

Benefits of Nucleotide Supplementation in Ruminants

Dr. Dina Krüger
New Product Development
Manager

Ohly GmbH:

Wandsbeker Zollstrasse 59,
D-22041 Hamburg
Germany
Tel: +49 40 68 293 0
Email: info@ohly.com

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. This is due to the fact that nucleotides enhance the immune system resulting in increased numbers of immune cells and antibodies, reducing the impact of pathogenic infections. Moreover, nucleotide supplementation was shown to increase milk yield and improve milk composition in lactating animals. Consequently, dietary nucleotides provide a valuable tool to the cattle producer as an alternative to antibiotics.

Keywords: Nucleotides, Ruminants, Antibiotic replacement

Introduction

Bacterial infections are an important problem for both health and productivity of ruminants. Traditionally, antibiotics were used sub-therapeutically by the cattle 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 livestock 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⁺). 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 livestock (Sauer *et al.*, 2011; Kehoe *et al.*, 2007).

Immune modulation: improved general health indicators

Maintaining a good immune status helps the animal protect itself against pathogens. Nucleotides have been shown to enhance the immune system after dietary supplementation (Boza and Martinez-Augustin, 2002). Also in ruminants, dietary supplementation with nucleotides has been shown to improve the general immune status. In sheep, dietary supplementation of nucleotides resulted in higher levels of white blood cells (Zomborszky-Kovács *et al.*, 1998) and lower levels of cholesterol (Krol, 2011). Moreover, nucleotide supplementation reduced the incidence of respiratory problems in dairy calves during the weaning period (Bach *et al.*, 2009).

Increasing rate of antibody formation after vaccination

Vaccines are an important component of ruminant disease prevention and control. Supplementation of nucleotides upon vaccination against Clostridia has been shown to result in higher IgG levels in dairy cows (Rodriguez-Prado *et al.*, 2017).

Improved passive immunity transfer to calves

Colostrum is known to provide passive immunity transfer from mothers to their newborns (Poulsen *et al.*, 2010).. However, due to higher availability and ease of administration calves are fed milk replacer instead of colostrum (Poulsen *et al.*, 2010). Calves fed a milk replacer

supplemented with nucleotides had a better passive immunity transfer indicated by higher levels of antibodies than those who weren't (Krol, 2011).

Improved development of the gut intestinal system

The gastrointestinal tract of weaning calves is still underdeveloped, resulting in a suboptimal nutrient digestibility. Supplementing with nucleotides resulted in longer intestinal villi which lead to an improved absorptive capacity of the intestine (Kehoe *et al.*, 2008). Moreover, nucleotide supplementation results in higher total bacteria counts in the rumen fluid (Krol, 2011) and results in higher concentrations of beneficial lactic acid bacteria (Kehoe *et al.* (2008).

Preventing neonatal diarrhea

Neonatal diarrhea causes more than half of calf mortality and is a large economic loss to the dairy industry. It is caused by pathogens that damage the gut system and could ultimately lead to death of the animal. Supplementation with nucleotides results in an improved intestinal morphology and subsequently decreased diarrhea in calves (Kehoe *et al.*, 2008) and improved fecal score which is an indication of better digestive health (Krol, 2011).

Boosting animal performance

Supplementation of animal diets with nucleotides has been demonstrated to improve growth performance of animals. The availability of nucleotides might be rate-limiting in rapidly dividing tissues, like in young calves. Exogenous added nucleotides do not only overcome this bottleneck, but also reduces the energy requirement of the animal, as de novo synthesis of nucleotides is an energy demanding process. This is especially important for animals during growth phases, reproduction and challenge periods (Bonato, 2017). Yeast nucleotides added to calf milk replacer lead to higher body weight as well as higher daily body weight gains, better feed uptake and

better feed conversion rates (Krol, 2011). Moreover, nucleotide supplementation improved milk production yields by 3%

and increased the content of nucleotides in milk greatly improving their nutritional and economical value (Xiaochun *et al.*, 2012).

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