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β-glucans and MOS For Immunomodulation and Intestinal Integrity in Poultry

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Key Points:

- Yeast cell wall β-glucans and mannan-oligosaccharide provide intestinal health benefits
- β-glucans in feed function to stimulate the immune system without a fever response
- Mannan-oligosaccharide (MOS) binds certain enterotoxic pathogens in the gut
- Maintaining poultry intestinal health and immune readiness can ensure keeping pathogens at bay and promoting less transmission of pathogens to progeny, and better food safety
- Quality Technology International's BacPack® products combine IMW50® and Q-Biotic® for optimum protection and productivity

Considering the worldwide pressure from consumers, the scientific community, and international regulatory agencies, to remove or decrease the application of the antibiotic performance enhancers and the rational use of the therapeutic form in animal production, maintaining the production versus animal's health versus food safety has been a challenge. The impact of antibiotics on the gut microbiota has been recently investigated. Researchers have shown that, in addition to altering the microbiota's composition, antibiotics can also affect the gene expression, protein activity, and overall metabolism of the intestinal microbiota. Microbial changes caused by antibiotics increase the immediate risk of infection and can also affect immunological homeostasis in the long term.

With this, it is imperative that the production chain adapts and applies a strict plan of management, health, and nutrition, since the transmission of pathogens could be through the ration, environment, or even vertically (from the breeder to her offspring), so proper management plan is essential in this control.

There are several alternatives on the market to control pathogenic bacteria, such as live attenuated vaccines (which act on *Salmonella* Gallinarum and *Salmonella* Typhimurium, also acting on *Salmonella* Enteritidis). Products that affect the feed as bactericidal antimicrobials or that act on the animal organism, such as probiotics, organic acids, plant extracts, prebiotics, etc., have a different mode of action, directly or indirectly modulating the microbiota and the response of the immune system.

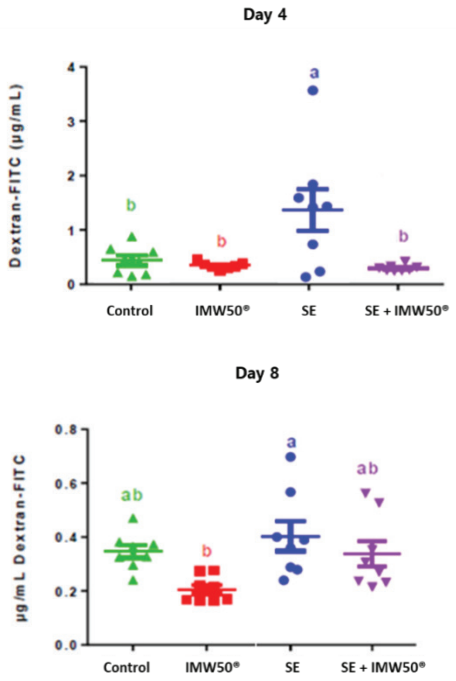
The yeast cell wall from *Saccharomyces cerevisiae* is one solution that can help with the pathogen control program since it is a natural solution that helps to reduce contamination and prevent the problem. Based on this concept, IMW50® stands out from other yeast products because it is composed of a Saccharomyces cerevisiae with dense yeast cell wall and high concentrations of β-Glucans and mannanoligosaccharides (MOS) with proven results and great cost/benefit.

MOS is known for its capacity to agglutinate pathogens. It will prevent pathogen colonization in the gut as it offers a binding site to harmful bacteria that possess type-1 fimbriae present in the intestinal tract. Because the β-glucans are indigestible, the "trapped" bacteria exit the animal's digestive system in the excreta. It is important to highlight that, to reach its full functionality, the yeast cell walls must have a low digestibility in the intestine. β-glucans are the indigestible portion of the yeast cell wall; thus, the higher the β-glucan concentration, the lower the digestibility of its cell wall.

The β-glucans present will modulate the animals' immune response as they are natural stimulants of the innate immune system. When the animal's phagocytic cells in the intestinal wall (antigen-presenting cells, APCs) contact β-glucans, they become activated and produce cytokines. The production of cytokines will trigger a "chain reaction," inducing a higher immune status in animals, making them able to resist opportunistic infections better. Thus, IMW50® supplementation ensures that birds maintain the balance of the intestinal microbiota and improve immune system

responses, resulting in decreased contamination and transmission of pathogenic bacteria to other organs of the body.

A recently published study by Bonato *et al.* (2020), where broilers were supplemented with IMW50® (0.5 kg/MT) and infected at two days old with *Salmonella* Enteritidis [SE] (orally at 10^8 CFU/broiler), showed that at four and eight days old (two and six days after infection, respectively) IMW50® had reduced marker passage (Dextran-FITC, 3-5 kD) to blood in challenged broilers (Graph 1). These results showed a significant improvement in intestinal permeability. SE can adhere to the mucosa through its fimbriae, produce toxins and damage tight junctions and epithelial cells (enterocytes), invade them and translocate into the bloodstream, other organs and tissues (Figure 1).



Graph 1. Evaluation of intestinal integrity (permeability). Higher values indicate higher permeability, which is indicative of lower mucosal integrity. Statistical relevance is indicated by different letters on each group. Differences were calculated by one-way analysis (one-way ANOVA) with Turkey's multiple comparisons test (P <0.05).

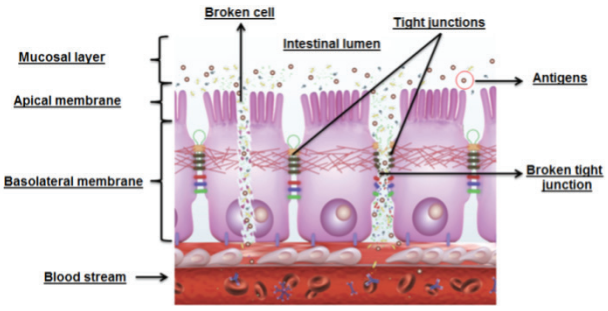
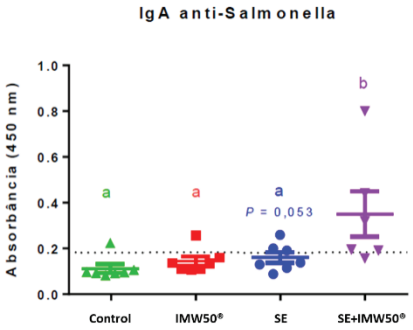


Figure 1. How bacteria damage tight junctions.

These results can be explained by quantifying circulating cells analyzed in the blood withdrawn from these broilers. It is important to note that blood leukocytes are mobilized to the gut during a normal infection process. However, if the bird has another type of infection, reduced total circulating leukocytes can impair this second antigen/site/tissue attack response. This can be especially dangerous when total leukocyte blood levels are deficient (leukopenia). In an analysis conducted in the study mentioned above, the group infected and supplemented with IMW50® had reduced blood leukocyte mobilization to the gut at 14 days. However, when this immune system was subdivided into different cells, there were more APCs and suppressor monocytes producted. The suppressor monocytes prevent an uncontrolled immune response. The group infected and supplemented with IMW50® also showed better response to helper T lymphocytes production (CD4) than the group of untreated challenged birds. The CD4 cells produce interleukins and stimulate the multiplication of cells that will attack the antigen.

The group of unchallenged birds supplemented with IMW50® showed intermediate responses between the challenged and the unchallenged control to the analyzed cells mentioned above. In addition, similar response to cytotoxic T lymphocytes (CD8) also was observed in the same group. The CD8 cells are important to prevent or control *Salmonella* invasion, as they can invade monocytes and then move to the liver and other organs.

Graph 2 below shows that supplementation with IMW50® resulted in higher production of anti-*Salmonella* IgA at 14 days old. This indicates that the immune system had a quicker and stronger specific response, using less energy and nutrients, as the inflammatory response seemed to be shorter.



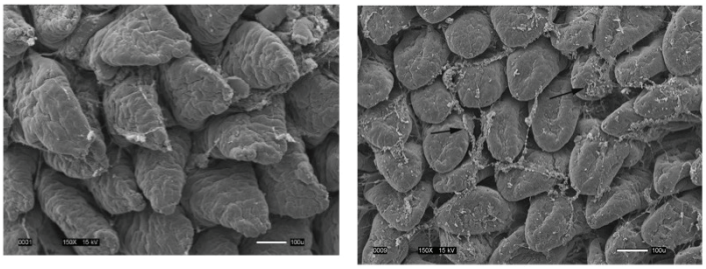
Graph 2. Relative IgA quantification in reagent serum against bacterial LPS. The cut-off line is shown. Different letters on each group indicate statistical relevance. ANOVA test with Tukey post-test (P<0.05, except when otherwise indicated).

SE can be a problem for broilers that still do not have a mature immune system, as they cannot fully control the infection. For this reason, most of the improved responses found in this study were observed up to day 14. Therefore, β-glucan supplementation can help broilers activate the immune system and have an early and quicker innate immune system response, reducing/minimizing the damage caused by pathogens and, consequently, performance impairment. This type of response is significant in animals at early development stages, during reproduction, periods of stress, and environmental challenges, acting as a prophylactic agent and increasing animal resistance, thus minimizing losses.

Another recent publication by Rahimi *et al*. (2019) with turkey poults showed that 21 days post-*Salmonella* Heidelberg (SH)

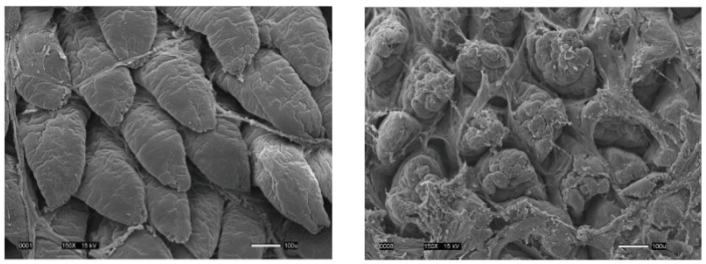
infection, SH in excreta samples decreased to zero when the birds were fed diets containing IMW50®. Ferreira *et al*. (2014) found similar results in a trial with IMW50® supplementation. Broilers infected with SH had a 50% reduction in pathogen presence in their crop and ceca compared to control infected birds.

Rahimi *et al*. (2019) also studied the effects of IMW50® on gut integrity in turkey poults infected or not infected with SH. For birds not infected with SH, the group fed a diet with IMW50® had significant (P<0.05) increases in mucosa thickness (44%), villus surface area (33%), and villus height (52%) when compared with the control group. For birds that were infected with the SH and supplemented with IMW50®, a significant increase (P<0.05) was observed in the villus surface area (12%). The scanning electron microscopy (SEM) photos of the ileum sections of birds fed the two treatments were also taken (Figures 2 and 3).



Control IMW50®

Figure 2. Scanning electron microscopy (SEM) photographs of ileum sections showing differences between the two dietary treatments without Salmonella challenge.



Control IMW50®

Figure 3. Scanning electron microscopy (SEM) photographs of ileum sections showing differences between the two dietary treatments with Salmonella challenge

The SEM photographs above confirm the live performance data found by the authors. Visually there was a higher presence of mucus in the IMW50® supplemented birds vs. control. In addition, the villus surface area was greater for IMW50® supplemented groups, infected or not, with *Salmonella*. These results are essential to show the β-glucans and MOS modes of action and benefits during a pathogenic challenge situation.

Several other studies have confirmed the efficacy of IMW50® in reducing pathogen contamination in broilers and eggs (Hofacre *et al*., 2017; Ferreira *et al*., 2014), reducing mortality and improving productivity (Bonato *et al*., 2016; Rivera *et al*., 2018; Koiyama *et al*. 2018), especially under challenge. However, it is important to highlight that there are no feed additives that can solve management problems, health plans, immunization, nutrition, and water quality. Additives are tools used to help control and prevent them. Intensive animal production is known to be highly challenging. Therefore, strengthening the immune system and controlling pathogens contamination will positively impact gut integrity and health, being one of the keys to higher productivity.

Poultry, including breeders, are typically under several kinds of challenges (pathogenic, stress, environmental, food restriction, vaccinations, egg production, etc), and yeast cell walls help these birds to strengthen and modulate the immune system, and reduce the pathogen contamination. The contamination of broilers with pathogens such as *Salmonella*, *Campylobacter*, and *E. coli* on the farm is a reality in commercial broiler production and is a major concern to consumers who worry that these pathogens may infect ready-to- cook meat and eggs. Thus, pathogen control in poultry is essential to ensure food safety. Yeast cell walls demonstrate a high capacity to agglutinate these pathogens in the intestinal contents of breeders and their broiler progeny, significantly reducing the presence of pathogens in or on eggs and meat.

Besides the benefits of balanced nutrition, a well-run sanitary plan, and good management, yeast cell wall supplemented poultry are better prepared for fighting against opportunistic pathogens, avoiding major production losses, and more fully expressing genetic potential. Research indicates that yeast cell walls, besides being a 100% natural ingredient, are successful in poultry due to immune response and pathogen agglutination actions, helping reduce the use of antibiotics. The BacPack® Q1+1 and BacPack® Q3+1 products from Quality Technology International combine IMW50 with the Q-Biotic single strain and IMW50 with the Q-Biotic multi-strain, respectively. The strategic and synergistic combination of Q-Biotic® direct fed microbial and IMW50® yeast cell wall (ICC, Brazil) provides a highly effective feed additive for poultry to improve gut health, feed utilization, livability, and food safety.

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