

# Benefits of Nucleotide Supplementation in Pigs

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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 animal feed with nucleotides improves animal productivity with respect to average daily gain and feed conversion ratio. This effect is especially pronounced in the first weeks after weaning, also resulting in a reduction of diarrhea. Moreover, nucleotides are known to enhance the immune system resulting in increased numbers of immune cells and antibodies, reducing the impact of pathogenic infections. Consequently, dietary nucleotides provide a valuable tool to the pig producer as an alternative to antibiotics.

**Keywords:** Nucleotides, Pigs, Antibiotic replacement

## Introduction

Bacterial infections are an important problem for both pig health and productivity. Traditionally, antibiotics were used sub-therapeutically by the pig industry to reduce the impact of bacterial infections. However, there are increasing consumer concerns about drug residues in meat products and the rise of antibiotic resistance of pathogenic bacteria. As a result, many countries have banned the inclusion of antibiotics in poultry diets as a routine means of growth promotion. Consequently, there is an increasing demand for alternatives to antibiotics (Liu *et al.*, 2018).

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<sup>+</sup>). 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 (Sauer, *et al.*, 2011). Moreover, the most commonly used feed ingredients contain relatively low amounts of nucleotides (Sauer, *et al.*, 2011).

After decades of studies, the health benefits of nucleotides have in the meantime been well established in humans (Grimble and Westwood, 2001), and they have therefore been added to human infant formulas for decades (Boza and Martinez-Augustin, 2002). An increasing body of evidence demonstrates similar benefits in pigs (Sauer *et al.*, 2011; Liu *et al.*, 2018).

### **Immune modulation: increasing resistance against pathogens**

Maintaining a good immune status of the gut, helps the animal to protect itself against pathogenic bacteria, viruses and parasites. Nucleotides have been shown to enhance the immune system after dietary supplementation (Boza and Martinez-Augustin, 2002). Also in pigs, dietary supplementation with nucleotides has been shown to increase the number of macrophages and lymphocytes (Di Giancamillo *et al.*, 2003; Domeneghini *et al.*, 2004) and plasma IgA concentrations (Sauer *et al.*, 2012a). Moreover, nucleotide supplementation results in an activation of lymphocytes (Lee *et al.*, 2007). Consequently, the severity of pathogenic infections was found to be less in pigs whose diet was supplemented with nucleotides (Hung, 2015). It has also been demonstrated that an improved supply of nucleotides via the diet improves the repair of damaged DNA in immune cells of pigs (Salobir *et al.*, 2005)

### **Improved growth, development and integrity of the intestine**

The involvement of dietary nucleotides in intestinal growth and maturation has been extensively documented (Boza and Martinez-Augustin, 2002). Domeneghini *et al.* (2004) have demonstrated that also in piglets nucleotides result in an increase in villi height and crypt depth, two

parameters that are indicative for an improvement of the integrity of the intestine.

### **Preventing post-weaning diarrhea**

There are many stress factors associated with the weaning period, like removal from the sow and the withdrawal of important nutrients such as milk nucleotides. This may lead to an intestinal gut dysfunction in the pigs, resulting in diarrhea. Martinez-Puig *et al.* (2007) have shown that nucleotide supplementation to diets for weaned piglets results in a 12% absolute reduction in diarrhea scores.

### **Boosting animal performance**

Supplementation of pig diets with nucleotides has been demonstrated to improve growth performance. The availability of nucleotides might be rate limiting in rapidly dividing tissues, like in young pigs. Exogenous added nucleotides do not only overcome this bottleneck, but also reduce the energy requirement of the animal, as *de novo* synthesis of nucleotides is an energy demanding process. Indeed, especially in the first week after weaning a large impact of nucleotide supplementation on the feed conversion ratio (>100% improvement) has been observed (i.e. Domeneghini, *et al.*, 2004, Weaver and Kim, 2014). Also the supplementation of nucleotides to the diet of sows has resulted in a better animal performance of piglets (Hung, 2015). Moreover, an increase of up to 11% in average daily gain (Waititu, *et al.*, 2016; Zomborszky-Kovacs *et al.*, 2000) have been reported in different pig trials. The animal performance benefits of nucleotides were especially pronounced when the pigs were raised under 'dirty' or challenged trial conditions, also resulting in lower mortalities (Hung, 2015).

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