Intestinal Integrity For Optimal Animal Health

Healthy gastrointestinal tract for optimal nutrient absorption and barrier for extraneous antigens

The gastrointestinal tract (GIT), a primary site for nutrient digestion and absorption, is constantly exposed to external harms happening through oral routes. Beyond nutrient utilisation, the intestine is a barrier against the invasion of pathogens and foreign materials. The lumen of the intestine is bordered by epithelial cells, which are held together by protein structures known as intercellular tight junctions. Together, these epithelial cells form macrostructures known as villi and microvilli that control the secretion of electrolytes into the lumen while allowing selective passage and uptake of certain molecules into the bloodstream for metabolism (Figure 1).

Figure 1 illustrates the intestinal epithelial cell lining separating the lumen from the internal environment (left). Individual epithelial cells are held together by intercellular tight junctions, forming an active barrier which only permits the passage of selective molecules (e.g., nutrients) while preventing the translocation of antigens and pathogens (middle). Certain conditions (e.g., mycotoxin poisoning or heat stress) compromise the integrity of the tight junctions and cause apoptosis of epithelial cells (right).

Factors compromise intestinal epithelium's integrity

The integrity and normal functions of the GIT and intestinal barrier are influenced by

intrinsic factors like health status, and extrinsic elements such as the composition of the diet. Indigestion due to poor diets can lead to the proliferation of pathogens including *Clostridium perfringens* and enterotoxigenic *Escherichia coli*. Certain microorganisms such as enterotoxigenic *Escherichia coli* and *Clostridium perfringens* can produce endotoxins that are known to interfere with the structure of tight junction proteins, thereby increasing the permeability of intestinal barrier. Infections by parasites (e.g., coccidiosis of poultry) can severely damage the intestinal epithelial lining, leading to lesions or predisposing the animals to gastroenteritis. Endotoxins and mycotoxins are important stressors that can lead to apoptosis of intestinal epithelial cells or worse, sub-clinical inflammation of the intestine.

Mycotoxin contamination of feed can have prominent cytotoxic effects on the epithelial cells even at very low dosages. Other stressors inducing heat stress have also been observed to escalate permeability of the intestinal barrier.

Butyrate improves intestinal health, prevents "leaky gut"

Butyric acid and its calcium salt form (collectively as "butyrates") are known to significantly enhance intestinal efficiency and morphology. Butyric acid serves as an energy source for epithelial cells. Studies have shown that butyric acid specifically stimulated the expression of genes such as *CaMKKβ coding* tight junction protein claudin-1 associated with the production of tight junction proteins that led to an enhanced intestinal barrier, reduced antigen translocation and lower incidence of leaky gut. There were also instances whereby butyric acid or its calcium salt form were shown to offer protection against certain intestinal injuries and improve recoveries.

Animals fed with coated butyrates (i.e., ButiPEARL™) developed healthy intestinal cells, with improved villi length/width and mean crypt depth compared to animals fed with diets without butyrate supplementation (Figure 2 and Table 1). Improved villi health is associated with increased efficiency of nutrient digestion and absorption.

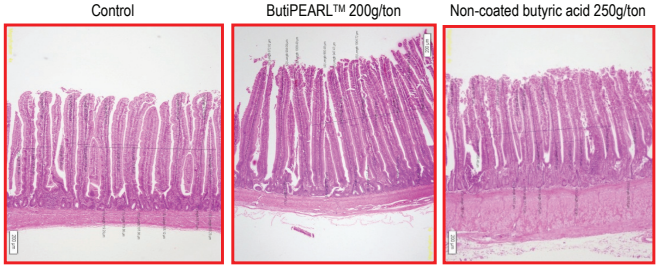

Figure 2 (from left to right) shows the intestinal villi histomorphometry of broilers fed with basal diets with no butyrate (control), diets containing 200g/ton ButiPEARL™, and diets containing 250g/ton of non-coated butyric acid. A summary of observations is provided in Table 1. All pictures: H&E 4X

Table 1: Villi characteristics of animals fed a diet with or without butyrate

Treatment	Jejunum			
	Mean Villi Height (µm)	Mean Villi Width (µm)	Mean Crypt Depth (µm)	Villi Density / 1000 µm
Control feed without Butyrate	760.0[a]	85.42[a]	130.6	8.7
Control feed with ButiPEARL™ (coated) 200g/t	994.9[b]	106.2[b]	128.6	8.8
Control feed with non-coated calcium butyrate 250g/t	729.7[a]	94.2[a]	107.7	7.7

Note: Mean values in the same column with different superscripts are significantly different P< 0.05

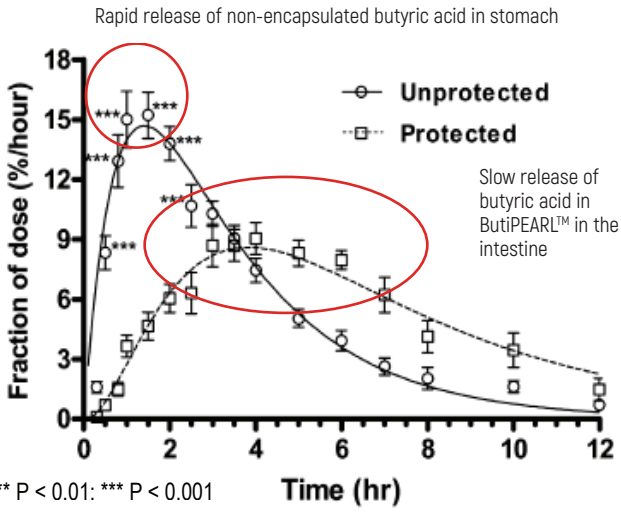

Figure 3 adapted from Smith et al. demonstrated the in vivo sustained release of encapsulated butyric acid (i.e. ButiPEARL™) fed to broiler chicks. The figure illustrates the evolution of [^{14}C] CO_2 from the metabolism of [1-^{14}C] butyrate in non-encapsulated and encapsulated forms (ButiPEARL™) over time. A higher percentage of [^{14}C] CO_2 detected in metabolism cage indicates greater evolution and metabolism of [1-^{14}C] butyrate. Food typically stays in the stomach within the first few hours upon ingestion. A higher level of [^{14}C] CO_2 is detected for non-encapsulated versus encapsulated [1-^{14}C] butyrate in the first few hours (e.g., 0 to 2 hours upon ingestion).

Encapsulation ensures slow-release of calcium butyrate along the GIT

Butyric acid is a short-chain fatty acid and can be quickly absorbed in the upper part of the GIT upon ingestion or volatilised from feeds kept open in the environment, thus reducing its beneficial effects in the intestine. Encapsulated butyrate, i.e.,ButiPEARL™ by Kemin Industries promises scientifically-proven sustained release of calcium butyrate along the intestine upon ingestion. This sustained release technology illustrated in Figure 3 was published in the Journal of Agricultural and Food Chemistry. Smith et al. conducted a trial using broiler chicks fed with diets supplemented with non-encapsulated and encapsulated calcium [1-^{14}C] butyrate. The fraction of butyric acid upon ingestion will be metabolised to produce CO_2 and in this case, [^{14}C] CO_2 that could be traced. Results from this study proved that the non-encapsulated form was immediately metabolised in the upper GIT within the first hours of ingestion, while the encapsulated calcium butyrate was released in a sustained manner in the intestinal tract upon its passage from the stomach.

Conclusion

Supplementing monogastric animals' diets with encapsulated butyrate improves intestinal conditions. Better intestinal integrity not only maximises health but also ensures efficient expenditure on feed through optimal nutrient utilisation. Healthy animals are expected to have less reliance on antimicrobial growth promoters (AGPs). Therefore, protecting intestinal integrity and health are important in expediting the withdrawal of AGPs from feed.

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