



# Improving The Productive Results Of Dairy Cows Through Intestinal Stimulation Beyond The Rumen: Nexulin

In dairy cows, during the transition period between gestation and lactation, the massive demand for glucose by the mammary gland means that glucose distribution is a key factor in improving the productive processes. Insulin is the main hormone involved in the regulation of the glucose mechanism and, as it is an anabolic hormone, it stimulates the uptake of glucose by skeletal muscles and adipose cells, inhibiting hepatic gluconeogenesis. Recent research has shown how certain bioactives can modulate the release of insulin into the blood flow through the pancreas during certain periods of metabolic challenges.

## Insulin regulation of the glucose metabolism

Dietary carbohydrates give animals energy. The carbohydrates are transformed

into glucose through various digestive metabolic pathways, and this glucose is subsequently released into the bloodstream. In the pancreas, the beta cells detect the increase in the levels of glucose and, in order to reduce them, the same beta cells release insulin into the blood. When the circulating insulin reaches the skeletal and adipose tissue, it binds to the cell surface receptors present and this act as a key in order to stimulate the translocation of the GLUT4 glucose transporter from intracellular locations to the surface. The circulating glucose can then subsequently penetrate the cell and be stored in the form of glycogen or glycerol.

## Glucose sparing – Insulin resistance in peripheral tissues

During early lactation studies, the

insulin response threshold increased and the skeletal and adipose tissues became more resistant to the signal from this hormone. Consequently, the uptake of glucose by the adipose tissue decreases and there is more glucose available for the mammary gland: this process is called glucose sparing.

## Insulin inhibition of gluconeogenesis

The liver produces glucose through two metabolic pathways: gluconeogenesis and glycogenolysis. Gluconeogenesis is the most important pathway and depends on the availability of substrates and hormonal regulations, especially insulin. Gluconeogenesis is a minor pathway since the quantities of glycogen present in the liver are even more limited. Furthermore, insulin has an inhibiting effect on the enzymes involved in the gluconeogenic pathway. Thus, when gluconeogenesis is limited and the demand for energy is increased, the liver produces Beta-hydroxybutyrate (BHBA) through the oxidation of NEFAs (non-esterified

fatty acids). BHBA acts as a replacement source of energy for glucose.

## Capsaicin decreases the release of insulin

Oleoresin capsicum is extracted from the capsicum fruits using hexane, the main active ingredient of which is capsaicin. Rumen-protected capsaicin is capable of decreasing blood insulin concentrations without affecting the glucose concentration (Oh et al., 2017). The inhibiting effect of capsaicin seems to be linked to the activation of the TRPV1 receptor (Transient Receptor Potential Cation Channel subfamily V), also known as the capsaicin receptor, the activation of which induces the secretion of CGRP (Calcitonin Gene-Related Peptide). This peptide plays a crucial role in reducing the secretion of insulin by the pancreas (Tanaka et al., 2013. Pettersson and Ahren 1990).

Nexulin is the first and only source available on the market based on capsaicin bypass. By activating TRPV1 in the intestine, Nexulin reduces the release of insulin

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and, as a result, prevents the inhibition of gluconeogenesis by subsequently supporting the glucose sparing effect. An increase in the glucose available for milk production, without requiring the mobilisation of energy reserves, leads to a direct increase in milk production, since it is the primary factor in determining its generation.

Following consecutive tests in dairy cows under experimental conditions (Oh et al, 2017) or in field conditions outside the EU (United States and New Zealand), Pancosma decided to conduct a European field experiment in order to validate the use of Nexulin in lactating cows.

Material and Methods

Location :

- Commercial farm located in Portugal (Ribatejo)

Animals and Housing:

- 500 Hostein Friesian lactating cows (LW: 700 kg)
- Animals milked in a milking parlour, housed in an open barn with free access to water and feed

Climate conditions:

- No specific events were recorded. Conditions recorded throughout the entire experimental test. According to the Livestock Weather Safety index, the THI (Temperature Humidity Index) maintained levels between 61.5 and 74.1

Experimental treatments:

- Experimental design: basic diet with 35.5% corn silage, 8.8% yeast, 12.4% brewers grains and 10.6% corn. Dry material, raw protein, and neutral detergent fibre were 51.5%, 15.5% and 33.8% respectively.
- Nexulin ON: from 1 January to 30 March 2018, with the inclusion of Nexulin PX (N60-3301) at a rate of 1 g/animal/day, in concentrate and administered to all the animals on the farm.
- Nexulin OFF (Control): from 1 April to 30 June 2018, without including the additive in the diet.

Controlled parameters:

- Individual data: daily milk production of 50 cows with < 100 DIM, in each period.
- Herd data: milk production and composition (fat, protein, somatic cells, urea, dry extract)

Statistical treatment:

- All the data was subjected to a Variance

Analysis using R Software version 3.5.1

Results

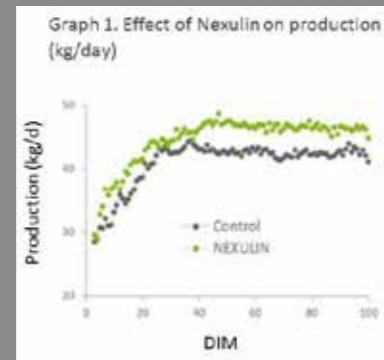


Table 1. Nexulin effects on milk compositions

	Control	NEXULIN	P-Value
Milk fat (%)	3.48	3.55	0.01
Milk protein (%)	3.16	3.18	0.14
Dry extract (%)	8.77	8.84	<0.001
SCC (*10 <sup>3</sup> cells/ml)	36.5	33.7	<0.001

The production responses to the inclusion of Nexulin are presented in Graph 1.

Cows treated with Nexulin produced more milk (+3.55 kg/day, P < 0.001) than the control cows. This increase in production did not lead to a drop in the quality of the milk.

The milk compositions for both groups are presented in Table 1. The fat content increased significantly (P < 0.01) with the addition of Nexulin, while the protein content was maintained. The somatic cell count was significantly lower with Nexulin, despite the already excellent results obtained in the control group.

On studying the historic data of the farm over a similar period (January to March), there is a significant increase in the herd's daily milk production (P<0.001). During the year the experimental test was conducted, production increased by 4.63 kg/day compared to 2017 and by 5.33 kg/day compared to 2016 (Graph 2). Regarding the milk quality, the milk protein (in %) was significantly higher in the year of the experiment (Graph 3), however, there were no significant differences in the fat percentage.

European conditions, while maintaining the milk solids composition. The previously observed stimulation of TRPV1 receptors and the associated modulation of insulin secretion help to contribute to productive results and productive optimisation during the glucose sparing phase.

1 Oh et al., (2017): J. Dairy Sci. 100:1-14



Sigfrid LÓPEZ FERRER, PhD. Technical Manager Mediterranean & Africa, Pancosma



Constantin Sebastian Bioactives Product Manager, Pancosma

Graph 2. Herd milk production (kg/day) over the last few years, January to March; P < 0.001



Graph 3. Milk composition (%) over the last few years, January to March; P < 0.001



Conclusions

Nexulin, at a field level, confirmed the

The Food and Agriculture Organization of the United Nations estimates the world population will reach 9 billion people by 2050 and as a consequence, livestock production must double to meet the demand for food. Sustainable livestock production is a field of intense research where ruminants play a great role since they can transform graze pastures, silage and high-fiber crop residues into high-quality human food (i.e. milk and meat). The goal is "sustainable intensification", meaning increased productivity while reducing the environmental impacts. In this context, feed efficiency (FE) has a particular importance, since it is directly related to productivity, greenhouse gas emission intensities, and resource use.

Due to its importance, more than two dozen feed efficiency measurements have been proposed to select efficient animals and from those, residual feed intake (RFI) is considered one of the most effective

One differentially expressed feature between high feed efficient and low feed efficient animals was found, but most importantly, one enriched pathway and two sets of highly correlated features significantly associated with feed efficiency were also found, which could be considered a potential molecular signature of feed efficiency in Nellore cattle before they enter the feedlot period.

# Identification Of A Metabolomic Signature Associated With Feed Efficiency In Beef Cattle

