Ohly Application Note

Benefits of Nucleotide Supplementation in Aquaculture: Fish

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Abstract: Nucleotides are semi-essential nutrients: under conditions of rapid growth, stress and disease the own synthesis capacity of animals is not sufficient. Supplementation of feed with nucleotides improves productivity with respect to body weight gain and feed conversion ratio. This effect is especially pronounced in the first weeks of life. This is because nucleotides supplementation especially results in an improved innate and adaptive immune system, thereby reducing the impact of pathogenic infections. Consequently, dietary nucleotides provide a valuable tool to the fish producer as an alternative to antibiotics.

Keywords: Nucleotides, Aquaculture, Fish, Antibiotic replacement

Introduction

Aquaculture is the global fastest growing animal food-producing sector. Intensive fish culture has led to serious problems with diseases and pathogen infections. Traditionally, antibiotics were used sub-therapeutically by the aquaculture industry to reduce the impact of bacterial infections. However, there are increasing consumer concerns about drug residues in food products and the rise of antibiotic resistance of pathogenic bacteria. As a result, many countries have banned the inclusion of antibiotics in fish diets as a routine means of growth promotion. Consequently, there is an increasing demand for alternatives to antibiotics (Ringo *et al*., 2012).

Nucleotides play a major role in almost every biological process. They are the building blocks of DNA and RNA and play a central role in cellular metabolism, i.e. as energy carriers (i.e. ATP), in cell signaling (i.e. cAMP) and are a building block for important cofactors (i.e. NAD+). Although cells can synthesize nucleotides themselves, they are considered semi-essential nutrients as under certain conditions the own synthesis capacity of animals is too low (Do Huu, 2016). Moreover, (non-fishmeal) aqua-feed ingredients contain relatively low amounts of nucleotides (Do Huu *et al*., 2012).

After decades of studies, the health benefits of nucleotides have in the meantime been well established in humans (Grimble & Westwood, 2001), and they have therefore been added to human infant formulas for decades (Boza & Martinez-Augustin, 2002). Although the use of nucleotides is relatively new in aquaculture, there is an increasing body of evidence showcasing their benefits (Do Huu, 2016; Ringo *et al*., 2012).

Enhancing the immune response

Maintaining a good immune status helps the animal protect itself against pathogens. Dietary nucleotides have been shown to improve the immune system response of various types of fish (Do Huu, 2016; Ringo *et al*., 2012). Nucleotide supplementation stimulated the innate immune response by increasing serum lysozyme activity, an important defense molecule of fish innate immune system, in tilapia (Xu *et al*., 2015) and rainbow trout (Hunt *et al*., 2016; Tahmasebi-Kohyani *et al*., 2011).

Enhanced resistance against Pathogens

Dietary supplementation with nucleotides results in an increased resistance against pathogens in salmonids (Burrells *et al*., 2001a), rainbow trout (Tahmasebi-Kohyani *et al*., 2011), hybrid striped brass (Li *et al*., 2004), and rohu (Baidya *et al*., 2015). Fish fed nucleotides had up to 39% higher survival rates following challenges by pathogenic infections (Burrells *et al*., 2001b; Shiau *et al*., 2015).

Reduction in Sea Lice Infections

Salmons with reduced or compromised immunity are more prone to infections by sea lice (Ringo *et al*., 2012). Burrells *et al*. (2001a) reported a 38% reduction in the numbers of infesting sea lice on salmons fed diets containing nucleotides.

Improving growth and development of the gut intestinal system

The improved structure of the intestine is a contributing factor to the enhanced growth of fish due to more efficient nutrient digestion and absorption (Xu *et al*., 2015). Fish fed nucleotides had a healthier intestinal system indicated by a 18-21% increase of the lateral branching and height of the intestinal folds (Burrells *et al*., 2001b), higher enterocyte height and microvilli height (Cheng *et al*., 2011), which resulted in an increase in the total gut surface (Burrells *et al*., 2001b; Xu *et al*., 2015).

Stronger and faster response to vaccinations

Dietary nucleotides also enhanced the efficacy of fish vaccination indicated by elevated antibody titers (Xu *et al*., 2015; Li *et al*., 2004).

Enhancement of osmoregulation ability

Atlantic salmon spend their juvenile phase in fresh water rivers or ponds before migrating to sea/being transferred to sea cages to grow and mature. During seawater transfer, salmon experience hyper-osmotic stress which results in low growth rates and high mortality (Handeland *et al.,* 1998). Nucleotide-fed Atlantic salmons had an increased capacity for seawater tolerance, resulting from greatly enhanced osmoregulatory ability (Burrells *et al.,* 2001b).

Boosting fish performance

Supplementation of diets with nucleotides has been demonstrated to improve growth performance of fish in the early stages of development (Ringo *et al*., 2012). There has been evidence of beneficial influence on various fish species. Nucleotides added to the feed of Atlantic salmon (Burrells *et al*., 2001b), rainbow trout (Tahmasebi-Kohyani *et al*., 2011), tilapia (Xu *et al*., 2015), carp (Baidya *et al*., 2015; Yin *et al*., 2015), meagre (Saenz de Rodriganez) or zebrafish (Guo *et al*., 2017) led to higher weight gain rates. Additionally, specific growth rate, feed conversion rates as well as protein efficiency ratio were significantly improved by nucleotide inclusion (Yin *et al*., 2015; Tahmasebi-Kohyani *et al*., 2011). Fish fed nucleotides were found to have a better muscle composition demonstrated by higher amounts of lipids and protein (Yin *et al*., 2015). Furthermore, Burrells *et al*. (2001b) demonstrated that nucleotide provision prior to and following stress periods such as saltwater transfer helped

negate the stressors' influence on growth rates of Atlantic salmon. The fish had a 15-22% weight advantage 5 weeks post-transfer.

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