



Applications of Nutraceuticals in Aquaculture: Improvement in Growth, Immunity and Disease Management

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ABSTRACT

Nutraceuticals are promising functional feed additives in aquaculture, providing natural approaches to improve growth, feed utilization, immunity, stress tolerance, and disease management. Derived from terrestrial and marine sources, they include amino acids, fatty acids, nucleotides, vitamins, minerals, polysaccharides, herbal extracts, probiotics, prebiotics, organic acids, and exogenous enzymes. Their use is increasing as sustainable alternatives to antibiotics and therapeutic chemicals, whose excessive application can contribute to antimicrobial resistance and environmental residues. Nutraceuticals enhance performance through antioxidant defense, non-specific immunity, gut microbiota modulation, improved nutrient digestibility, and stress reduction. Immunostimulants such as β -glucans and chitin enhance disease resistance, while probiotics, prebiotics, and synbiotics promote intestinal health. Exogenous enzymes improve plant-feed digestibility, and dietary administration offers a practical delivery method, although nanodelivery may enhance targeted delivery. Despite their potential, further research is needed on species-specific doses, synergistic interactions, mechanisms, delivery, and regulation. Overall, nutraceuticals support healthier, productive, and sustainable aquaculture.

KEYWORDS

Nutraceuticals, Aquaculture nutrition, Immunity, Stress mitigation, Disease management

Introduction

Hippocrates, roughly 2500 years ago, originally proposed the concept of using appropriate foods for health and medicinal purposes. Dr. Stephen D. Felice defined "nutraceuticals" in 1989 as a food or substance that provides health and therapeutic benefits, such as illness prevention and therapy (Kalra, 2003). Nutraceuticals include nutrient-dense foods like Spirulina and garlic, as well as particular chemicals such as vitamins, lycopene, and omega-3 fatty acids. Gupta et al. (2010) report difficulty distinguishing between food, nutraceuticals, dietary supplements, functional foods, and medications. This approach was previously acknowledged for improving human health, but has recently gained prominence in animal feeding. Natural food products from both terrestrial and marine sources provide significant medicinal benefits. Nutraceuticals refer to goods produced from both terrestrial and marine sources, including isolated nutrients, nutritional supplements, genetically altered foods, herbal items, processed foods, and beverages.

Types of Nutraceuticals

On the basis of bio-functional properties of bioactive compounds derived from both terrestrial and marine sources can be classified as follows:

Dietary Supplements

According to (Food and Administration, 1995) USA, dietary supplements are considered those preparations which are made up of "dietary constituents taken orally in order to supplement the nutritional requirements of diet." Dietary constituents mean bioactive compounds like amino acids, vitamins, minerals, fibers, metabolites and some enzymes. Dietary

supplements also include extracts in functional food is considered as a usual food that includes one or more ingredients that have a therapeutic effect and nutritional benefits (Jalili et al., 2001). In contrast, in Japan functional foods include certain criteria as (1) functional food is taken from natural sources and should be taken in their natural form rather than being processed into various dosage forms such as tablets, capsules or powder; (2) should be taken regularly as part of the normal daily diet, and (3) they work both ways to prevent disease and treat them (Arai, 1996).

Medicinal Food

The medicinal food is specially formulated food products that are recommended for consumption under the supervision of a doctor, aimed at managing a certain disease through the diet with specific nutrient requirements that can be obtained only via special formulation rather than regular diet. Dietary supplements or functional foods do not fall into this category (Radhika et al., 2011).

Role of nutraceuticals in aquaculture

Use of nutraceuticals has been widely encouraged for improved production performance, growth promotion, increased immunity, and feed utilization efficiency (Sinha et al., 2007; Tejpal et al., 2021). Different categories of nutraceuticals currently used in the aquafeed industry and farms include enzymes, methyl donors, immunostimulatory chitin and chitosan, extracts of polychaete and tunicates, vitamins, antioxidants, minerals, amino acids, growth hormones, organic acids, carotenoids, and so forth. Nutraceuticals have been seen as less worrisome in the aquafeed industry as they are likely to yield positive results in relation to feed utilization, immunity,

meat quality, stress tolerance, reproductive and productive performance, and improved water quality in culture through reduced feed wastage and better feed utilization. The lack of growth in the output of marine products along with the increase in demand for the product led to the need for improvement in aquaculture production. Land and water limitation causes the inland farming system to be more intensive, hence more likely to have diseases because of stress, reducing the immunity of the fishes. There are several pathogens in the aquatic ecosystem that wait for a chance to affect the fishes. Several outbreaks of diseases in aqua farms have been witnessed in recent times. To prevent diseases from happening in aquaculture, the application of antibiotics and drugs has become popular. The uncontrolled use of these chemicals leads to antibiotic resistance, buildup of residues in the aquatic ecosystems, and other negative impacts. Some studies suggest that nutraceuticals possess the capacity of stimulating growth and boosting immunity of fishes.

The studies show that nutraceuticals can promote an increase in feed consumption in fish; provide anti-stress and antimicrobial capabilities and stimulate maturation without causing any negative effects. In addition, some types of feed additives in aquaculture may also be considered as nutraceuticals (Brower, 1998). There are numerous causes behind stress for fish living in aquaculture environment. High stocking density, changes in climatic conditions, exposure to pesticide or insecticides, malnutrition, utilization of plant products with anti-nutritional factors may cause stress for fish in an aquaculture environment. However, today many scientists have developed various compounds that may be able to mitigate stress in fish. Such compounds can be classified based

on their functions and chemical composition. Some common nutraceuticals used in aquaculture include:

Traditional

The ancient cultures such as Indian, Chinese, Egyptians, and Sumerians have been quite aware about the significance of foods as medicines and these facts have been documented in their epics and other such documents. As an instance, the ancient Indian medical science Ayurveda has clearly indicated about the significance of food as medicines. The traditionally utilized simple and natural foods are regarded as traditional nutraceuticals, while commercially available products having additional nutrients through breeding or hybridization techniques are considered as nutraceuticals.

Based on the chemical nature

Amino acids and peptides

Essential Amino Acids (EAA)

Some amino acids can serve as essential nutrients as well as stress-reducing agents while peptides can act as antimicrobial agents. Many important AAs such as tryptophan, pyridoxine, tyrosine, glycine, and arginine have been known to reduce stress effect. For example, tryptophan is a very important AA which is used in the synthesis of serotonin (5-HT). Serotonin has an important role to play in reducing stress in fish species (Hoseini et al., 2019). Several studies have shown that tryptophan has the ability to reduce the stress effect in rainbow trout (Lepage et al., 2002), rohu (Akhtar & Abdullah, 2021) (Kumar et al., 2014), mrigal (Tejpal et al., 2009) and juvenile grouper (Höglund et al., 2007). Laboratory studies conducted by FNBP in ICAR-CIFE

have shown that tryptophan (1.36%) significantly reduces the stress effect (Akhtar et al., 2013). Tyrosine, as the precursor of catecholamines, works similarly to noradrenalines and reduces the stress in fishes. Besides, glycine and arginine are the other important AAs which help the immune system and antioxidants of the fish. In addition, glycine, an amino acid, has an important role to play in osmoregulation while the survival of oysters transferred from freshwater to seawater increases with the supplementation of glycine (Takeuchi, 2007).

Fatty acids

Polyunsaturated fatty acids (PUFA) which are a part of the n-3 and n-6 group of fatty acids act as precursors of eicosanoids, which are biologically active substances (Bakhle, 1983). According to JOLLY, 1999, n3 PUFA increased the immunity of rohu fingerlings. But according to (Fontana et al., 1999), the diet containing PUFA at a concentration of 3% inhibits immunity in juveniles.

Nucleotides

Supplementation with nucleotides in diet increases immunity in fishes (Beale et al., 1999; Snyderman et al., 1999). Studies have revealed that supplementation with nucleotides in diet in salmon increases the overall health of fish (JOLLY, 1999; Sukumar et al., 1999). Besides, Pepin et al. (1999) have concluded that inclusion of RNA in diet increases survival of fish.

Vitamins

Vitamins are the primary micronutrients that are needed in small amounts for various functions in the animals. Vitamins A, C, and E play significant roles in antioxidant activities and

fish immunity. A high concentration of ascorbic acid (3000 mg/kg diet) enhances immune activity and complements function (Soliman, 1985). Chen et al. (2004) reported that addition of vitamin C in more than 100 mg/Kg in fish diets enhanced immunity. Supplementing vitamin E reduced nitrite stress in rohu (Ciji et al., 2012), whereas in channel catfish, vitamin E supplementation improved immunological activity (Zhu et al., 2012). Vitamin A and Beta Carotene are strong antioxidants in biological systems; astaxanthin administration showed an immunomodulatory effect in rainbow trout (Thompson et al., 1995). Pyridoxine, commonly known as Vitamin B6, plays an effective role in reducing stress due to increased levels of serotonin and GABA. A dose standardization study conducted in our laboratory revealed that addition of 100 mg/kg of pyridoxine proved effective for stress management and improved growth performance (Akhtar et al., 2013). Pantothenic acid reduces the cortisol release and manages stress.

Minerals

Minerals are inorganic nutrients that can serve as anti-stress agents. Mineral supplementation, both organic and inorganic, can effectively reduce stress in fish. Supplementation with zinc picolinate reduced oxidative stress in rainbow trout (Kucukbay et al., 2006). According to Rider et al. (2009), organic selenium in the diet can lower oxidative stress in grouper fish.

Polysaccharides

Polysaccharides primarily target the non-specific immune systems of aquatic animals. Many polysaccharides, including microbial levan, beta glucan, chitin, lactoferrin, and inulin, have been employed as immune-stimulants in recent years. β -glucans are glucose polymers having a backbone of β -(1-3)

connected β -glucose. D-glucopyranosyl units. It can attach to several cellular receptors and activate them. Zhang et al. (2014) found that β -glucan improved fish resistance to bacterial and viral diseases.

Herbal extracts

Herbal extracts are compounds capable of neutralizing reactive oxygen species and boosting the immune systems of animals. Various plant extracts exhibit immune-enhancing and stress-reducing effects in fish (Harikrishnan et al., 2011; Serradell et al., 2020). Bioactive substances like Rutin (Toonasinensis) have been identified as potent antioxidants and anti-stress bioflavonoids, proving effective for crustaceans. A laboratory study on guava and mango leaf extracts demonstrated that a 0.5% inclusion of either guava or mango leaf extract in the diet improves immunity in *Labeo rohita* fingerlings (Fawole et al., 2016).

Based on the functions

Anti-stress & antioxidant nutraceuticals

This category is constituted by most of the vitamins, minerals, and herb extracts. Supplementation with bovine lactoferrin in an amount of 1200 mg/kg of feed in the groupers decreased salinity stress (Saichiro et al., 2006). The herbs *Astragalus membranaceus* and *Astragalus paniculatus* have proved to be stress relieving in the case of *Cyprinus carpio* and tilapia fish (Wu et al., 2007).

Immunostimulants

The immune system of fish and shellfish is not as complex as that of the terrestrial animals, and most often the main emphasis is placed on the non-specific immune system. A number of polysaccharides and oligosaccharides enhance

the non-specific immunity in fish and shellfish. It was observed that addition of 5 mg/kg of levamisole in the feeds of carp fish enhanced their phagocytosis. (Boonyaratpalin and New, 1995) found that black tiger shrimps were more tolerant to dissolved oxygen and had enhanced immunity with the administration of peptidoglycan. Also, beta-glucan showed better resistance against bacteria and viruses in crustaceans (Misra et al., 2006). Addition of 1% Microbial Levan was found to enhance the immune status of young rohu fish along with inulin. A few plant extracts such as saponin, tannin, glycyrrhizin, and azadirachtin improve the immune system of fish and shellfish.

Antimicrobial and viral nutraceuticals

Antimicrobial properties are possessed by many nutraceuticals such as onion, garlic, thioles, sulphides, terpenes such as oregano, turmeric, and ginger, phenolic such as cloves, nutmeg, cinnamic acid, glycosides such as sugar, citral, citronellol, esters and alcohols. At present, most aquaculture applications are in their experimental stages. Extracts from plants and immunostimulants such as glucan, chitin, lactoferrin, levamisole have antimicrobial properties.

Growth promoters

Various natural substances and minerals enhance the growth of fish. As per Abdel-Tawwab et al. (2008), addition of spirulina enhances the growth of tilapia. Spirulina, rich in carotenoid and phenolic substance, has been reported to enhance development and phosphatase activity in rohu under metallic stress (James, 2010). Extracts from yeast and seaweed enhance the growth of fishes. Growth enhancing herbs have been reported to enhance the process of transcription, hence increasing the growth rate. As per Chitra (1995),

enrichment of artemia nauplii with herbs like stressol I & II enhance the growth of *Penaeus indicus*.

Acidifiers

Organic acids, either singularly or in mixture, can serve to improve digestion, gut microflora, and general health. These are also referred to as acidifiers. Incorporation of acidifiers in the diet enhances the longevity of the feed, helps in digestion by enzyme activity and acts as an intermediate in the TCA cycle. In our laboratory, we observed that when citric acid (3%) and exogenous phytase were used in mixture, their efficiency was increased in rohu (Baruah et al., 2007). Some other acidifiers commonly used in animal diets include formic acid and acetic acid. The mechanism of action of organic acids is as follows:

Prebiotics, probiotics and synbiotics

The probiotics are defined as microorganisms that enhance the properties of the resident flora on being used in humans and animals (Havenaar, 1992). The prebiotics are the non-digestible components of food which stimulate growth and development of the gut microflora. The synbiotics refer to the simultaneous use of the prebiotics and probiotics to create synergy. The common carp (Staykov et al., 2007). The probiotics reduce the bacterial infections and stimulate the production of immune-stimulating metabolites. Some of the probiotics commonly used in aquaculture are *Lactobacillus*, *Enterococcus*, *Bifidobacterium*, *Bacillus*, and *Streptococcus*. The prebiotics used in aquaculture systems include Mannan oligosaccharides (MOS), Xylan oligosaccharides (XOS) and Fructan oligosaccharides (FOS). Studies have indicated that use of the MOS in the fishes improves survival, immunity, and growth in rainbow trout

(Staykov et al., 2007), channel catfish (Welker et al., 2007), and common carp (Staykov et al., 2007).

Nutrizymes/exogenous enzymes

Nutrizymes are extracellular enzymes used as nutraceuticals which increase digestibility and growth. Additives in the plant feed usually include antinutritive factors and cellulose. This leads to digestive problems in fish and calls for more enzymes to counteract the adverse effects. Digestive enzymes like lipase, cellulase, protease, glucanase, phytase, and microbial amylase increase the digestibility in fish that are being fed on plant-based feed. It has been shown that gluconase increases digestibility of proteins in soy beans by 74-95% while phytase increases mineral and protein utilization through complexation with phytic acid (Coon 1998). Exogenous chitinase aids in improving the digestibility of chitin compounds in the diet. Addition of exogenous carbohydrate increases the glucose uptake in carnivores. It has been found that addition of non-gelatinized maize and microbial α -amylase in the diet of *L. rohita* fingerlings at lower than optimal protein level increased their growth and size.

Mode of delivery

Nutraceuticals can be administered through many routes, including parental, oral, and dietary supplements. A study on nucleotides found that oral yeast RNA supplementation improved phagocytic activity in common carp (Sakai et al., 2001), while high dietary RNA supplementation impacted the development and protein accretion of European seabass (Peres and Oliva-Teles, 1999). Injecting chitin improved fish immunological function. Research suggests that dietary supplementation in a safe manner is more cost-effective and efficient. Nutraceutical nanodelivery is an

emerging field that requires further research. Also, Nano delivery technologies offer advantages such as focused tissue delivery, reduced micronutrient loss, and cost reduction.

Future scope

Several forms of disease outbreaks in shrimp and fish farms have occurred in recent years, including WSSV and EMS, resulting in the loss of a huge volume of crops worldwide. This occurred mostly as a result of the fish's lower immunological condition. Although various publications have been published, there is still room for research on species-specific dose standardization and effective delivery methods. The field of nutraceuticals in aquafeed is still in its early stages, requiring control and regulatory measures similar to those for pharmaceutical products. Further research is needed to determine the effectiveness of nutraceuticals in aquafeeds, including species-specific dose standardization, synergistic effects, nanodelivery technologies, and mechanisms of action.

Conclusion

Fisheries and aquaculture can contain a variety of nutraceuticals. Antioxidants, for example, help to protect fish against the detrimental effects of free radicals, which can cause cell and tissue damage. They can also aid to boost the immune system and avoid illness. Methyl donors are important substances that aid in the synthesis of DNA and RNA. They are also necessary for the metabolism of lipids and proteins. Immunostimulants strengthen the immune system, making fish more resistant to disease. They can also assist to alleviate the severity of illnesses. Probiotics are living microorganisms that improve the gut health of fish. They can enhance nutrient absorption and prevent illness. Herbal extracts contain

chemicals that can improve fish health. Herbal extracts can enhance fish flavor, alleviate stress, and promote development. Although the use of nutraceuticals in aquaculture is still in its early stages, there is increasing evidence that they can improve fish health and production. More research is needed to discover appropriate nutraceutical doses and combinations for various fish species.

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