Mitigating a Feed Induced Immune Response

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Inflammation is an important mechanism that is used by the immune system to repair damaged tissue after injury or infection. If well-regulated, an inflammatory response will re-establish normal tissue function. Uncontrolled inflammation can however lead to a chronic response with a subsequent loss of tissue function[1].

The intestine must provide an effective barrier that prevents the translocation of toxins and bacteria from the intestinal lumen into the body but still allow for the absorption of nutrients[1]. The physical intestinal barrier consists of intestinal enterocytes linked together by transmembrane tight junction (TJ) proteins to form a tight seal preventing the translocation of bacteria and toxins from the intestine into the bird's body. The breakdown of these TJ proteins results in a leaky gut and the translocation of bacteria and toxins from the intestine into the body, resulting in an inflammatory response and further damage to the intestinal barrier which can lead to a systemic inflammatory response and septicaemia[4].

Feed fed to broilers, breeders and layers is formulated for the birds to achieve as close as possible to 100% of their genetic potential. The feed however can contain components that challenge intestinal immunity triggering a low-grade inflammatory response[1].

If left unchecked this low-grade inflammatory response can result in chronic inflammation. A chronic inflammatory response will lead to a reduction in intestinal function and nutrient diversion away from production to maintain the inflammatory response resulting in a reduced performance. Up to 3% of birds metabolizable energy has been estimated to be redirected to the maintenance of a feed induced immune response (FIIR)[3]. Dietary components that can trigger a low-grade immune response or FIIR in the intestine include non-starch polysaccharides, excess protein and mycotoxins[1&2].

Non-Starch polysaccharides (NSP)

Carbohydrates present in plants are divided into starch and non-starch polysaccharides (NSP) also called structural carbohydrates or fibres. NSP can be further classified into soluble and non-soluble NSP. Soluble NSP consist of arabinoxylans, glucans, fructans, pectins, and hemicelluloses. Monogastric animals do not produce enzymes that can digest NSP. Soluble NSP form a jelly in the small intestine of poultry after contact with mucous in the intestinal tract. The jelly covers the digesta and the intestinal enterocytes limiting feed contact with enzymes resulting in lowered digestion and absorption of nutrients[1].

The increase in digestive viscosity will decrease the rate of digesta transit. Decreasing the rate of digesta transit will increase the proliferation of pathogenic bacteria such as *Clostridium perfringens*. Proliferation of *Clostridium perfringens* will stimulate an intestinal inflammatory response (FIIR), break down in intestinal TJ proteins and leaky gut. Leaky gut will result in translocation of bacteria from the intestine into the blood resulting in systemic inflammation and septicemia[1].

Soybean meal can contain 1 – 1.6% insoluble NSP called mannans and galactomannans. The cell wall of many pathogens contains mannans. Mannans present in feed can be recognised by pathogen recognition receptors of the intestinal innate immune system. Recognition of mannans in feed will thus result in an innate immune response that can lead to an energy depleting FIIR[3].

Excess proteins

Broilers have been selected for a high growth rate and high feed intake. This high feed intake often exceeds the acid production capacity of the proventriculous, resulting in an increase pH of preventriculous and an increase in undigested protein entering the intestine. Damage to the intestinal epithelium as a result of coccidiosis or other insults can lead to leaky gut. This results in translocation of intestinal content including undigested protein across the intestinal barrier triggering an intense inflammatory response (FIIR) resulting in further damage to the intestine and worsening of leaky gut.[5]

Undigested proteins reaching the ceaca are a predisposing cause for the development of necrotic enteritis (NE) from an increased proliferation of *Clostridium perfringens* in the ileum and ceaca. NE will result in inflammation and damage to the nutrient absorptive capacity of the intestine and a FIIR.[1]

Mycotoxins

Mycotoxins are secondary metabolites produced by fungi that contaminate grains. Mycotoxins when absorbed can induce various systemic effects. The intestinal barrier is the first tissue that comes into contact with feed mycotoxins and acts as a filter for mycotoxins. Intestinal enterocytes that form the intestinal barrier will thus potentially suffer toxic effects from the mycotoxins.[1,6&7]

There is a rapid turnover of intestinal enterocytes in a healthy intestine which is in turn dependent on a rapid turnover of proteins especially TJ proteins. Mycotoxins including T-2, DON and Ochratoxin (OTA) are known to inhibit protein synthesis. Intestinal enterocytes are thus prime targets for the negative effects of mycotoxins. Inhibition of TJ protein synthesis by mycotoxins will result in a breakdown in the intestinal barrier resulting in leaky gut and FIIR. This will result in translocation of bacteria and toxins from the intestine into the body resulting in a systemic inflammatory response and septicaemia.[1,4,6&7]

How can a FIIR be mitigated?

Exogenous enzymes

The addition of exogenous enzymes for example xylanases (Xygest™ HT Dry), amylases and β glucanases will assist in breaking down NSPs. Breaking down NSPs will decrease the viscosity of the feed, increase the digestibility of the feed and increase feed transit thus lowering the risk of a *Clostridium perfringens* overgrowth in the small intestine[1], thus decreasing the risk for the development of a FIIR.

Exogenous mannanase enzymes added to poultry feed will hydrolyse undigestible mannans into mannan oligosaccharide fragments that are not recognised by mannose receptors and thus will not stimulate a FIIR[3].

Exogenous protease enzymes (KEMZYME® Protease Dry) added to poultry feed will increase the digestion of protein. Thus, decreasing the amount of undigested protein in the small intestine thus decreasing the risk of developing a FIIR and necrotic enteritis[1].

ButiPEARL™

An important side effect of a FIIR is the breakdown of the intestinal barrier function and development of leaky gut. Butyric acid maintains the intestinal barrier via upregulating the assembly of intestinal TJ proteins (preventing the development of leaky gut) and via down regulating the production of pro inflammatory cytokines thus down regulating the inflammatory response associated with a FIIR.[8&9]

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The high volatility and pungent odour of butyric acid complicates the use of free Butyric acid as a feed additive. The challenge of using butyric acid as a feed additive can be solved by encapsulating butyric acid using Kemin's MicroPEARL™ technology to form ButiPEARL™. ButiPEARL™ is a slow release source of Ca Butyrate that releases Ca Butyrate along the length of the small intestine.[10] ButiPEARL™ can be used to mitigate the effects of FIIR via lowering the inflammatory response and preventing the formation of leaky gut.

Toxfin™ Dry

The development of a FIIR from mycotoxins can be mitigated via using a mycotoxin binder (Toxfin™ Dry) to bind mycotoxins and ButiPEARL™ to mitigate the effect of mycotoxins on the intestinal barrier.

CLOSTAT™

NSPs and excess proteins in the small intestine creates an environment favourable for the growth of *Clostridium perfringens* increasing the risk of developing NE and FIIR. CLOSTAT™ contains the probiotic *Bacillus subtilis* PB6. Apart from the probiotic effect of PB6[12], PB6 secretes an anticlostridial factor that inhibits *Clostridium perfringens*[11]. CLOSTAT™ can therefore be used to mitigate the development of a FIIR via supressing the overgrowth of *Clostridium perfringens*.

Conclusion

FIIR can result in a marked decrease in poultry production. The Kemin solutions, CLOSTAT™, ButiPEARL™, KEMZYME® Protease dry, Toxfin™ Dry and Xygest™ HT Dry can be used strategically to mitigate the development of FIIR in poultry.

REFERENCES
Available on request.