nutrex NV

the finishing touch for nutrition

# EndoBan®

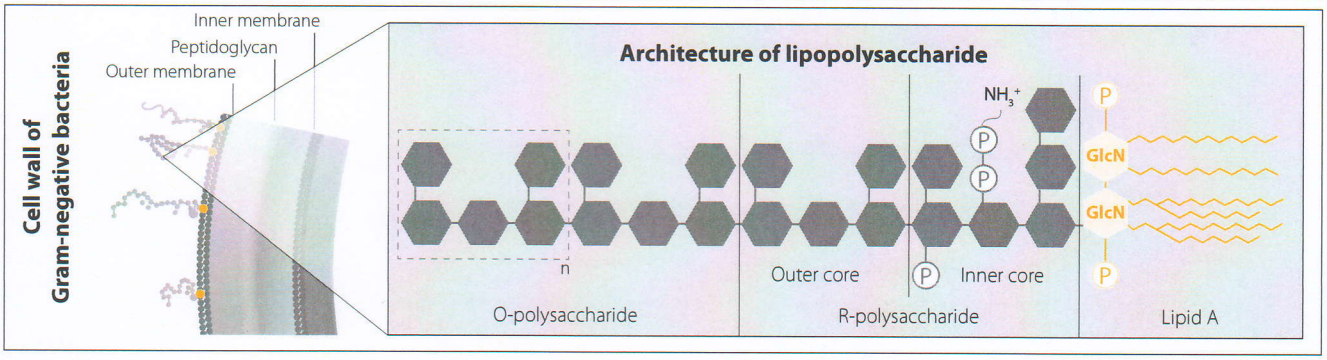
## Disarm the endotoxins

ENDOTOXIN SOLUTIONS

# Introduction

Endotoxins are toxic molecules which are part of the bacterial cell wall structure. The most well-known endotoxins are lipopolysaccharides (LPS). These are the building blocks of the outer membrane of Gram-negative bacteria. LPS are released into the environment when the bacteria multiply or when their cell membranes rupture through bacterial lysis. For this reason, endotoxins are present everywhere in the environment: in the air, in the water, in the soil and also in the gastrointestinal tract of animals. LPS are chemically composed of an outer O-polysaccharide chain, an inner R-polysaccharide chain and lipid A (Figure 1). The latter is the toxic part of the molecule.

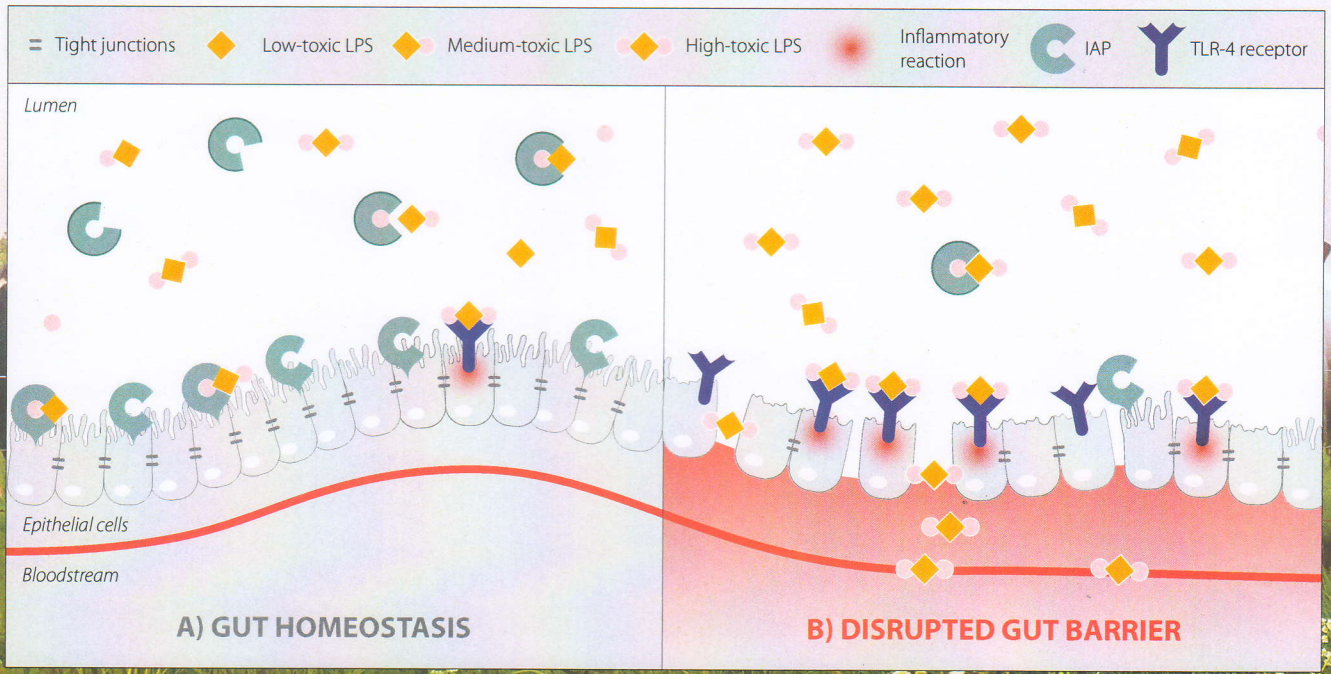
**FIGURE 1: CHEMICAL STRUCTURE OF LPS**




# Transfer of endotoxins

In production animals the gastrointestinal tract is the main risk site where endotoxins can be transferred from the lumen into the bloodstream, where they exert their toxic effects. In healthy animals, the permeability of the gut is tightly controlled. The gut barrier is composed of gut epithelial cells (enterocytes) which are connected by tight junction proteins. This keeps endotoxins on the luminal side of the gut where they are not toxic to the animal. The immune system constantly 'senses' these endotoxins by specific receptors (TLR-4) present on the membrane of enterocytes. In addition, enterocytes produce an enzyme (intestinal alkaline phosphatase, IAP) which detoxifies endotoxins. These mechanisms protect the animal against the constant threat of endotoxins (Figure 2A).

**FIGURE 2: REACTIONS TOWARDS ENDOTOXINS IN A HEALTHY AND IN AN INFLAMED GUT**



Several external factors are known to increase gut permeability. Further, a disrupted gut barrier is characterised by a lower IAP activity (lower endotoxin detoxification capacity) and a higher number of TLR-4 receptors (excessive triggering of the immune system). Altogether, this promotes leakage of endotoxins into the bloodstream (Figure 2B).

In ruminants, the translocation of endotoxins into the blood circulation can also take place across the rumen epithelium. This epithelium has a multi-layer structure and is covered by keratinised cells, which act as a protective barrier. Moreover, TLR-4 receptors are also present to protect the animal against endotoxins. However, a low ruminal pH and a high osmolality reduce the epithelial barrier function and increase endotoxin translocation from the rumen into the blood.

## Endotoxemia

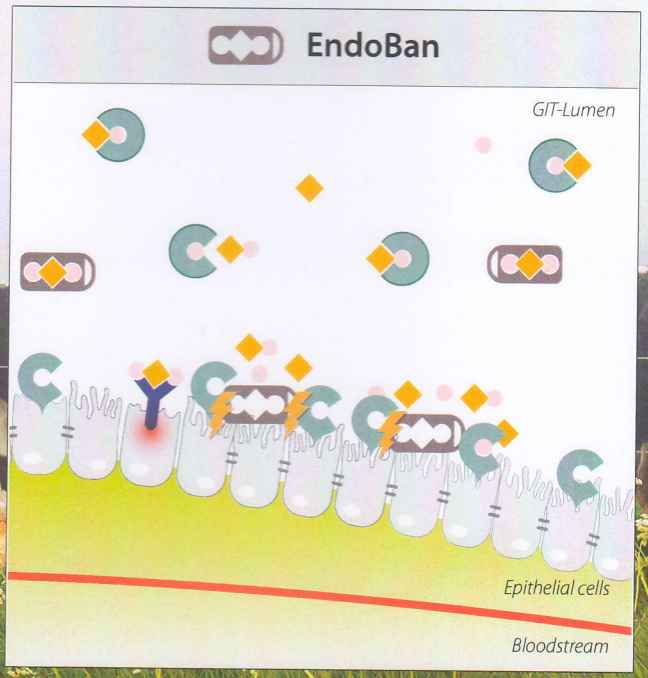
Once in the bloodstream, endotoxins induce an inflammatory immune response: they bind to TLR-4 receptors present on the membrane of macrophages after which these produce inflammation markers, such as IL-6, TNF-α and IL-1β. These inflammatory markers modulate the functioning of different tissues and they trigger the liver to produce acute phase proteins. Generally, these excessive immune processes consume a lot of energy and nutrients which come at the expense of the production of meat, eggs, and milk. In the worst case, high amounts of endotoxins can result in septic shock and even death.

## EndoBan

It is clear that measures should be taken to effectively remove or detoxify endotoxins before they can pass through the gut barrier and lead to inflammation and disease.

**EndoBan** was developed by combining different strategies to help farmers and feed mills to reduce the negative effects of endotoxins before they can reach the bloodstream, thereby lowering the potential for endotoxemia and the subsequent effects on animal performance (Figure 3).

**FIGURE 3: REDUCTION OF ENDOTOXIN ACTIVITY BY ENDOBAN**

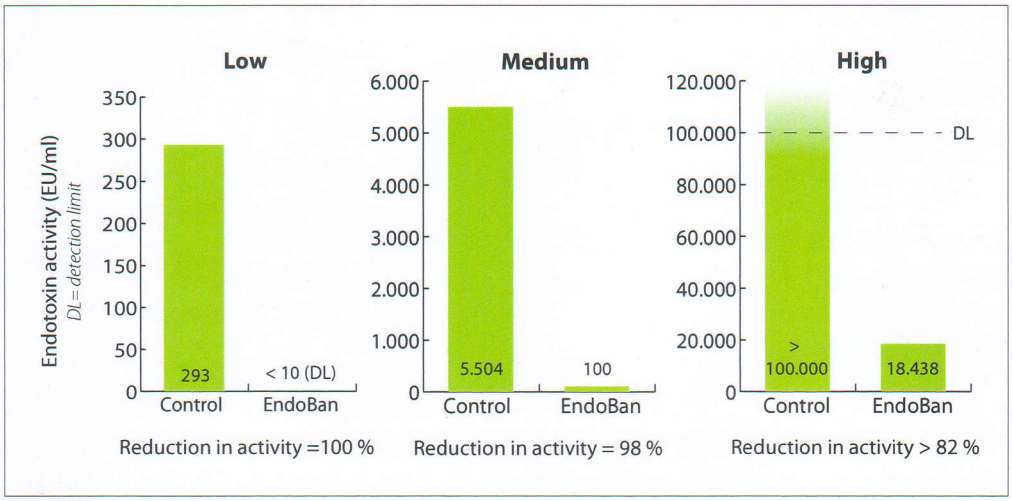


# Trial results

**EndoBan** was tested to evaluate its capacity to reduce the amount of (potentially harmful) endotoxins. Therefore, LPS from E. coli O111:B4 was used at 3 different concentrations which correspond to a low, medium and high level of contamination in practice. Next, the LPS solutions were treated with an equivalent of 1 kg/ton **EndoBan** and the endotoxin activity was verified by the Endosafe-PTS test.

As shown in Figure 4, **EndoBan** was able to efficiently reduce the activity of endotoxins at different levels of contamination. It is clear that **EndoBan** can help to reduce the levels of free endotoxins in the digestive tract, thereby limiting the potential passage through the gastrointestinal barrier.

**FIGURE 4: ENDOTOXIN ACTIVITY AT DIFFERENT LEVELS OF CONTAMINATION**




# Use

It is recommended to use **EndoBan** under following circumstances, when there's increased occurence of endotoxins:

## POULTRY

- At the onset of lay
- For hens housed in cage-free systems, which are affected more frequently by intestinal disorders
- After antibiotic treatment
- In high fat diets
- During heat stress
- Fatty liver
- In general when gut health is compromised

## CATTLE

- A diet high in rapidly fermentable carbohydrates
- Heat stress
- After antibiotic treatment
- Generally, when gut health is compromised, which can be caused by different environmental, social and dietary factors

**TABLE 1: ENDOBAN DOSAGE LEVEL**

| | (g/kg feed) | (g/cow/day) |
|---|---|---|
| Preventive | 0.5 – 1 | 15 |
| In case of severe problems | 1.5 – 2 | 25-30 |

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