaculture have demonstrated promising antioxidative effects of beneficial additives such as probiotics, prebiotics, and synbiotics across various fish species (Dawood et al., 2018; Van Doan et al., 2020; Hoseinifar et al., 2021). This highlights the importance of investigating the use of beneficial microorganisms to ameliorate antioxidant defense in aquaculture practices.

Despite these advancements, several gaps persist in our knowledge of fish digestive health and the role of oxidative stress and antioxidant defense in fish health. First, there is a need for more comprehensive studies on the diversity and function of the fish gut microbiome across species and environmental conditions (Burns et al., 2016; Yan et al., 2016; He et al., 2017; Nie et al., 2017; Smith et al., 2017). This includes understanding how external factors, such as diet, water quality, and stress, impact the composition and activity of the gut microbiota. Second, research on the ontogeny of the fish digestive system is limited, hindering our understanding of how digestive processes change during different life stages. Third, the influence of environmental pollutants on fish digestive health remains an underexplored area, with potential implications for both wild and farmed fish populations (Sullam et al., 2012; Schmidt et al., 2015; Yan et al., 2016; Nie et al., 2017).

Addressing these research gaps requires a multidisciplinary approach. Future studies should integrate molecular biology, ecology, and aquaculture science to provide a holistic understanding of fish digestive health. Investigating the impact of environmental stressors, such as climate change and pollution, on fish digestive physiology is crucial for predicting and mitigating potential adverse effects. Additionally, continue advancements in omics technologies can facilitate in-depth analyses of the fish gut microbiome, enabling researchers to uncover novel interactions between the microbiota and host physiology (Sullam et al., 2012). Collaboration between researchers, industry stakeholders, and policymakers is essential for translating research findings into practical applications. Developing strategies to enhance digestive health in aquaculture settings can improve fish growth rates, feed efficiency, and disease resistance. Furthermore, understanding the role of the fish gut in nutrient cycling within aquatic ecosystems is vital for managing and conserving wild fish populations. By addressing these gaps and adopting a holistic approach that considers the diverse factors influencing digestive physiology, researchers can contribute to developing sustainable aquaculture practices and conserving wild fish populations. The integration of emerging technologies and collaboration across disciplines will be instrumental in advancing our knowledge of this complex and vital aspect of fish biology.

3.1 Overview of probiotics, prebiotics, and synbiotics: advantages in the context of fish farming

Probiotics are live microorganisms that confer health benefits to the host when administered in adequate amounts (Fuller, 1989; FAO/WHO, 2001; FAO, 2011; Ferreira, 2014; Newaj-Fyzul et al., 2014; Jesus et al., 2016; FAO, 2016). In the case of fish, these microorganisms are usually bacteria or yeast strains that promote a balanced and beneficial microbial community in the fish gut (Nayak, 2010; Iribarren et al., 2012; Ferreira, 2014; Newaj-Fyzul et al., 2014). The gut microbiota plays a crucial role in nutrient absorption, immune system regulation, and overall health (Figures 1–3). Probiotics for fish farming are commonly chosen from *Lactic acid* bacteria (LAB) such as *Lactobacillus* and *Bacillus* species (Balcázar et al., 2006; Dotta et al., 2011; Ferreira, 2014; Torres, 2014; Paixão et al., 2017; Yu et al., 2017; Zhai et al., 2017; Didinen et al., 2018; Amenyogbe et al., 2021; Amenyogbe et al., 2022a; Amenyogbe et al., 2022b; Amenyogbe et al., 2022c). Probiotics are recognized for their capacity to produce beneficial enzymes that aid in digestion and protect the gastrointestinal tract (GIT) (Sumon et al., 2018). The proper use of probiotics can enhance the balance of intestinal microorganisms, leading to improved activity of digestive enzymes, enhanced food absorption, and reduced pathogenic issues in the GIT (Figure 3) (Balcazar et al., 2007; Dotta et al., 2011; Muñoz-Atienza et al., 2013; Ferreira, 2014; Torres, 2014; Azevedo et al., 2016; Paixão et al., 2017; Yu et al., 2017; Zhai et al., 2017; Didinen et al., 2018; Linh et al., 2018; Chen et al., 2019; Amenyogbe et al., 2021; Ringø et al., 2022; Amenyogbe et al., 2022a). Scientists suggest that a key way probiotics benefit organisms in cultivation is by enhancing their nutrition through the generation of extra digestive enzymes. This leads to improved feed efficiency, accelerated growth, and the mitigation of intestinal disorders and antinutritional factors (Verschuere et al., 2000; Suzer et al., 2008). Following transit through the stomach, probiotics multiply within the intestine and utilize diverse carbohydrates to support their growth, while also producing vital digestive enzymes including lipase amylase, and protease (Suzer et al., 2008), by adding additional enzymes to those naturally produced by the host, the overall levels of digestive enzymes in the host's gut are increased.

Amylases are enzymes that break down starch into smaller carbohydrates like glucose, maltose, and maltotriose, making them available for absorption by the host (Mardani et al., 2018). These enzymes are found throughout the intestinal tract of fish, with their activity varying depending on the fish species. Research indicates that the modulation of amylase activity is influenced by the type of food and supplements, as well as the administration of probiotics (Murashita et al., 2018). Studies have shown that dietary supplementation with probiotics, such as PrimaLac®, can significantly increase (5.45% compared to the control) amylase activity in Caspian white fish (*Rutilus frisii* kutum), leading to improved feed utilization and growth performance (Mirghaed et al., 2018). Probiotics, whether used individually or in conjunction with other bacterial strains, have been shown to increase the levels of

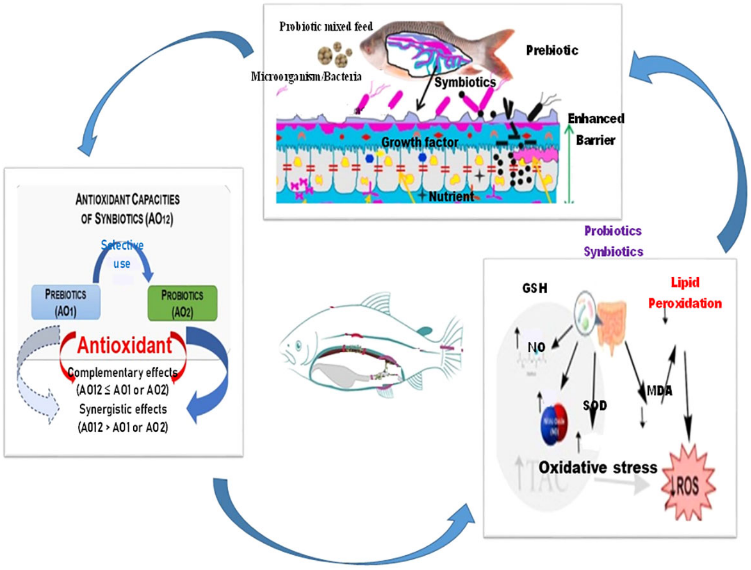

FIGURE 1
The mechanism by which probiotics, prebiotics and synbiotics act in the guts of host animals. Probiotics, Prebiotics, and Synbiotics plays a crucial role in nutrient absorption, immune system regulation, decreased oxidative stress and overall health, indicating that these microorganisms may have a significant protective effect via enhancing enzymatic and non-enzymatic antioxidant ability, non-specific immune response and reduced oxidative stress effect (Heshmati et al., 2018; Lin et al., 2019; Hosain and Liangyi, 2020; Rohani et al., 2021; Mounir et al., 2022). Note: The arrow indicates the various functions of probiotics, prebiotics and synbiotics in protecting aquatic species especially fish.

amylase activity in various types of fish. For example, tilapia (*Oreochromis niloticus*) fed with a diet supplemented with *B. subtilis* HAINUP40 exhibited significantly higher (185.71%) amylase activity in the digestive tract (Liu H. et al., 2017). Similar positive effects on amylase activity and growth were reported in catfish and shrimp when supplemented with specific probiotics. The positive impact of probiotics on amylase activity extends to various fish species, including Nile tilapia (16.46%, 44.02%, and 37.03% respectively when fed with supplemented with *Bacillus subtilis* NIOFSD017, *Lactobacillus plantarum* NIOFSD018, and *S. cerevisiae*) (Essa et al., 2010), catfish (*Clarias* sp.) (63.64% increased when supplemented with *Bacillus megaterium* PTB 1.4) (Afrilasari and Meryandini, 2016), shrimp (about 44.74% increase when fed with supplanted *B. subtilis*) (Wang, 2007). Additionally,

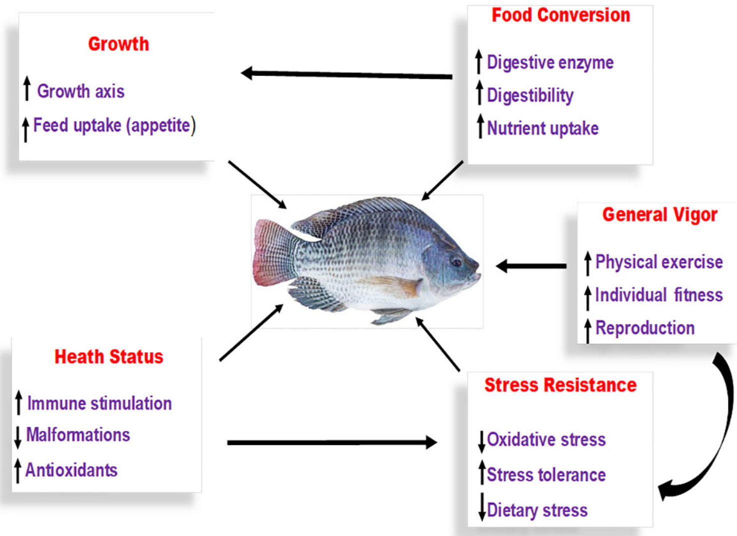

FIGURE 2
Method of exploit of probiotics, prebiotics and synbiotics. Probiotics function through various mechanisms to benefit fish, such as promoting growth and appetite, optimizing feed conversion through the secretion of microbial enzymes for digestion, enhancing the nutritional value of feed by augmenting both macro and micronutrient absorption, boosting stress resilience, and bolstering overall health by activating the fish's immune response and enrichment of overall vigor (Wuertz et al., 2021).

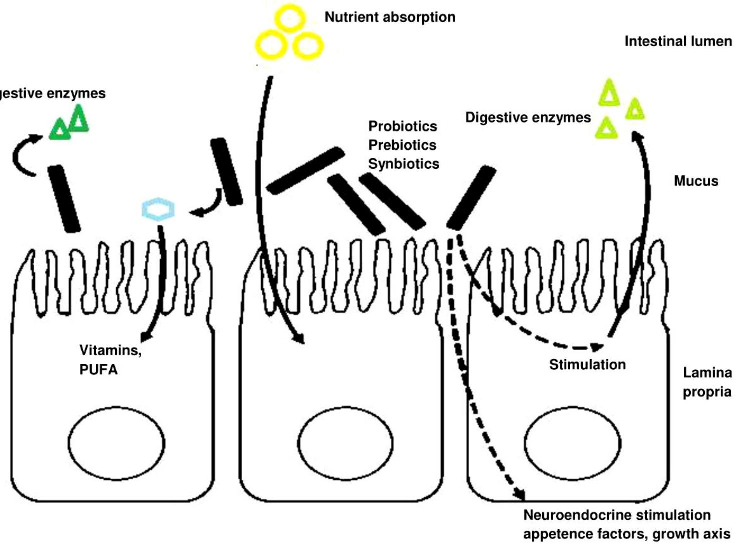

FIGURE 3
Nutrition- and growth-related effects (modes of action) of probiotics in the gastrointestinal tract (GIT). Probiotics exert various effects within the gastrointestinal tract (GIT) that influence nutrition and growth. These effects encompass direct actions, such as the release of digestive enzymes and the facilitation of (micro) nutrient absorption, including cofactors, vitamins, and polyunsaturated fatty acids. Additionally, probiotics indirectly enhance nutrient uptake and absorption while stimulating enzyme secretion. Furthermore, they contribute to neuroendocrine modulation, promoting appetite and fostering growth (Wuertz et al., 2021).

the use of specific probiotics like *Bacillus amyloliquefaciens*, *B. cereus*, and *B. subtilis* has been associated with substantial increases (approximately 170.00%, 265.00%, and 62.50%) in amylase activity in catfish. In prawn *Macrobrachium rosenbergi*i, the supplementation of *Clostridium butyricum* in the diet led to a significant increase (55.56%) in digestive amylase activities (Sumon et al., 2018).

Furthermore, a combination of photosynthetic bacteria and *Bacillus* sp. was found to enhance (approximately 44.74%) amylase activity in shrimp (*Penaeus vannamei*). Probiotic supplementation in a study by Sankar et al. (2017), using *Micrococcus* MCCB 104 and *Bacillus* MCCB 101, was linked to increased (approximately 9.41% and 61.18% correspondingly) intestinal amylase in Mozambique tilapia (*Oreochromis mossambicus*). Carnivorous fish, specifically snakehead (*Channa striata*) fingerlings, showed higher amylase specific activities when fed with Lactobacillus acidophilus-supplemented diets compared to prebiotic-supplemented diets (Munir et al., 2016). Interestingly, there were instances where amylase activities increased in fish infected with *Aphanomyces invadans* when fed with *Saccharomyces cerevisiae* (Devi et al., 2019). European seabass (*Dicentrarchus labrax*) also exhibited increased amylase activities when fed with a diet containing *Bacillus subtilis*, *Lactococcus lactis*, and *Saccharomyces cerevisiae* (Tovar et al., 2002). However, the supplementation of *Debaryomyces hansenii* CBS 8339 led to a reduction in amylase activity in European seabass compared to the control diet (Tovar-Ramírez et al., 2004). These findings collectively highlight the significant role of various factors, including probiotics and specific bacteria, in modulating amylase activity and influencing the digestive performance of different fish species.

The significance of proteases in digestion lies in their ability to break down protein in food by hydrolyzing peptide bonds, releasing essential amino acids for the body (Naidu, 2011). The addition of probiotics has been demonstrated to boost the digestibility of proteins in fish, leading to enhanced performance in those fed with probiotic-included diets (Allameh et al., 2017). Studies have reported increased protease activity in various fish species when fed diets supplemented with specific probiotics. For instance, Wang (2007) found a significant 78.38% increase in the protease activity of shrimp (*Penaeus vannamei*) when fed a diet supplemented with *Bacillus* sp. compared to the control. Similarly, Wang (2011) observed an 18.18% increase in protease activity in grass carp (*Ctenopharyngodon idella*) when supplemented with *Bacillus coagulans*. Essa et al. (2010) documented elevated digestive protease activity in Nile tilapia fed probiotics *Lactobacillus plantarum* NIOFSD018 (76.92% increase) and *Bacillus subtilis* NIOFSD017 (73.08% increase). *Bacillus megaterium* PTB 1.4 was reported to boost catfish protease activity by 245.00% (Afrilasari and Meryandini, 2016), and Mirghaed et al. (2018) observed a similar effect in Caspian white fish with PrimaLac® supplementation.

In Nile tilapia, Liu H. et al. (2017) noted a 133.33% rise in protease activity within the digestive tract following an 8-week regimen of a diet enriched with *B. subtilis* HAINUP40. Prawn (*Macrobrachium rosenbergii*) juveniles treated with the probiotic *Clostridium butyricum* demonstrated an 86.67% increase in digestive protease activity compared to control groups (Sumon et al., 2018). Similarly, Wang and Xu (2006) observed heightened digestive protease activities in *C. carpio* juveniles upon supplementation with a *Bacillus* sp. probiotic diet. Experiments conducted by Zhou et al. (2009) revealed that the probiotic *B. coagulans* SC8168, when introduced as a water additive, significantly elevated protease activities in shrimp larvae. *B. subtilis* consistently elicited increased digestive protease activity in shrimp, as evidenced by studies from Liu et al. (2009), Wang (2007), and Zokaeifar et al. (2012). Reda et al. (2018) noted a significant enhancement in protease activity in Clarias gariepinus when their diets were enriched with native strains of *B. amyloliquefaciens*, *B. cereus*, and *B. subtilis*. In contrast, Wang et al. (2015) documented a decrease of 0.78% in protease activity in sea cucumber (*Apostichopus japonicus*) following treatment with probiotic *Rhodotorula benthica* D30.

Lipases play a crucial role in catalyzing various biochemical reactions, including the hydrolysis of triglycerides into glycerol and free fatty acids, as well as the hydrolysis, transesterification, and synthesis of esters (Thakur, 2012). These enzymes exhibit enantioselective properties. Widely distributed in bacteria, plant, and animal tissues, lipases are renowned for their involvement in fat digestion in the small intestine, acting as a class of digestive enzymes (Bruno, 2010). Numerous studies have explored the impact of probiotics on the lipase activity of various fish species. For instance, Tovar-Ramírez et al. (2004) investigated the modulation of digestive enzymes in European sea bass larvae using the live yeast *Debaryomyces hansenii*, observing increased survival, growth parameters, and a substantial rise in lipase activity (approximately 833.33% higher than the control). In juvenile *C. carpio*, Yanbo et al. (2006) observed a notable increase in lipase activity after the application of *Bacillus* sp. Likewise, the incorporation of *Lactobacillus* spp. into the diet of gilthead sea bream larvae resulted in elevated lipase activity, approximately 1.69% higher than the control group (Suzer et al., 2008). Additionally, in shrimp larvae, the presence of *B. coagulans* SC8168 not only provided various benefits but also led to a significant increase in lipase activity, approximately 20.00% higher (Zhou et al., 2009).

In addition, Sankar and colleagues (2017) observed elevated levels of intestinal lipase enzymes in *O. mossambicus* following dietary supplementation with *Micrococcus* MCCB 104 and *Bacillus* MCCB 101, showing approximately a 26.32% and 7.02% increase, respectively. Similarly, Wang (2011) demonstrated a significant enhancement in lipase activity in *Labeo rohita* when the diet was enriched with *Bacillus coagulans*. Furthermore, Essa et al. (2010) documented increased digestive lipase activity in Nile tilapia after administration of the probiotics *Bacillus subtilis* NIOFSD017 and *Lactobacillus plantarum* NIOFSD018. Additionally, Wu et al. (2012) observed a substantial increase (approximately 65.22%) in lipase activity in grass carp (*Ctenopharyngodon idella*) following dietary administration of *Bacillus subtilis* compared to the control treatment. In summary, probiotics exhibit positive effects on the activity of digestive enzymes, including amylases, proteases, and lipases, in cultured fish. Fish are poikilothermic animals, meaning their body temperature fluctuates with the environment (Frick et al., 2018). Optimal digestive function is critical for their metabolic processes, especially in varied environmental conditions. These effects contribute to enhanced nutrient absorption, feed efficiency, and overall growth performance. However, outcomes may vary depending on the specific probiotic strains and fish species involved. A healthy gut microbiota contributes to optimal growth performance in fish. Probiotics have been shown to mitigate the adverse effects of stress on fish by promoting a stable gut environment (Amenyogbe et al., 2022c). A balanced microbial community in the fish gut can contribute to the breakdown of organic matter, helping to maintain good water quality in aquaculture systems. In fact, using probiotics, in fish farming is a promising strategy to enhance the health and productivity of farmed fish (Amenyogbe, 2023). It involves manipulating the gut microbiota to create a favorable environment that supports the well-being of the fish and minimizes the risk of diseases. Probiotics can produce substances like organic acids, bacteriocins, and hydrogen peroxide, inhibiting harmful bacteria growth (Tremaroli and Bäckhed, 2012; Falcinelli et al., 2018; Liu et al., 2021). Probiotics can improve nutrient absorption by enhancing the intestinal mucosa's surface area (Figure 1) (Heshmati et al., 2018; Lin et al., 2019; Hosain and Liangyi, 2020; Rohani et al., 2021; Mounir et al., 2022). The choice of probiotic strains is critical and should be species-specific. Strains should be resistant to environmental stressors, bile salts, and gastric acid to survive the passage through the digestive tract (Amenyogbe et al., 2021). Encapsulation of probiotics in feed helps protect them from environmental conditions, ensuring their viability until they reach the intestines (Simo´n et al., 2021). Studies have shown that fish supplemented with probiotics exhibit improved growth rates, feed conversion efficiency, and biomass production (Table 1) (Panigrahi and Azad, 2007; Muñoz-Atienza et al., 2013; Chen et al., 2019; Assan et al., 2022). Probiotics contribute to enhanced nutrient utilization, leading to better growth outcomes. Probiotics bolster the immune system by stimulating the production of immune-related molecules (Zapata and Lara-Flores, 2012; Xu et al., 2013; Amenyogbe et al., 2020; Amenyogbe, 2023). Probiotics can contribute to the sustainability of aquaculture by reducing the need for antibiotics and other chemical treatments (Amenyogbe et al., 2021). Challenges include the need for strain-specific research, optimizing delivery methods, and understanding the interactions between probiotics and the fish microbiome (Amenyogbe, 2023). The use of probiotics in fish digestive health is a promising avenue in aquaculture. Through their diverse mechanisms of action, probiotics contribute to improved digestion and growth, disease prevention, and environmental sustainability. Continued research will provide further insights into probiotics' specific applications and benefits in different fish species and aquaculture systems. As research in this field continues (Supplementary 4), further insights into specific strains, dosages, and application methods will likely lead to more efficient and sustainable aquaculture practices.

Prebiotics, on the other hand, are non-digestible compounds that stimulate the growth and activity of beneficial microorganisms, such as probiotics, in the gastrointestinal tract. In fish farming, prebiotics are often carbohydrates like oligosaccharides and fructooligosaccharides (Assan et al., 2022). Over the last three decades, the conventional use of antibiotics in aquaculture has faced criticism due to concerns about the emergence of antibiotic-resistant bacteria, the presence of antibiotic residues in aquatic food, disruption of microbial ecosystems in aquacultural environments, and the potential suppression of the immune systems in aquatic animals (Ringø et al., 2010). As an alternative approach to antibiotics, prebiotics have garnered significant attention in the field of aquaculture. Ingredients rich in dietary fiber, such as plant-based materials (cellulose, hemicellulose), can serve as prebiotics for fish. Fiber promotes the growth of fiber-degrading bacteria in the gut, enhancing the overall microbial diversity. Oligosaccharides, including fructooligosaccharides (FOS) and inulin, are commonly used prebiotics in fish diets (Ganguly et al., 2013; Ringø et al., 2014; Di Gioia and Biavati, 2018). These compounds resist digestion in the upper gastrointestinal tract and reach the lower intestine, where they selectively stimulate the growth of beneficial bacteria (Ganguly et al., 2013; Ringø et al., 2014). Mannan-Oligosaccharides (MOS), derived from yeast cell walls, have been recognized for their prebiotic properties in fish (Song et al., 2014; Akhter et al., 2015; Di Gioia and Biavati, 2018). They can bind to pathogenic bacteria, preventing their attachment to the gut epithelium and facilitating their removal from the digestive system.Mannan oligosaccharides are structurally complex carbohydrates derived from yeast cell walls, primarily composed of mannose (Mata-Sotres et al., 2016). The addition of prebiotics, particularly mannan, to sturgeon feeds emerges as a viable alternative for enhancing feed efficiency and promoting sturgeon health (Pryor et al., 2003; Akrami et al., 2009). The effects of mannan prebiotics have been extensively studied in various aquatic species, including tilapia fingerlings (Hisano et al., 2007), channel catfish (Welker et al., 2007), juvenile Nile tilapia (Sado et al., 2008), rohu (Andrews et al., 2009), Japanese flounder (Ye et al., 2011), and grass carp (Shaker Khoshroudi, 2011). These compounds serve as a food source for beneficial bacteria, promoting their proliferation and enhancing their positive effects on the host fish. By fostering the growth of beneficial bacteria, prebiotics contribute to a more stable and resilient gut microbiota in fish Assan et al., 2022). This, in turn, can improve the fish's overall health and disease resistance (Mata-Sotres et al., 2016; Assan et al., 2022).

The role of prebiotics in fish digestive health is a subject of growing interest in aquaculture research. Prebiotics are non-digestible compounds that selectively promote the growth and activity of beneficial microorganisms in the gastrointestinal tract, ultimately improving the overall health and performance of the host organism (Gatesoupe, 2010; Xu et al., 2022). In the context of fish, the digestive system is a crucial aspect of their well-being, as it directly influences nutrient absorption, disease resistance, and growth. In this study, we explore the importance of prebiotics in fish digestive health, their sources, mechanisms of action, and potential applications in aquaculture. Fish require a balanced intake of proteins, fats, carbohydrates, vitamins, and minerals for growth and development (Roberfroid, 2007). Prebiotics play a crucial role in enhancing nutrient absorption by promoting the growth of beneficial bacteria that aid digestion and breakdown of complex nutrients (Hanley et al., 1995; Geraylou et al., 2013). Polysaccharides, synonymous with prebiotics, refer to non-digestible feed ingredients that stimulate the growth of beneficial microbiota in the gastrointestinal tract (Song et al., 2014). Numerous studies in aquaculture have illustrated this phenomenon. For instance, *Astragalus polysaccharides* were shown to enhance the activity of digestive enzymes in *O. niloticus* (Yu et al., 2022). Similarly, *Sparus aurata* exhibited increased digestive enzyme activity when fed fructooligosaccharides (Guerreiro et al., 2016). In the case of *Channa striata*, feeding with β-glucan, galactose-oligosaccharide, and mannaoligosaccharide demonstrated a similar positive effect (Munir et al., 2018). Additionally, *Diplodus sargus* displayed improved digestive enzyme activity when fed a diet supplemented with xylooligosaccharides, small chain fructooligosaccharides, and galactoseoligosaccharides, respectively (Guerreiro et al., 2016).

A well-balanced microbial community helps in preventing the colonization of harmful pathogens (Landers et al., 2012; Tzivara et al., 2013; Amenyogbe et al., 2021; Amenyogbe et al., 2022c). Aquaculture environments can expose fish to various stressors, such as water quality, handling, or transportation changes (Hoseinifar et al., 2010; Daniels and Hoseinifar, 2014). Stress can negatively impact the digestive system. Prebiotics have been shown to mitigate the effects of stress on fish by stabilizing the gut microbiota and promoting the production of bioactive compounds that positively influence stress response (Gatesoupe, 2010; Di Gioia and Biavati, 2018; Xu et al., 2022). The selective stimulation of prebiotics helps in maintaining a balanced microbial community, contributing to a healthier gut environment (Gatesoupe, 2010; Xu et al., 2022). Prebiotics promote competitive exclusion by providing a substrate for beneficial bacteria to outcompete pathogenic microorganisms for resources and attachment sites in the gut (Xu et al., 2022).

Studies have demonstrated that the inclusion of prebiotics in fish diets can lead to improved growth rates, feed conversion efficiency, and overall performance (Hoseinifar et al., 2011a, Hoseinifar et al., 2011b; Geraylou et al., 2013; Xu et al., 2022; Gatesoupe, 2010; Ta'ati et al., 2011; Ringø et al., 2010; Mohajer Esterabadi et al., 2010);. Prebiotics have shown promise in preventing and controlling fish diseases by enhancing the immune response and inhibiting the growth of pathogenic bacteria. By improving nutrient utilization and reducing the environmental impact of aquaculture operations, prebiotics contribute to the sustainability of fish farming practices (Geraylou et al., 2013; Xu et al., 2022).The effectiveness of prebiotics can vary among fish species, highlighting the need for species-specific research to optimize prebiotic supplementation in different aquaculture systems. Determining the optimal dosage and formulation of prebiotics in fish diets is a complex task, as it depends on factors such as fish species, age, and environmental conditions (Gatesoupe, 2010; Di Gioia and Biavati, 2018; Xu et al., 2022). The interactions between prebiotics and other dietary components need further exploration to ensure a balanced and effective nutritional profile for fish.

As aquaculture continues to evolve, optimizing the use of prebiotics offers a promising avenue for enhancing the sustainability and productivity of fish farming operations. Further research in this field will further refine our understanding of the specific requirements for different fish species and contribute to developing tailored aquaculture prebiotic strategies.

Synbiotics refer to the combination of probiotics and prebiotics, creating a synergistic effect to enhance the health-promoting benefits in the host organism (Mohapatra et al., 2013). In fish farming, the use of synbiotics aims to maximize the colonization and activity of probiotics in the gut by providing a suitable nutritional environment through prebiotics. The combination of probiotics and prebiotics can have several advantages, such as improved survival rates of probiotics during storage and transportation, increased adherence of probiotics to the gut lining, and sustained activity of beneficial microorganisms in the fish gastrointestinal tract.

4 Interconnection of digestive enzymes, oxidative stress, and significance of antioxidant defense in maintaining fish health

All aerobic organisms, including those in aquatic environments, require molecular oxygen (O_2) for essential metabolic processes and energy production (Hoseinifar et al., 2021). However, the oxygen dependence poses a risk of oxidative stress, creating a paradox known as the 'aerobic-life paradox' or 'oxygen paradox' (Ahmad, 1995; Davies, 1995; Hoseinifar et al., 2021). Oxygen can exist in atomic form (O), a free radical, a free bi-radical (Davies, 1995). Reactive oxygen species (ROS) are generated during partial oxygen reduction, with superoxide anion (O_2^-), hydroxyl radical (OH), and hydrogen peroxide (H_2O_2) being the most physiologically active (Schieber and Chande, 2014; Halliwell and Gutteridge, 2015; Hoseinifar et al., 2021).

Superoxide dismutase (SOD) eliminates superoxide by converting it into oxygen and hydrogen peroxide. Hydroxyl radicals have a short half-life and are highly reactive, causing significant harm. Hydrogen peroxide, produced during O_2 reduction, can be partially eliminated by enzymes like catalase (CAT) and glutathione peroxidase (GPx) (Halliwell and Gutteridge, 2015; Li et al., 2016; Hoseinifar et al., 2021). ROS, produced through normal metabolism, play essential roles in physiological functions, but excessive concentrations lead to cellular damage, including lipid peroxidation, protein modifications, and DNA alterations (Schieber and Chande, 2014; Dong et al., 2017).

To maintain balance, organisms utilize antioxidant mechanisms from endogenous and exogenous sources (Wang et al., 2013; Franco and Martınez-Pinilla, 2017; Hoseinifar et al., 2021). Fish and shellfish possess adapted enzymatic systems, including SOD, CAT, and GPx, along with lower-molecular-weight antioxidants such as vitamins like vitamin E, K and C, carotenoids, amino acids, and peptides (Birnie-Gauvin et al., 2017; Prego-Faraldo et al., 2017; Biller and Takahashi, 2018; Ji et al., 2018; Parolini et al., 2019; Hoseinifar et al., 2021). The antioxidant system helps prevent or repair oxidative stress effects (Li et al., 2016; Cao et al., 2019; Devi et al., 2019; Parolini et al., 2019). Enzymes like SOD and CAT play crucial roles in eliminating ROS, while non-enzymatic antioxidants like vitamin C and vitamin E act as powerful scavengers and reducers, contributing to the overall antioxidant defense system in fish and shellfish (Narra et al., 2015; Cheng et al., 2018; Hossain et al., 2018. The intricate balance between ROS formation and elimination is crucial for maintaining cellular functions and preventing oxidative stress-related damage.

Proper digestion ensures optimal nutrient absorption, providing essential building blocks for antioxidant synthesis. Efficient lipid and carbohydrate digestion contribute to energy production, which is essential for antioxidant defense mechanisms. Environmental stressors affecting digestion can contribute to oxidative stress. Antioxidant defense helps mitigate the adverse effects of stress (Halliwell and Gutteridge, 2015; Li et al., 2016; Yang et al., 2018; Hoseinifar et al., 2021). Antioxidants play a role in immune function, aiding the defense against pathogens and reducing the likelihood of oxidative damage during infections. The interplay between digestive enzymes, oxidative stress, and antioxidant defense is intricate and vital for fish health (Yang et al., 2018). A balanced diet, optimal digestion, and a robust antioxidant defense system contribute to fish's overall well-being and resilience in both natural and aquaculture settings.

5 Evidence of prebiotics influencing digestive enzyme activity in fish

The influence of prebiotics on digestive enzyme activity in fish has been a subject of increasing interest in aquaculture research. In the context of fish nutrition, understanding how prebiotics impact digestive enzyme activity is crucial for optimizing feed formulations and promoting efficient nutrient utilization. The gastrointestinal tract of fish contains various enzymes such as proteases, lipases, and carbohydrases, which are responsible for the digestion of proteins, lipids, and carbohydrates, respectively (Assan et al., 2022). Prebiotics, acting as substrates for beneficial gut bacteria, have been shown to influence the gut environment and subsequently impact the activity of these digestive enzymes (Ta'ati et al., 2011; Hoseinifar et al., 2011a, Hoseinifar et al., 2011b; Geraylou et al., 2013; Munir et al., 2016; Xu et al., 2022).

Prebiotics, often in the form of non-digestible carbohydrates like fructooligosaccharides (FOS) and inulin, serve as substrates for beneficial gut bacteria (Bartlett, 1937). Prebiotics contribute to the maintenance of a balanced microbial community in the gut. A well-balanced microbiota is essential for the production of certain enzymes that aid in the digestion and absorption of nutrients (Amenyogbe et al., 2022a, Amenyogbe et al., 2022b, Amenyogbe et al., 2022c). The presence of beneficial bacteria can positively influence the expression and activity of digestive enzymes through complex interactions within the gut microbiome (Amenyogbe et al., 2022a, Amenyogbe et al., 2022b, Amenyogbe et al., 2022c). Several studies have provided evidence supporting the influence of prebiotics on digestive enzyme activity in fish: Research conducted on various fish species, including tilapia and rainbow trout, has shown that dietary supplementation with prebiotics can enhance lipase activity in the intestinal tract (Hoseinifar et al., 2011a; Mehrabi et al., 2012; Geraylou et al., 2013; Munir et al., 2016; Xu et al., 2022; Rodriguez-Estrada et al., 2009; Ta'ati et al., 2011). The increased lipase activity is attributed to the modulation of gut microbiota and the production of microbial metabolites that positively affect enzyme secretion. Studies on carnivorous fish, such as salmon, have demonstrated that prebiotic supplementation can influence protease activity in the stomach and intestine (Jeney and Jeney, 2002; Mahious et al., 2006; Aly et al., 2008; Rodriguez-Estrada et al., 2009; Mohajer Esterabadi et al., 2010; Ai et al., 2011; Geng et al., 2011; Ta'ati et al., 2011; Ye et al., 2011; Hoseinifar et al., 2011a, Hoseinifar et al., 2011b; Mehrabi et al., 2012; Abid et al., 2013; Cerezuela et al., 2013; Munir et al., 2016). The stimulation of protease activity is often associated with changes in the gut microbiota composition and the release of microbial enzymes (Munir et al., 2016). Prebiotics, particularly those with a carbohydrate-based structure, have been linked to enhanced carbohydrase activity in fish. This effect is often observed in herbivorous and omnivorous species (Abdel-Tawwab et al., 2008; Munir et al., 2016). Improved carbohydrase activity is thought to result from the fermentation of prebiotics, leading to the production of SCFAs that stimulate the secretion of digestive enzymes (Dhanasiri et al., 2023).

Understanding the impact of prebiotics on digestive enzyme activity in fish has practical implications for aquaculture. Enhanced digestive enzyme activity in farmed fish, facilitated by prebiotics, can improve nutrient utilization, leading to better growth and feed conversion ratios while promoting a balanced gut microbiota and disease resistance. This contributes to sustainable aquaculture by reducing nutrient excretion into the water. Prebiotics influence enzyme activity through microbial fermentation and gut microbiota modulation, offering potential for optimized diets to enhance growth, disease resistance, and environmental sustainability in aquaculture. Further research is required to refine recommendations for different fish species.

6 Probiotics and synbiotics effects on digestive enzymes in fish

Probiotics are commonly associated with promoting gut health by modulating the composition and function of the gut microbiota (Yanbo et al., 2006; Sumon et al., 2018). Probiotics can influence digestive enzymes through various mechanisms (Verschuere et al., 2000; Suzer et al., 2008; Assan et al., 2022). Probiotic strains such as Lactobacillus and Bifidobacterium can enhance lactase activity. Lactase is the enzyme responsible for breaking down lactose, the sugar found in milk (Mardani et al., 2018). Increased lactase activity can be beneficial for individuals with lactose intolerance, allowing for better digestion of dairy products. Some probiotics produce proteases, enzymes that break down proteins (Naidu, 2011). These proteases may complement the host's digestive enzymes, aiding in the breakdown of dietary proteins into smaller peptides and amino acids (Afrilasari and Meryandini, 2016; Allameh et al., 2017; Mirghaed et al., 2018). Probiotics may influence amylase activity, which is responsible for breaking down carbohydrates into simpler sugars (Murashita et al., 2015; Mardani et al., 2018; Murashita et al., 2018). By modulating carbohydrate metabolism, probiotics can impact the availability of nutrients for both the host and the gut microbiota. Probiotics, such as certain strains of Lactobacillus and Bifidobacterium, may possess bile salt hydrolase activity (Liu H. et al., 2017). This enzyme plays a role in bile salt metabolism and can impact the digestion and absorption of dietary fats.

While prebiotics are not enzymes themselves, prebiotics indirectly influence digestive enzymes through their effects on the gut microbiota SCFAs, can influence the activity of various digestive enzymes, including amylases and proteases (Akrami et al., 2015). The fermentation of prebiotics by gut bacteria can alter the pH of the gut environment (Ganguly et al., 2013; Hoseinifar et al., 2014; Song et al., 2014; Dawood and Koshio, 2016). Changes in pH can influence the activity of digestive enzymes, creating an environment that may be more or less conducive to their function (Merrifield et al., 2014; Feckaninova et al., 2017; Ringø et al., 2018).

The interaction between probiotics and prebiotics can profoundly impact digestive enzymes; Prebiotics can serve as a source of energy for probiotics, promoting their growth and survival in the gut (Dawood and Koshio, 2016). This can enhance the overall impact of probiotics on digestive enzyme activities. Synbiotics work together to stimulate the growth of beneficial bacteria selectively (Dawood and Koshio, 2016). This selective stimulation can influence the overall balance of the gut microbiota, potentially affecting the production and activity of various digestive enzymes. Probiotics, prebiotics, and synbiotics can exert a multifaceted influence on digestive enzymes (Ganguly et al., 2013; Hoseinifar et al., 2014; Song et al., 2014; Dehaghani et al., 2015; Dawood and Koshio, 2016). These interactions contribute to the overall maintenance of gut health and highlight the intricate relationship between the microbiota and host digestive processes. The field of research in this area continues to evolve, providing deeper insights into the specific mechanisms by which these components modulate digestive enzyme activities.

Different fish species have unique digestive systems and nutritional requirements. Tailoring synbiotic formulations to specific species ensures optimal results. Synbiotics contribute to maintaining a healthy microbial balance in the gut and surrounding water, thus positively influencing overall water quality (Di Gioia and Biavati, 2018). Identifying the most effective probiotic strains for different fish species remains a challenge. Continued research is needed to understand the specific requirements of diverse aquatic organisms. Various environmental factors, such as temperature and water quality, influence aquaculture systems. Future developments in synbiotic applications should consider these factors for consistent and reliable outcomes. Synbiotics represent a promising avenue for promoting digestive health in fish. By combining the strengths of probiotics and prebiotics, aquaculturists can optimize the gut microbiota, leading to improved nutrient utilization, growth, and overall resilience against diseases. Further research and development in this field will uncover new insights and refine the application of synbiotics in the dynamic context of fish farming.

7 Probiotics, prebiotics, and synbiotics impact on oxidative stress in fish

Studies have shown that probiotics can positively influence the antioxidant defense system in fish (Van Doan et al., 2020; Hoseinifar et al., 2021). These microorganisms can enhance the activity of antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) (Supplementary Table 1; Figure 1) (Lin et al., 2019; Hosain and Liangyi, 2020; Hoseinifar et al., 2021; Rohani et al., 2021; Mounir et al., 2022; Abdel-Latif et al., 2023; Wang C. et al., 2019; Dawood et al., 2018; Heshmati et al., 2018). By doing so, probiotics contribute to the elimination of reactive oxygen species (ROS) and reduce oxidative stress in fish tissues (Dawood et al., 2018; Ringø et al., 2018; Hoseinifar et al., 2021). Additionally, probiotics may help maintain the balance of gut microbiota, promoting a healthy gut environment. A well-balanced gut microbiota is crucial for the absorption of nutrients and can indirectly impact the antioxidant status of the fish. Prebiotics indirectly affect oxidative stress by supporting the growth of probiotics (Dawood et al., 2018; Abdel-Latif et al., 2023). By providing a favorable environment for beneficial bacteria in the gut, prebiotics contribute to the maintenance of a healthy gut microbiota. This, in turn, helps in the prevention of oxidative stress by ensuring optimal nutrient absorption and gut function.

The combination of probiotics and prebiotics in synbiotics often results in enhanced effects on oxidative stress compared to individual administration (Supplementary Table 2) (Hoseinifar et al., 2021; Mohammadi et al., 2021; Puvanasundram et al., 2021; Wang C. et al., 2019; Dawood et al., 2018; Ringø et al., 2018). Synbiotics can promote the survival and activity of probiotics in the gut, creating a more resilient and diverse microbial community (Lin and Yen, 1999). This enhanced gut health can lead to improved antioxidant defense mechanisms and a reduced risk of oxidative stress in fish (Dawood et al., 2018; Ringø et al., 2018; Hoseinifar et al., 2021; Abdel-Latif et al., 2023).

Different strains of probiotics may have varying effects on oxidative stress (Dawood et al., 2018; Ringø et al., 2018). Understanding the specific strains and their interactions is crucial for designing effective probiotic formulations. The efficacy of probiotics, prebiotics, and synbiotics in mitigating oxidative stress can be influenced by the dosage and duration of administration (Ahire et al., 2013). Optimal levels need to be determined through careful experimentation. Responses to probiotics and prebiotics can vary among fish species (Ringø et al., 2016; Dawood et al., 2016a; Li et al., 2019; Van Doan et al., 2020). Research should consider the specific requirements and characteristics of the target species. Water quality, temperature, and other environmental factors can influence the effectiveness of these supplements. A holistic approach that considers both biological and environmental factors is essential. Probiotics, prebiotics, and synbiotics play pivotal roles in influencing oxidative stress in fish through their effects on gut health and the antioxidant defense system (Supplementary Table 2). Ongoing research in this field is vital for optimizing formulations and application strategies to enhance the health and well-being of cultured fish species.

8 The relationship between probiotics, prebiotics, synbiotics, and antioxidant defenses in fish

The relationship between probiotics, prebiotics, synbiotics, and antioxidant defenses in fish is a complex and fascinating area of research. In this review, we broke down each component and discussed their roles in enhancing antioxidant defenses in fish. Several studies suggest that probiotics positively influence antioxidant defenses in fish through various mechanisms (Supplementary Tables 1–3) (Wang C. et al., 2019; Dawood et al., 2018; Gobi et al., 2018; Yi et al., 2018). Probiotics have been shown to possess free radical scavenging abilities, helping to neutralize reactive oxygen species (ROS) in fish (Hussain et al., 2003; Brzozowski et al., 2006; Gomez-Guzman et al., 2015; Trinder et al., 2015; Salem et al., 2018). This reduces oxidative stress, a critical factor in cellular damage. The immune system and antioxidant defenses are closely linked. Probiotics can modulate the immune response in fish, leading to a more efficient defense against oxidative stress.

The connection between prebiotics and antioxidant defenses in fish can be understood through the following points; by promoting the growth of beneficial gut bacteria, prebiotics indirectly contribute to antioxidant defenses (Gibson, 2004; Guerreiro et al., 2016). The enhanced microbial activity can lead to the production of bioactive compounds that have antioxidant properties (Hoseinifar et al., 2017a, b). Prebiotics often exhibit anti-inflammatory effects, which can reduce oxidative stress (Gibson, 2004; Zhang et al., 2014; Guerreiro et al., 2016). Inflammation is closely linked to the generation of free radicals, and by mitigating inflammation, prebiotics contribute to improved antioxidant status.

Synbiotics refer to a combination of probiotics and prebiotics, where prebiotics serve as the fuel for probiotic microorganisms (Huynh et al., 2017; Abdel-Latif et al., 2023; Hoseinifar et al., 2015a, b). The synergistic effects of probiotics and prebiotics provide additional advantages for antioxidant defenses in fish; Prebiotics act as a substrate for probiotics, promoting their growth and survival in the gut (Rurangwa et al., 2009; Zhang et al., 2013; Llewellyn et al., 2014). This ensures a sustained and effective presence of probiotics, leading to prolonged antioxidant benefits. The combination of probiotics and prebiotics often results in a more comprehensive approach to enhancing antioxidant defenses (Kumar et al., 2018; Devi et al., 2019; Ashouri et al., 2020; Abdel-Latif et al., 2023; Hoseinifar et al., 2017a, b; Zhang et al., 2014). This can include both direct antioxidant activity and indirect effects through modulation of the gut microbiota and immune system (Kumar et al., 2018; Devi et al., 2019; Ashouri et al., 2020).

In fact, probiotics, prebiotics, and synbiotics play pivotal roles in enhancing antioxidant defenses in fish through various mechanisms. These include direct scavenging of free radicals, stimulating antioxidant enzyme production, modulation of immune responses, and promoting beneficial gut microbiota. Integrating these components in aquaculture practices holds promise for improving fish's overall health and stress resistance, contributing to sustainable and efficient aquaculture systems. However, it is important to note that the specific effects can vary depending on the fish species, environmental conditions, and the particular strains of probiotics used. Ongoing research in this field will likely provide more insights and refine the application of these strategies in aquaculture.

9 Factors such as fish species, diet, environmental conditions, and dosage affect the efficacy of probiotics, prebiotics, and synbiotics

The efficacy of probiotics, prebiotics, and synbiotics in aquaculture is influenced by a variety of factors, including fish species, diet, environmental conditions, and dosage (Cerezuela et al., 2013; Zoumpopoulou et al., 2018; Cavalcante et al., 2020). The activity of digestive enzymes like amylase, protease, and lipase in fish is influenced by factors such as fish species, age, dietary enzymes, and food habits (Falc´on-Hidalgo et al., 2011; Assan et al., 2022). Host-produced digestive enzymes are regulated in response to nutrient intake (Gisbert et al., 2018). For example, feeding rainbow trout (*Oncorhynchus mykiss*) diets deficient in fish oil led to decreased lipase activity (Ducasse-Cabanot et al., 2007). High-protein diets activated trypsin and chymotrypsin activity in rainbow trout (Rungruangsak-Torrissen et al., 2009), while red seabream (*Pagrus major*) on soybean meal diets exhibited decreased hepatopancreatic enzymes and protease activity compared to fishmeal-based diets (Murashita et al., 2018). This difference in digestive enzyme activities may be attributed to antinutritional factors in soybean, not necessarily reduced nutrient intake (Yasothai, 2016; Assan et al., 2022).

A comparative study of amylase and proteolytic activities in six fish species revealed that omnivorous species, like gilthead seabream, had higher amylase activity, whereas carnivorous species exhibited greater proteolytic enzyme activity (Hidalgo et al., 1999). In larval Yellow catfish (*Pelteobagrus fulvidraco*), pepsin and trypsin activity increased initially and then decreased with age (Wang et al., 2006). Older abalone (*Haliotis laevigata*) showed a decrease in trypsin and amylase activity compared to younger ones (Bansemer et al., 2016), indicating age-dependent variations in digestive enzyme activity (Infante and Cahu, 2001).

Stocking density also indirectly affects digestive enzyme activity; higher density results in decreased lipase, amylase, and trypsin activities in fish and shrimp (Liu G. et al., 2017; Dong et al., 2018; Liu et al., 2018), likely due to reduced appetite and stress. Intestinal brush border enzyme development, seasonal changes, diet variations, probiotic supplementation, and rearing environment impact gastrointestinal microbial communities, with unfavorable conditions leading to stress, decreased appetite, and subsequently lower digestive enzyme activity. Rearing temperature influences digestive enzymes, with decreased activity observed at lower temperatures (Bansemer et al., 2016). It is crucial to consider these factors in dietary formulation for fish, as decreased digestive capacity can lead to reduced growth (Iqbal et al., 2016; Zeng et al., 2016). Despite the positive effects of probiotics in modulating digestive enzyme activities, careful consideration of the mentioned factors is necessary for optimizing probiotics' digestive enzyme modulation capacity.

In the realm of digestive enzymes, beyond the primary categories like amylase, protease, and lipase, there are noteworthy subclasses such as cellulase (related to amylase) and alginase, both influenced by probiotics. These enzymes hold significance, particularly for omnivorous and herbivorous fish, which predominantly consume plants containing cellulose and algin. Some fish species lack the synthesis of cellulase and alginase or produce them in insufficient quantities, necessitating supplementation (Clements, 1997; Assan et al., 2022).

While literature on the modulation of alginase by probiotics is limited, available studies confirm increased alginase activities in South African abalone (*Haliotis midae*) (approximately 58.33%) (ten Doeschate and Coyne, 2008) and juvenile sea cucumber (*Apostichopus japonicus*) (97.47%) (Wang et al., 2015) associated with probiotic diet supplementation. Other research indicates the production of alginase by probiotic bacteria (Huddy and Coyne, 2014; Escamilla-Montes et al., 2015).

It is noteworthy that some fish generally lack cellulose due to its plant origin, and the presence of cellulase enzymes in fish intestines is likely a result of ingested microbial flora. Inclusion of probiotic bacteria in fish diet becomes essential for cellulase activity. Although cellulose is strictly derived from plants, herbivorous fish exhibit a higher population of cellulase-producing bacterial strains due to the presence of microbial flora in their digestive tracts (Kar and Ghosh, 2008). Yet, only a few studies have touched upon the modulation of cellulase in fish concerning probiotic activities. For instance, Bairagi et al. (2004) reported exogenous and extracellular digestive cellulose production by certain Bacillus spp. strains in rohu (*Labeo rohita*) fingerlings. Similarly, probiotic supplementation was found to elevate the activities of digestive cellulase enzymes in Mori (*Cirrhinus mrigala*) and shrimp (*Penaeus vannamei*) (Ullah et al., 2018). Table 1 provides a summary of the source, dose, and duration of probiotics used to modulate digestive enzymes in cultured fish.

Different fish species have varying physiological and immunological characteristics. Therefore, the response to probiotics, prebiotics, and synbiotics can be species-specific (Ringø and Song, 2016; Huynh et al., 2017). The microbial communities in the gut, which interact with these supplements, may vary among species. Understanding the specific requirements of the target species is crucial for the successful application of these supplements (Dawood and Koshio, 2016; Huynh et al., 2017; Cavalcante et al., 2020). The fish diet plays a significant role in the efficacy of probiotics, prebiotics, and synbiotics. The composition and nutritional content of the feed can impact the survival and proliferation of beneficial microorganisms (Akhter et al., 2015). Some probiotics may require specific nutrients for growth, and prebiotics can serve as a substrate for beneficial bacteria. The diet's balance between probiotics and prebiotics is essential for optimal performance.

Environmental factors, such as water quality, temperature, and salinity, influence the gut microbiota of fish (Hura et al., 2018; Hlordzi et al., 2020; Amenyogbe et al., 2021). Probiotics and prebiotics may be sensitive to environmental conditions, affecting their viability and functionality (Kuebutornye et al., 2019). High temperatures or abrupt changes in water quality can stress fish, compromising their immune system and making them more susceptible to diseases (Hoseinifar et al., 2018; Ringø et al., 2018; Kuebutornye et al., 2019; Hlordzi et al., 2020; Van Doan et al., 2020). Therefore, maintaining stable and suitable environmental conditions is crucial for the effectiveness of these supplements. The dosage and method of administration significantly impact the efficacy of probiotics, prebiotics, and synbiotics (Cerezuela et al., 2013; Kumar et al., 2018; Zoumpopoulou et al., 2018; Cavalcante et al., 2020). The optimal dosage can vary based on factors like fish size, age, and health status. Overdosing may lead to competition among microorganisms for resources, while underdosing may not provide the desired benefits. The method of administration, whether through the feed or water, also affects the contact time between the supplements and the gut microbiota.

Interaction with other feed additives, such as antibiotics or immunostimulants, can influence the efficacy of probiotics, prebiotics, and synbiotics (Banerjee et al., 2013; Simo´n et al., 2021). Some additives may enhance or inhibit the activity of beneficial microorganisms. Understanding these interactions is crucial for formulating a balanced and effective feed regimen (Hura et al., 2018; Hlordzi et al., 2020). The health status of fish is a critical factor affecting the success of probiotics and prebiotics. In stressed or diseased fish, the gut microbiota may be altered, making it challenging for probiotics to establish themselves (Hoseinifar et al., 2018; Ringø et al., 2018; Kuebutornye et al., 2019; Hlordzi et al., 2020; Van Doan et al., 2020). Addressing the underlying health issues before introducing these supplements is essential in such cases.

The choice of probiotic strains is paramount. Different strains exhibit distinct properties, including resistance to environmental conditions, adhesion to the gut epithelium, and production of bioactive compounds (Cerezuela et al., 2013; Zoumpopoulou et al., 2018; Cavalcante et al., 2020). Selecting strains with proven benefits for the target species under specific conditions is crucial for achieving the desired effects (Akhter et al., 2015; Dawood and Koshio, 2016; Huynh et al., 2017; Cavalcante et al., 2020). The duration of administering probiotics, prebiotics, or synbiotics is an important consideration. Some benefits may take time to manifest, and prolonged administration might be necessary for sustained effects (Amenyogbe, 2023). Conversely, continuous use without periodic evaluation may lead to a decline in efficacy.

Therefore, a holistic approach that considers the interplay of fish species, diet, environmental conditions, dosage, interactions with other feed additives, health status, strain selection, and duration of administration is essential for optimizing the efficacy of probiotics, prebiotics, and synbiotics in aquaculture. Researchers and aquaculturists need to tailor their strategies based on a thorough understanding of these factors to promote the health and performance of fish populations.

10 Current challenges and future directions in implementing probiotics, prebiotics, and synbiotics in fish farming

Different fish species have unique gut microbiomes and nutritional requirements. Identifying probiotic strains that are effective across a range of species is challenging. Tailoring probiotic formulations to specific fish species is crucial for optimal performance (Amenyogbe, 2023). Probiotics need to survive and remain viable during the manufacturing process, storage, and administration to the fish. Harsh environmental conditions can reduce their effectiveness. Improving the encapsulation techniques and storage conditions is essential for enhancing probiotic viability (Hoseinifar et al., 2018; Ringø et al., 2018; Kuebutornye et al., 2019; Hlordzi et al., 2020; Van Doan et al., 2020). Determining the optimal dosage and duration of probiotic supplementation is complex. Too little may be ineffective, while excessive amounts can be wasteful and may lead to unintended consequences (Akhter et al., 2015; Dawood and Koshio, 2016; Huynh et al., 2017; Cavalcante et al., 2020). Conducting long-term studies to understand the sustained effects of probiotics on fish health and growth is necessary (Amenyogbe, 2023).

The interaction of probiotics with different feed components and additives needs to be better understood. Some compounds in feed may inhibit or enhance the efficacy of probiotics. Investigating the compatibility of probiotics with various feed formulations is critical for successful integration (Kuebutornye et al., 2019; Amenyogbe et al., 2021). Environmental conditions in aquaculture systems, such as temperature, pH, and water quality, can impact the performance of probiotics (Kuebutornye et al., 2019; Amenyogbe et al., 2021). Adapting probiotic formulations to diverse environmental conditions is a challenge. Research on developing robust probiotic strains that can withstand a range of environmental variables is needed. The need for standardized regulations for probiotic use in aquaculture poses a challenge (Amenyogbe et al., 2020). Obtaining regulatory approval for probiotics is crucial for their widespread adoption. Establishing international standards and guidelines for probiotics in aquaculture is essential for ensuring product safety and efficacy.

Understanding the host-microbiome interactions to develop species-specific probiotic interventions is necessary (Kuebutornye et al., 2019; Amenyogbe et al., 2021). Research on innovative encapsulation methods to enhance the survival and targeted delivery of probiotics to the fish gut is needed. Exploring nanotechnology and other advanced delivery systems for efficient probiotic administration are areas that can be looked at. Conducting dose-response studies to determine the optimal concentration of probiotics for different fish species and life stages are necessary. Investigating the potential for developing time-release formulations for sustained probiotic delivery is very much needed. Systematic analysis of the interaction between probiotics and various feed components to optimize feed formulations. Identifying feed additives that synergistically enhance the efficacy of probiotics is an area that researchers can look at. Assessing the ecological impact of probiotics on the overall aquatic environment, including non-target species and microbial communities, is important. Investigating the potential for developing eco-friendly probiotic formulations is a way to go.

Long-term studies to evaluate the extended effects of probiotic supplementation on fish health, disease resistance, and overall performance are very much needed attention. Exploring the potential for probiotics to mitigate the impact of stressors in aquaculture systems is also needs to be fully understood and needs much research. Collaborative efforts among researchers, industry stakeholders, and regulatory bodies to establish standardized guidelines for probiotic use in fish farming are the uttermost important. Addressing the current challenges and exploring these suggested research directions can contribute to the successful implementation of probiotics, prebiotics, and synbiotics in fish farming, ultimately improving the sustainability and efficiency of aquaculture practices.

11 Our viewpoints on methodological evaluation and standardization in probiotic, prebiotic, and synbiotic studies in fish farming

Research on probiotic, prebiotic, and synbiotic interactions in fish farming is a complex and evolving field with essential implications for aquaculture sustainability. Existing methodologies, however, show variations that hinder cross-study comparisons and data extrapolation. The selection and characterization of probiotics, prebiotics, and synbiotics in existing studies is often inconsistent. It is important to note that strain sources, identification methods, and strain-specific traits can significantly impact results. The reproducibility of strain isolation, identification (e.g., molecular techniques), and characterization (e.g., viability, adhesion capacity) must be ensured using standard methods. Identifying dose-response relationships can be challenging because dosing strategies vary widely among studies. Considering fish species, weight, and environmental conditions, standardized dosing protocols are crucial. Transparent reporting of administration routes (e.g., feed, water) and frequency will facilitate the replication of experiments. Existing studies have a variety of experimental designs, durations, and environmental conditions that make comparisons difficult. The framework for an investigation must be standardized, with appropriate controls and statistical analyses. The long-term effects of probiotics, prebiotics, and synbiotics would be better understood through longitudinal studies with consistent environmental parameters.

Variability in methodologies for assessing digestive enzymes complicates result interpretation. Standardized assays for specific enzymes relevant to fish digestion should be adopted, considering substrate concentration and reaction time factors. Enzyme activity should be expressed consistently, allowing for meaningful comparisons. Inconsistencies in oxidative stress and antioxidant defense measurements undermine the result's reliability. Standardized assays (e.g., lipid peroxidation, antioxidant enzyme activities) with validated protocols must be employed. Additionally, reporting basal and induced stress conditions will enhance understanding of the system's resilience.

Implement internationally recognized protocols for isolating, identifying, and characterizing probiotic, prebiotic, and synbiotic strains to ensure uniformity across studies. Develop standardized dosing guidelines based on fish species, weight, and environmental conditions. Researchers should clearly document administration routes and frequency to facilitate replication. Establish a standardized experimental framework, including appropriate controls and statistical analyses. Encourage longitudinal studies with consistent environmental parameters to assess long-term effects.

Researchers should adopt standardized assays for digestive enzyme analysis, accounting for factors like substrate concentration and reaction time. Enzyme activity reporting should be consistent for meaningful cross-study comparisons. Developing and endorsing standardized assays with validated protocols for oxidative stress and antioxidant defense assessments is essential. Researchers are encouraged to report basal and induced stress conditions to capture the system's resilience. Standardizing methodologies in fish farming in probiotic, prebiotic, and synbiotic studies is imperative for advancing the field and facilitating cross-study comparisons. Implementing uniform strain characterization, dosing guidelines, experimental protocols, and measurement techniques will enhance the findings' reliability and applicability, contributing to aquaculture's sustainable development. Researchers, industry stakeholders, and regulatory bodies must collaborate to establish and endorse these standardized approaches for the benefit of the aquaculture sector.

12 Investigation gaps and approaching perspectives

Despite significant progress, there still needs to be more in our understanding of the mechanisms through which probiotics, prebiotics, and synbiotics exert their effects on digestive enzymes, oxidative stress, and antioxidant defense in fish. Specific gaps include a need for standardized protocols for evaluating the efficacy of these supplements, a need for standardized information on optimal dosages and administration methods, and long-term studies to assess sustained effects. While there is substantial literature and research on the impact of microbial feed additives on factors such as growth performance, immune response, and disease resistance in fish, there is a noticeable lack of studies specifically addressing the modulation of antioxidant defense through the use of functional feed additives. Exploring the significance of these environmentally friendly feed additives on antioxidant defense represents a clear avenue for future research. Additionally, there are proposed mechanisms of action related to the modification of antioxidant defense activities after treatment with functional feed additives, and it is essential to conduct thorough investigations to validate and confirm these suggested modes of action in fish. The interaction between host genetics, diet, and the gut microbiome in response to these supplements requires further exploration. More research is needed to identify suitable biomarkers that accurately reflect the health status of fish in response to probiotics, prebiotics, and synbiotics. Research should address the species-specific responses to these supplements, as different fish species may exhibit variations in their gut microbiota and physiological responses. Future research should explore the environmental impact of probiotics, prebiotics, and synbiotics in aquaculture, considering sustainability and potential ecological consequences. While existing research provides valuable insights into the positive effects of probiotics, prebiotics, and synbiotics on digestive enzymes, oxidative stress, and antioxidant defense in fish farming, further investigation is necessary to address species-specific variations, and long-term impacts for sustainable aquaculture practices. Researchers should focus on filling these gaps to optimize the effective use of these supplements in fish farming.

13 Conclusion

In conclusion, the application of probiotics, prebiotics, and synbiotics in the aquaculture industry holds great promise for improving digestive health and reducing oxidative stress in fish populations. These interventions offer multifaceted benefits, highlighting their potential as effective tools for sustainable aquaculture practices. Probiotics, particularly beneficial bacteria such as *Lactobacillus* and *Bacillus* species, have shown significant improvements in gut microbiota composition and function. These microorganisms play crucial roles in aiding nutrient absorption, inhibiting pathogenic bacteria, and modulating immune responses. By establishing a balanced microbial community within the gastrointestinal tract, probiotics promote optimal digestion and nutrient utilization, contributing to the overall resilience of fish. Complementing the effects of probiotics, prebiotics are non-digestible compounds that selectively stimulate the growth and activity of beneficial microorganisms. Prebiotics such as fructo-oligosaccharides (FOS) and inulin support the establishment of a robust gut microbiome, facilitating nutrient assimilation and bolstering the immune system. When combined with probiotics, these prebiotics create synbiotics, offering a holistic approach to promoting digestive health in fish. This cooperative strategy reinforces positive outcomes in growth performance, disease resistance, and stress tolerance. Furthermore, probiotics, prebiotics, and synbiotics play a crucial role in managing oxidative stress in fish. Oxidative stress, resulting from an imbalance between the productions of reactive oxygen species (ROS) and antioxidant defense mechanisms, can have detrimental effects on fish health. These bioactive compounds enhance antioxidant enzyme activities, scavenge free radicals, and reduce lipid peroxidation, serving as effective mitigating agents against oxidative stress.

As the aquaculture industry continues to evolve, integrating probiotics, prebiotics, and synbiotics into fish diets represents a proactive approach toward sustainable and responsible farming practices. However, it is essential to acknowledge that their efficacy can be species-specific and influenced by various environmental factors. Therefore, ongoing research and tailored approaches are crucial to optimizing their application for different fish species and production systems. The utilization of probiotics, prebiotics, and synbiotics offers a promising avenue for enhancing digestive health and managing oxidative stress in fish. These interventions contribute to the overall well-being of fish populations and align with the broader goals of sustainable aquaculture by reducing reliance on antibiotics and promoting ecological balance within aquatic ecosystems.

Author contributions

EA: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing. ED: Data curation, Formal analysis, Investigation, Writing – review & editing. CL: Formal analysis, Investigation, Methodology, Writing – review & editing. GB: Formal analysis, Investigation, Methodology, Writing – review & editing. RD: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. EA: Data curation, Investigation, Methodology, Writing – review & editing. JH: Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Supervision, Validation, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This work was supported by grants from the National Key R&D Program of China (2022YFD2401203), the Zhanjiang Marine youth talent innovation project in 2021 (2021E05026); Key scientific research platforms and projects of ordinary universities in Guangdong Province in 2022 (2022KCXTD013).

Acknowledgments

We acknowledge all funders of this work.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmars.2024.1368436/full#supplementary-material

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