The potential of phytogenics in animal nutrition

by Dr Basharat Syed, Micro-Plus Konzentrate GmbH, Am Güterbahnhof 7a D-37627 Stadtoldendorf, Germany.

Gastro-intestinal disorders caused by inflammation processes are an all too common experience in animal production. This article provides the reader with a detailed animal physiology insight into the key fundamental factors that cause these upsets.

The latest research findings at the University Giessen, Germany demonstrate how digestarom can have a beneficial impact on such situations. It belongs to the group of phytogenic feed additives and has been classified as a flavour according to the EC Regulation No 1831/2003 of the European Parliament and Council.

The product is a combination of essential oils, herbs, extracts and spices. In addition to the flavouring effect, which arouses the animal's appetite, digestarom stimulates the internal secretions.

The increased secretion of the endogenous digestive enzymes optimises digestion and the degradation of metabolic products, as well as the absorption and metabolic conversion of the supplied feed nutrients.

For many years Micro-Plus has considered not only the zootechnical performance by the supplementation of digestarom, but also its influence on the genetic information and inflammatory processes in the intestine.

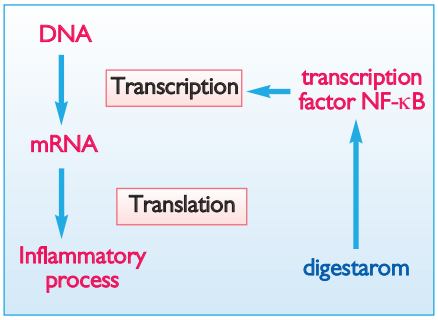

Fig. 1. Functioning of the transcription factor NF-κB.

Several pathological stimuli, including bacteria and viruses, are known to stimulate inflammatory processes in the intestinal mucosa by cytokine-mediated activation of the pro-inflammatory transcription factor NF-κB.

NF-κB is considered the master regulator of inflammation because its activation causes an up-regulation of a series of genes mediating the inflammatory response.

Through the subsequent release of inflammatory mediators, like TNFα, IL-6, or INFγ, which enter the circulation, the inflammatory process is not only restricted to the intestine but may also affect other tissues.

For instance, inflammatory mediators cause a stimulation of protein catabolism in skeletal muscle by activation of the ubiquitin-proteasome-system, which is the most important system for intracellular protein degradation in mammalian cells, and an increase in the formation of acute phase proteins in the liver.

Considering that such processes lead to an impairment of animal performance, the inhibition of inflammatory processes in the intestine is a reasonable approach to maintain performance and health characteristics of livestock animals.

Effect of phytogenics

A large body of evidence exists in the literature to show that phytochemicals, which are important constituents of essential oils, are capable of attenuating inflammatory processes in the intestine by blocking the pro-inflammatory transcription factor NF-κB. Recent studies showed that phytochemicals exert protective effects on tissues including the intestine by activating the Nrf2 pathway.

Activation of the Nrf2 pathway leads to the induction of genes responsible for cellular defence against reactive oxygen species

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Fig. 2. Inhibition of the expression of NF-κB target genes in intestinal cells.

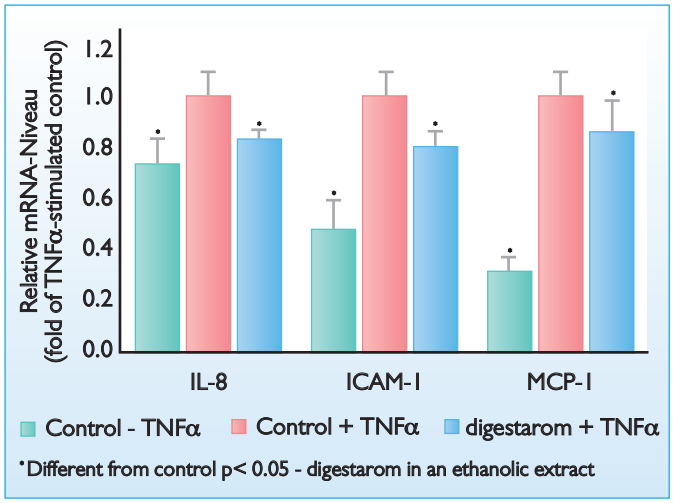
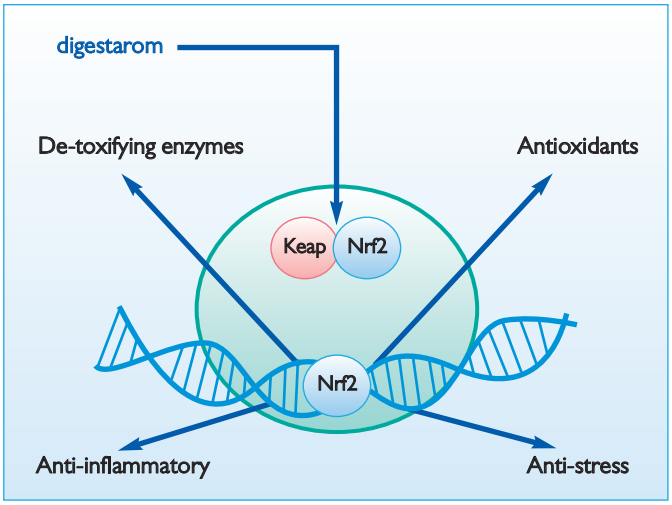


Fig. 3. Functioning of the transcription factor Nrf2.



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and detoxification of xenobiotics. In this university study, the objective was to explore the anti-inflammatory potential of the phytogenic additive digestarom, which is rich in essential oils, by using Caco-2 intestinal epithelial cells.

Caco-2 cells express characteristics of enterocytic differentiation upon reaching confluence, and are therefore an established in-vitro model for intestinal epithelial cells.

To evaluate the anti-inflammatory action of digestarom, its effect on TNFα-induced transactivation of NF-κB and TNFα-induced mRNA levels of selected NF-κB target genes, interleukin-8 (IL-8), chemokine (C-X-C motif) ligand 10 (CXCL 10), intercellular

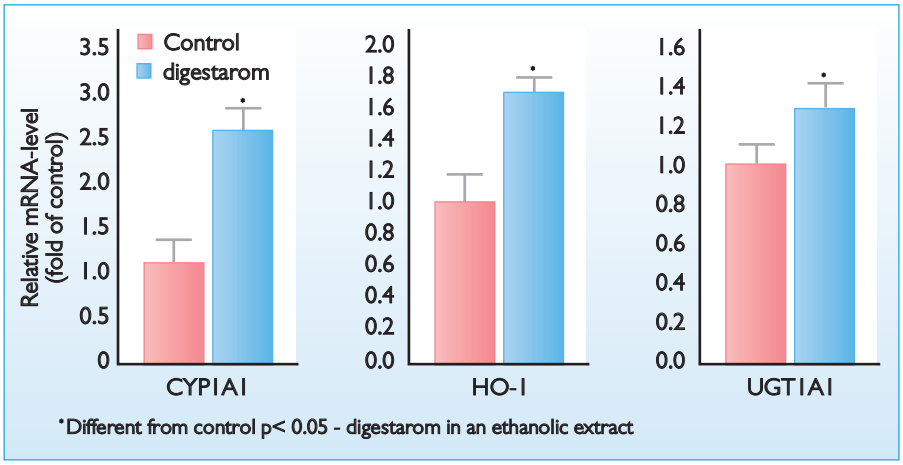

Fig. 4. Up-regulation of Nrf2 target genes in intestinal cells.

adhesion molecule-1 (ICAM-1) and monocyte chemoattractant protein-1 (MCP-1) were investigated.

To study the effect of digestarom on activation of the Nrf2 pathway, the mRNA levels of selected Nrf2 target genes, heme oxygenase-1 (HO-1), cytochrome P450 isoform 1A1 (CYP1A1) and UDP-glucuronosyltransferases isoform 1A1 (UGT1A1) were determined.

Research findings

Supplementation of digestarom in the ration reduces the activation of the complex transcription factor NF-κB, so that the damages caused by inflammatory processes are substantially reduced.

The mode of functioning of NF-κB is represented in Fig. 1.

It was found that digestarom significantly reduced the mRNA levels of the NF-κB target genes IL-8, ICAM-1, and MCP-1 which initiate and maintain inflammatory reactions in Caco-2 cells contracted with lipopolysaccharides functioning as antigens to provoke inflammatory reactions and added TNFα (tumour necrosis factor alpha) which intensifies the inflammation.

The product is also able to stimulate and raise the activity of the transcription factor Nrf-2 responsible for anti-oxidative activity.

Positive effects

Digestarom is capable of inhibiting transactivation of the pro-inflammatory transcription factor NF-κB, thus it is able to counteract the inflammatory processes.

It is able to activate the transactivation of Nrf2 and thus stimulate the expression of antioxidant enzymes and enzymes of xenobiotic metabolism (phase 1 and 2 enzymes) in the liver.

Digestarom is able to reduce the hypersensitivity of the intestines due to inflammation and, eventually, reduce the incidence of the onset of enteric diarrhoea provoked by the activity of inflammatory transcription

factor NF-κB. It assists and promotes the immune system to enhance its resistance capacity to defend any potential inflammatory or oxidative factors.

Economic benefits

Through its prophylactic nature, digestarom prevents excess inflammation and, eventually necrosis, in the intestinal tract, thereby promoting optimal animal performance and reduced mortality. It also helps in the reduction of sub clinical gastro-intestinal disorders during feed changes, which reduces production losses.

Due to its stimulation of Nrf2 the product indirectly prevents the hypersensitivity of intestines to oxidative stress. The extra-hepatic detoxification, in which Nrf2 plays an important role by promoting the formation of detoxifying enzymes, then helps in the breakdown of undigested feed and metabolic toxins thus assisting the liver.

By stabilising the immune system digestarom plays an important role in situations of peak production performance when the organism is metabolically burdened, stressed and unstable, thus saving energy and therefore production costs.

A graphic representation in Fig. 5 shows the cardinal signs of inflammation, the appearance and damage of these are mitigated by the continuous supplementation of digestarom in the diet, which prevents economic losses caused by these classical signs and symptoms.

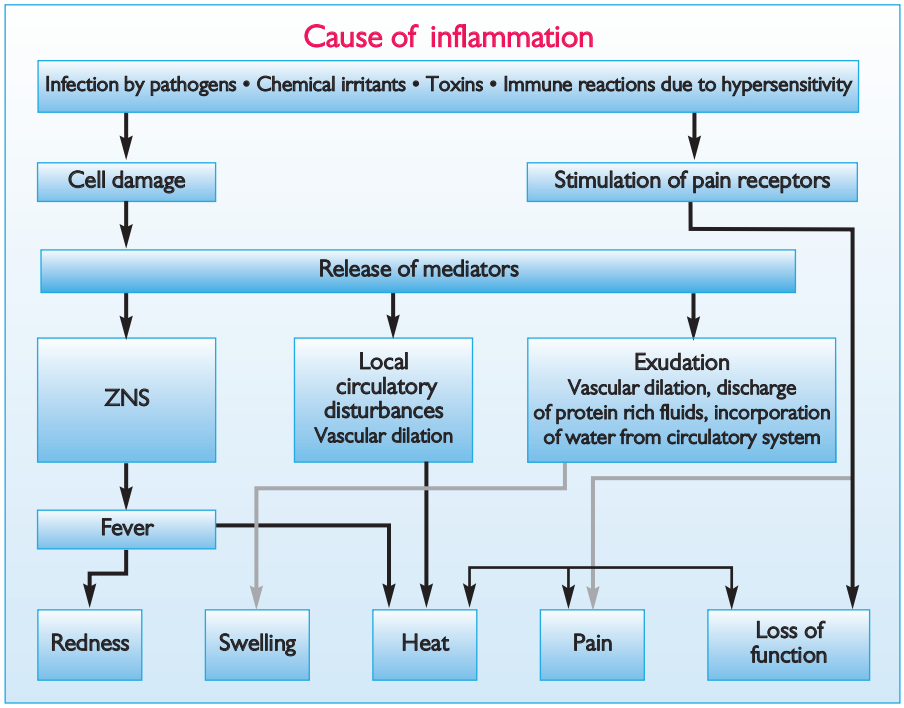

Fig. 5. Representation of the appearance of cardinal signs of inflammation.

Regular supplementation in the ration acts as a prophylactic against inflammatory reactions in the gastro-intestinal tract by inhibiting the NF-κB factor and stimulating the anti-oxidative factor Nrf2.

This activity interrupts the damaging circle of the release of inflammatory mediators that otherwise would provoke intensive inflammation and the resulting necrosis. ■