

Abstract

Poultry production in Poland and worldwide has become one of the best developed and most important among animal productions for decades. Broiler chickens are subjected to intensive selection, which has a series of negative consequences, including deterioration of the overall welfare and health of the animals. One of the major challenges in chickens' health status are necrotic enteritis caused by *C. perfringens* and colibacteriosis caused by *E. coli*. Due to the European Union's prohibition on the preventive use of antibiotics (Regulation 1831/2003/WE), there has been an increase in the incidence of these infections in broilers. Bacterial pathogens can impair the function of the gastrointestinal tract and intestinal barrier by disrupting tight junctions, initiating inflammatory cascades, and through epigenetic and oxidative changes. These diseases cause huge losses to the poultry industry, and the industry itself will continue to contribute a serious threat to human health due to its role as a vector for zoonotic diseases and its contribution to the rise in antibiotic resistance due to inappropriate drug use. Over the past decade, research has been conducted into alternative methods of reducing inflammation in broilers that at the same time maintain bird performance and are safe for consumers with no contribution to the development of antibiotic resistance. Effective infection control strategies can be achieved by identifying the interactions occurring in the gastrointestinal tract of birds and understanding the relationship between the condition of the gastrointestinal tract and bioactive nutrients such as cannabidiol (CBD) and nano-selenium (nano-Se).

As part of this dissertation, two experiments were conducted on broiler chickens. The first was aimed at evaluating the effects of diets enriched with CBD and nano-Se on gastrointestinal function under physiological and pathophysiological conditions. The second experiment analyzed how infection with *C. perfringens* bacteria or exposure to *E. coli* lipopolysaccharide affects intestinal barrier structures and functions. Both avian production indices and a number of biological parameters were evaluated using spectrophotometric methods (including determination of intestinal collagen levels, blood concentrations of fluorescein isothiocyanate-dextran and activity of bacterial enzymes in the cecum), histological analyses (evaluation of morphological structures, histopathological and ultrastructural changes of the small intestine), real-time qPCR techniques (expression of genes related to, among others, related to intestinal barrier integrity, oxidative stress and immune response), immunoenzymatic assays (including analysis of intestinal health markers and epigenetic and oxidative changes), and determination of hemoglobin concentration in the blood.

The results of own studies showed that both *C. perfringens* infection and action of LPS *E. coli* may cause adverse changes in the structures and functions of the gastrointestinal tract, including weakening of the integrity of the intestinal barrier.

These processes are associated with impaired expression of tight junction proteins, impaired protective function of the intestinal epithelium and compromised immune response of chickens. In addition, negative epigenetic and oxidative modifications were observed in both the gastrointestinal tract and blood, depending on the infectious agent. The model of subclinical *C. perfringens* infection used did not produce typical clinical signs or changes characteristic of advanced infection, on macroscopic and microscopic examination, which confirms that the disease can develop in a latent manner. Despite the absence of necrotic changes typical of acute intestinal inflammation, a decrease in collagen levels and abnormalities in small intestinal morphology were found, which may further impair intestinal barrier function.

Dietary supplementation with CBD and nano-Se demonstrated protective and regulatory effects against the gastrointestinal tract and intestinal barrier. Both compounds, irrespective when used separately or in combination, had a beneficial effect on maintaining the structural and functional integrity of the intestines and supporting the body's immune responses, without causing adverse effects and negative qualitative changes in the structures of the small intestines or interactions under physiological and pathophysiological conditions. Under conditions of infection-related stress, their synergistic effects were manifested in the attenuation of the inflammatory response, a more controlled immune response, improvement of the integrity of the intestinal barrier and modification of bacterial enzyme activity, which may affect the efficiency of energy utilization during infection. Nano-Se contributed to an increase in blood hemoglobin levels, which may be relevant to overall broiler health status, while CBD promoted mechanisms to protect intestinal cells from the cytotoxic effects of *C. perfringens*.

Taken together, the results of own study indicate that understanding the mechanisms of action of CBD and nano-Se is highly relevant to developing preventive strategies for intestinal enteropathies in broiler chickens. In addition, the present study provided new information on the biological action and mechanisms of both additives and the pathophysiology of *C. perfringens* infections and LPS *E. coli* exposure in birds.