ANEVIS™
Rumen-protected niacin

QualiTech

ANEVIS supplementation optimizes many health factors in growing beef cattle

Background

Niacin plays important roles as a cofactor in lipid, protein, and carbohydrate synthesis. Therefore, supplementation may be justified when high forage levels result in lower niacin concentrations. Rumen-protected niacin (Anevis) has been widely used in dairy cattle due to its numerous metabolic advantages, such as its vasodilatory, antioxidative, and antilipolytic effect. In this study, we investigated the effect of supplementation with Anevis on beef cattle liver transcriptome (i.e., genes present in the DNA).

Design

A group of 6 Angus × Simmental, weaned steers (n = 4) and heifers (n = 2) with average body weight (BW; 299 ± 7 kg) and age of 7–9 months old were randomly allocated in two groups based on dietary treatment: Anevis (n = 3), and Control (n = 3). After a training period of ~10 d, animals were successfully adapted to Calan gates. The diet offered was *ad libitum* Bermudagrass hay combined with a nutritional supplement composed of 1.61 kg of endophyte-free tall fescue seeds, and 1.61 kg of pellets composed of 46.5% ground corn, 46.5% soybean meal, 5% wheat middlings, and 2% soybean oil; and 0.1 kg of molasses per animal per day. Anevis was supplemented at 6 g/h/day (4.2 g niacin). Liver samples were obtained 30 days after the beginning of the supplementation with Anevis. The total RNA of liver samples was extracted and analyzed through RNA-sequencing; a technique that determines the level of expression of differentially expressed genes (DEG) in the whole genome (DNA). DEG were clustered based on their related metabolic pathways (KEGG pathway; Figure 1).

Results

A list of 1,192 genes were differentially expressed between treatments. These DEG were significantly altered by administration Anevis as compared with the Control. They resulted in alterations to the following metabolic pathways:

<u>Downregulation of arachidonic acid metabolism pathway</u>

- Inhibitory effect of niacin on lipolysis.
- Anevis supplementation may improve liver health status by preventing hepatic lipid accumulation.

<u>Downregulation of Cholesterol metabolism</u>

- Inhibitory effect of niacin on total cholesterol decreasing metabolic pathways.
- Anevis supplementation downregulates genes that encode for proteins of glycan biosynthesis, which might suggest that glycation could potentially be inhibited, leading to decreased VLDL and LDL synthesis, which is beneficial to liver health.

<u>Increased the expression of genes that are critical regulators of liver size</u>

- The decrease in organ size could be explained also by the lipolytic effect of niacin in liver adipose tissue content.

<u>Promotion of anti-inflammatory effects</u>

- Mediated via HCA2-dependent mechanisms in monocytes and macrophages.
- Inhibition of adhesion and accumulation in adipose tissue by oxidized LDL.
- Inhibition of angiotensin II-induced ROS production in vascular endothelium.

<u>Promotion of a vasodilator effect</u>

- Niacin derived activation of genes that attenuate the increment of hepatic vascular resistance.
- Anevis supplementation produced an inhibition of the Phospholipase D pathway, which causes vasoconstriction and regulates blood pressure.

<u>Causing an inhibition on cell migration through actin reorganization and cell proliferation</u>

- Niacin interferes with the signaling cascade of chemo-attractants in macrophages.
- This leads to the macrophage proinflammatory responses of niacin.

<u>Inhibition of inflammation and increased activation of angiogenesis</u>

- Observed in the HIF1 pathway (an oxygen-sensing metabolic pathway).
- Anevis activates an early response gene involved in hepatic tissue proliferation and liver regeneration.
- The FOXO signaling pathway was downregulated, potentially inhibiting oxidative stress resistance and DNA repair, glucose metabolism and immunoregulation.

For more information, please visit qualitechco.com

Potential antifibrotic properties

- Anevis also inhibited the conversion of mechanical forces into biochemical signals through the RAP1 pathway, leading to attenuation of collagen accumulation exerting of niacin.

Downregulation of Insulin signaling suggests an improved insulin sensitivity

- Downregulation of G6PD, which encodes for a key enzyme involved in the last step of gluconeogenic and glycogenolytic pathways, suggesting gluconeogenesis inhibition.
- Anevis treatment is associated with an increase of adiponectin, an important insulin-sensing hormone.

Conclusion

Anevis supplementation presented a significant list of potential benefits observed at the liver transcriptomics level. Several metabolic pathways revealed positive effects of Anevis. The most impacted pathways showed that rumen-protected niacin had a down-regulatory effect on the expression of genes related to lipolysis, inflammatory responses, atherosclerosis, oxidative stress, and fibrosis, and enhancing vasodilation. Therefore, results from our study could potentially promote supplementation of rumen-protected niacin on beef cattle backgrounding operations or new arrivals to a feedlot, especially during the acclimation period when health status is often compromised. Finally, it is important to remark that our study seeks to bring light on the specific role of niacin in growing beef cattle, and caution must be exercised when translating our findings to other species or cattle breeds (i.e., transition dairy cows).

Reference

https://doi.org/10.1371/journal.pone.0289409

Figure 1. Results of flux and impact uncovered by Kyoto Encyclopedia of Genes and Genomes (KEGG) database analysis of the bovine liver transcriptome of growing beef cattle supplemented with ANEVIS.

KEGG category	KEGG subcategory	KEGG pathway	Impact	Flux
Metabolism	Lipid Metabolism	Arachidonic acid metabolism		
Environmental Information Processing	Signal Transduction	VEGF signaling pathway		
Environmental Information Processing	Signal Transduction	HIF-1 signaling pathway		
Environmental Information Processing	Signal Transduction	TNF signaling pathway		
Environmental Information Processing	Signal Transduction	Notch signaling pathway		
Environmental Information Processing	Signal Transduction	FoxO signaling pathway		
Environmental Information Processing	Signal Transduction	Rap1 signaling pathway		
Environmental Information Processing	Signal Transduction	Phospholipase D signaling pathway		
Environmental Information Processing	Signaling Molecules and Interaction	ECM-receptor interaction		
Cellular Processes	Cellular community - eukaryotes	Focal adhesion		
Cellular Processes	Cell Motility	Regulation of actin cytoskeleton		
Organismal Systems	Immune System	Fc epsilon RI signaling pathway		
Organismal Systems	Immune System	B cell receptor signaling pathway		
Organismal Systems	Immune System	T cell receptor signaling pathway		
Organismal Systems	Immune System	Toll-like receptor signaling pathway		
Organismal Systems	Immune System	Chemokine signaling pathway		
Organismal Systems	Immune System	Neutrophil extracellular trap formation		
Organismal Systems	Endocrine System	Thyroid hormone signaling pathway		
Organismal Systems	Endocrine System	Regulation of lipolysis in adipocytes		
Organismal Systems	Endocrine System	Adipocytokine signaling pathway		
Organismal Systems	Endocrine System	Insulin signaling pathway		
Organismal Systems	Digestive System	Carbohydrate digestion and absorption		
Organismal Systems	Digestive System	Protein digestion and absorption		
Organismal Systems	Digestive System	Cholesterol metabolism		

'Impact' represents the change in the expression of the genes belonging to a specific pathway due to the supplementation of ANEVIS; and 'flux' as the report of the average direction in the expression as downregulation, upregulation, or neutral or no change. Flux represents the direction of each subcategory belonging to 'Metabolism' KEGG category: green color represents inhibition, yellow neutrality, whereas red color shows activation. Color intensity depicts flux level. Blue lines show the impact of each category and the corresponding subcategory (P value < 0.05).