Ann. Anim. Sci., Vol. 20, No. 1 (2020) 29–41 *DOI: 10.2478/aoas-2019-0077*

EFFECT OF SODIUM BUTYRATE ON INTESTINAL HEALTH OF POULTRY – A REVIEW

Shaaban S. Elnesr[1], Mahmoud Alagawany[2♦], Hamada A.M. Elwan[3], Mohamed A. Fathi[4], Mayada R. Farag[5]

[1]Poultry Production Department, Faculty of Agriculture, Fayoum University, Fayoum, 63514, Egypt
[2]Department of Poultry, Faculty of Agriculture, Zagazig University, Zagazig 44511, Egypt
[3]Animal and Poultry Production Department, Faculty of Agriculture, Minia University, El-Minya, 61519, Egypt
[4]Animal Production Research Institute, Agricultural Research Center, Ministry of Agriculture, Dokki, Giza, Egypt
[5]Forensic Medicine and Toxicology Department, Veterinary Medicine Faculty, Zagazig University, Zagazig 44511, Egypt
♦Corresponding author: dr.mahmoud.alagwany@gmail.com

Abstract

Health of the intestine is one of the main reasons that affects the bird's performance, and thus the economic yield in the poultry sector. Various studies have examined how to improve the intestinal health using dietary supplements, including organic acids such as sodium butyrate (SB). The efficacy of the dietary supplementation in poultry is often assessed using an important parameter such as intestinal integrity, which is often assessed as a measure of high villus height and the ratio of villus height to crypt depth, or count of goblet cell numbers. In broilers, the villus length and width were increased by the addition of dietary SB. Since, at day 21 and 42, the villus length was increased by 55 and 27%, and 39 and 18% for birds fed 0.5 and 1 g/kg, respectively, compared with the control diet. Furthermore, SB plays an important role in development of poultry intestinal epithelium. It can be employed by the intestinal epithelial cells as an energy source to stimulate their differentiation and proliferation, and to improve intestinal barrier function. SB is effective against acid intolerant species such as *Salmonella, Clostridium perfringens* and *E. coli*. In addition, use of butyric acid at 0.6% reduced the pH of gastrointestinal segments. For this, SB could be a potential alternative in maintaining the health of gastrointestinal tract and improving the productive performance of poultry. This review refers to the expanding horizons in the research on SB supplementation in poultry health and nutrition.

Key words: poultry, organic acid, mucosa, gut, antimicrobial activity

In poultry, growth and production depend upon the digestion and absorption for the diet accomplished by the intestinal health. Good intestinal health is important to reach the optimal feed efficiency and growth rates (Alagawany et al., 2018 a, b;

Al-Sagheer et al., 2019). The importance of gastrointestinal tract health in poultry has been increasingly documented due to its contribution to their overall health and performance. If the intestine health and its functions are damaged, the digestion and absorption are affected (Sugiharto, 2016; Abdelnour et al., 2018). The intestinal mucosa of poultry plays a very significant role in providing an active barrier between the host internal tissues and the hostile luminal content. So, it is an important element of gut health and birds performance (Rinttila and Apajalahti, 2013). One of the most important factors affecting the functions of the intestinal mucosa is the dynamic balance among the epithelial cells, mucus layer, microbiota and immune cells in the parts of the intestine (Schenk and Mueller, 2008). Therefore, in poultry nutrition we need to use supplements that improve the bird's performance through promoting their intestine health without the use of antibiotics (Alagawany et al., 2019; Farag and Alagawany, 2019; Geetha and Chakravarthula, 2018; Saeed et al., 2019). One of these supplements is SB. It has been described that SB plays a vital role in depressing intestinal pH with the controlling harmful microbial colonization and growth, and stimulating the growth of intestinal absorptive cells, and finally, promotion of the growth performance of birds.

Several studies have shown the development of nutritional approaches to improve the performance without the use of antibiotics, such as the study of Shahir et al. (2013) who stated that sodium butyrate (SB) addition may improve intestinal health. The use of SB in poultry nutrition is well accepted due to its pH reduction effect that limits the pathogen development (Sikandar et al., 2017 a) and helps in the protein digestion (Jankowski et al., 2012).

Butyrate is the most important energy source of the colonocytes (Roediger, 1982). It regulates the differentiation and proliferation of the gastrointestinal epithelium (Gálfi and Neogrády, 2002) and boosts apoptosis in the genetically disordered cells (Leu et al., 2009). Also, it plays an extensive role in gut homeostasis, including support for the gut barrier function (Hodin, 2000). Antimicrobial agents, such as SB, are known to lessen levels of the intestinal pathogen, which in turn reduces the presence of toxins that causes alterations in morphology of the intestine (villi and the crypts). Butyrate is of special interest due to its various positive effects on the intestinal tissues and gut health. Generally, supplementation of SB augmented both crypt depth and villus height. Feeding diets containing SB through the whole growth period show positive impact on the physiological indices and intestinal health of birds (Elnesr et al., 2019). Scientific reports interested in supporting the poultry industry are always trying to show the beneficial role of any supplement can be utilized in the poultry diet as an antimicrobial agent and good for the intestine health. The purpose of this review is to describe the possible and potential action of SB in improving the intestinal health of poultry through improvement of the intestine morphometery and gut microbial ecosystem.

Sodium butyrate and its multiple effects

Sodium butyrate ($C_4H_7NaO_2$) is a short chain fatty acid (SCFA) that has effects on the molecular, cellular, and tissue level. As shown in Figure 1 A, when butyric acid ($CH_3CH_2CH_2COOH$) loses its H ion it converts to butyrate ion ($CH_3CH_2CH_2COO$).

Sodium butyrate (SB) is the sodium salt of butyric acid (BA), which contains Na atom in place of H of -OH group. SB was used as a source of BA which is known for its beneficial impacts in the gut, since it is solid, stable and much less odorous (Jiang et al., 2015). Generally, the advantage of salt over free acids is that it is odourless and makes the feed manufacturing process easier to handle owing to their solid and less volatile character. Butyrate plays a role in stimulating the intestinal epithelium development (Hu and Guo, 2007), and lessening pathogenic bacteria (Fernández-Rubio et al., 2009). Figure 2 summarized the multiple effects of SB in the intestine of birds.

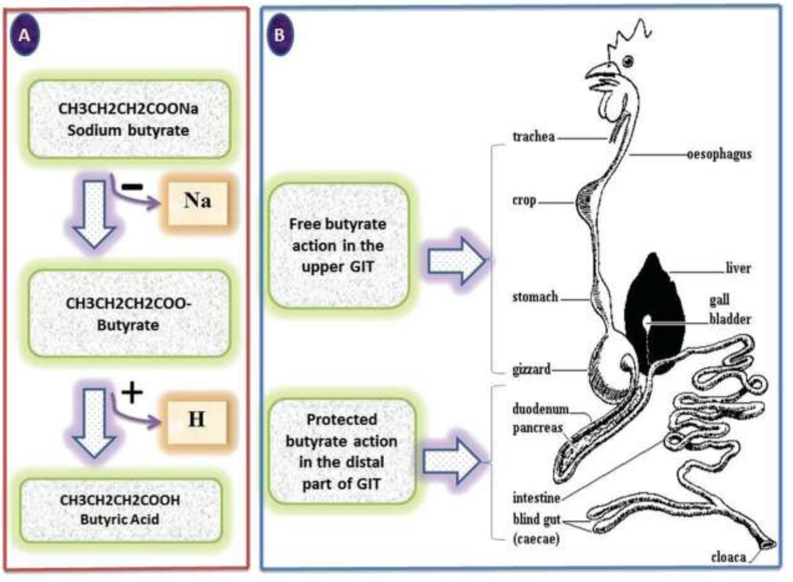

Figure 1. (A) Conversion of sodium butyrate to butyric acid; (B) Place action of butyrate in the gastrointestinal tract

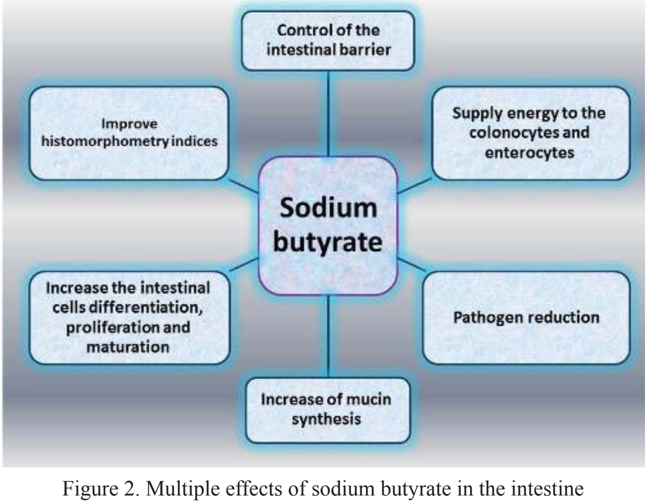

Figure 2. Multiple effects of sodium butyrate in the intestine

Many investigations have been made on how SB does improve the intestinal health of poultry. Mode of action is that once SB reaches the bird stomach, it rapidly releases the first fraction (Na ion) and due to the low pH, the other fraction (butyrate) is quickly converted to the undissociated form, termed the BA. This form (BA) is the one answer for the antimicrobial action, where it is sturdily lipophilic and can diffuse across the bacterial membrane. Adding SB to poultry diets can lower the gastric pH, accelerating the conversion of pepsinogen to pepsin, which enhances the absorption rate of nutrients such as proteins, amino acids and minerals (Youn et al., 2005). This low pH destroys pathogenic bacteria by the depletion of metabolic energy and the reduction of cell membrane metabolism, the outflow of cellular fluids, and the blockage of the nutrients use (Kirchgessner and Roth, 1982). Therefore, the main target of dietary SB supplementation is to maintain good health of poultry intestine by decreasing the level of pathogenic bacteria.

Butyrate efficacy in the gastrointestinal tract

The small intestine plays a main role in digestion and absorption of nutrients (Svihus, 2014). The cecum is the main site for unabsorbed nutrient fermentation and maintaining gut microbiota balance (Svihus et al., 2013). Investigations have revealed that earlier releasing of products such as SB in the small intestine can increase the nutrient digestibility, and stimulate the villus development, and later releasing time in the cecum has an inhibitory effect on gut pathogenic bacteria (Fernández-Rubio et al., 2009; Guilloteau et al., 2010). Liu et al. (2017 b) stated that post ingestion releasing, 30 min to 2.5 h is the suitable time for the encapsulated products that improve nutrient digestibility and stimulate epithelial cell development in the small intestine, and also, 2.5 to 4 h is an optimal range of these products that focus on hind-gut bacterial control.

Butyrate is easily absorbed in the upper gastrointestinal tract (GIT) (the crop) when fed in the free salt form (Van der Wielen, 2002). The BA salt needs to be in an undissociated state before reaching the hind-gut to exert its antimicrobial effect (Warnecke and Gill, 2005). Coated BA in the chicken diet protects from cecal colonization of *Salmonella* (Van Immerseel et al., 2005). The common way to protect SB from early absorption in GIT is to use vegetable fat to encapsulate the SB and control its releasing time in GIT. The vegetable fat protection allows butyrate to reach the distal parts of the GIT (Figure 1 B). Efficacy of butyrate was improved when it is fed in a coated form such as encapsulation (Smith et al., 2012).

Effect of SB on relative organ weight or length of the intestine

BA enhanced the intestinal weight (Abdelqader and Al-Fataftah, 2016). Eshak et al. (2016) stated that there were increased intestinal diameter and length in birds fed diet containing SB compared with the control. The weight and length of the entire gut were increased in BA-supplemented birds compared with the control birds (Aghazadeh and Tahayazdi, 2012). The dietary SB supplementation significantly increased the length and weight of intestinal segments of broilers at 21 and 42 d compared with the control without SB (Wu et al., 2018). Addition of SB increased the relative weights of the total GIT, the duodenum, and the jejunum of broiler chickens at 21 day of age (González-Ortiz et al., 2019). On the other hand, relative length of the duodenum was not influenced by SB supplementation at all ages (14, 28 and 42 days of age). But, the relative lengths of the small intestine and jejunum were longer with SB at d 14 as compared to control (Chamba et al., 2014). Also, the longer (Aghazadeh and Tahayazdi, 2012) and heavier small intestines (Adil et al., 2011) have been recorded with SB. High level of SB improved lengths of jejunum and small intestines (Mahdavi and Torki, 2009). Furthermore, Reilly et al. (1995) stated that SB increases blood flow to the small intestine that leads to better tissue growth and oxygenation.

Table 1. Effect of butyric acid forms supplemented at various levels in poultry diet on the improvement rate (%) in villus length (previous studies)

Bird type	Age	Improvement rate (%) compared with the control (without SB)	Intestinal part	Tested level and form	Reference
1	2	3	4	5	6
Broiler chicken	22 days	7.3	Duodenum	0.2% butyrate	Panda et al., 2009
		8.9	Duodenum	0.4% butyrate	
		8.2	Duodenum	0.6% butyrate	
Broiler chicken	35 days	0.1	Duodenum	0.5 g butyric acid/kg	Abdelqader and Al-Fataftah, 2016
	42 days	0.9	Duodenum		
Broiler chicken	36 days	19.0	Duodenum	2 g butyric acid/kg	Qaisrani et al., 2015
Broiler chicken	21 days	27.4	Duodenum	sodium butyrate 0.5 g/kg	Sikandar et al., 2017 b
		36.6	Jejunum		
		13.6	Ileum		
	35 days	17.1	Duodenum		
		12.7	Jejunum		
		5.2	Ileum		
Broiler chicken	21 days	27.9	Duodenum	sodium butyrate 1.0 g/kg	
		41.0	Jejunum		
		18.4	Ileum		
	35 days	33.4	Duodenum		
		21.9	Jejunum		
		7.3	Ileum		
Broiler chicken	35 days	21.7	Jejunum	SB: starter diet 1 g/kg, grower diet 0.5 g/kg and finisher diet 0.25 g/kg	Awaad et al., 2016

Table 1 – contd.

1	2	3	4	5	6
Japanese quail	21 days	21.9	Duodenum	sodium butyrate 1.0 g/kg	Elnesr et al., 2019
		68.2	Jejunum		
		39.7	Ileum		
Japanese quail	42 days	20.3	Duodenum		
		70.1	Jejunum		
		29.3	Ileum		
Broiler chicken	30 days	5.8	Jejunum	300 mg SB/kg	Czerwiński et al., 2012
		7.9	Ileum		
Broiler chicken	42 days	8.2	Duodenum	2 g SB/kg	Shahir et al., 2013
		8.7	Jejunum		
		3.4	Ileum		
Broiler chicken	21 days	25.6	Duodenum	1 g SB/kg	Jiang et al., 2015
		6.1	Jejunum		
Broiler chicken	42 days	7.3	Duodenum	2% butyric acid	Adil et al., 2010
		13.5	Jejunum		
		9.3	Ileum		
Broiler chicken	42 days	20.9	Duodenum	3% butyric acid	
		14.3	Jejunum		
		29.6	Ileum		
Broiler chicken	21 days	55.2	Duodenum	0.5 g SB/kg	Mallo et al., 2012
	42 days	39.2	Duodenum		
	21 days	27.2	Duodenum	1 g SB/kg	
	42 days	18.2	Duodenum		
Laying hens	73 weeks	6.1	Duodenum	300 g/ton	Sánchez Herrera et al., 2009
		14.8	Duodenum	500 g/ton	
Broiler chicken	42 days	19.9	Ileum	0.3 g protected butyrate/kg	Kaczmarek et al., 2016
Broiler chicken	21 days	6.4	Duodenum	500 ppm sodium butyrate	Liu et al., 2017 a
		6.8	Jejunum		
		1.0	Ileum		

Effect of SB on the intestinal morphology

The digestion and absorption of nutrients depend on the intestinal villus (Awad et al., 2015). The villus height is related with contact surface area with the nutrients. Larger villus height improves villus function, and then a better growth performance of the bird. In many previous studies, it turned out that SB improved the villus height in the intestine parts (duodenum, jejunum and ileum) relative to the control treatment as shown in Table 1. In principle, increased villus height and decreased crypt depth in the small intestine were used as signs of intestinal health, because both are indicators for proper absorption of nutrients (Chiang et al., 2010). The villus length and width were affected by the addition of dietary SB for broilers. At day 21, the villus length was increased ($P<0.001$) by about 55 and 27% for birds fed 0.5 and 1 g/kg, respectively, and at 42 days, the villus length was increased ($P<0.001$) by about 39 and 18% for birds fed 0.5 and 1 g/kg, respectively compared with the control diet (Mallo et al., 2012). An improvement in villi height and crypt depth has been detected after butyrate supplementation in poultry diets (Leeson et al., 2005). Butyric acid has been shown to stimulate growth of intestinal villi (Guilloteau et al., 2010). Villus height and absorptive epithelial cell area were augmented in response to BA administration. The increase in the villi surface area is significant and can be correlated with an increased proliferation rate of mucosal cells (Abdelqader and Al-Fataftah, 2016). SB supplementation was linked to improved intestinal morphological measurements compared with the control (Hassanin et al., 2015). SB has been described to be useful in the maintenance of the intestinal villus structure (Leeson et al., 2005). This improvement in the epithelia structure may participate in the maintenance of intestinal epithelial integrity by diminishing breaks in the mucosal barrier, which limit luminal antigens passage to the bloodstream (Söderholm and Perdue, 2006). Sikandar et al. (2017 b) found an improvement in histomorphometry indices (height of villus having intact lamina propria and villus surface area) in the jejunum and duodenum of SB-treated groups compared to the control. Elnesr et al. (2019) found a better growth of intestinal villi in the quail fed diet with SB compared to the quail fed diet without SB (Wu et al., 2018). The SB addition to poultry diets may stimulate restitution of the intestinal epithelial cell and encourage growth of the intestinal mucosa (Hu and Guo, 2007). Elnesr et al. (2019) suggested that SB action in the improvement of intestine status may be due to that butyrate stimulates the intestinal blood flow and the gastrointestinal hormone synthesis. Also, BA leads to increase the secretion of peptides which lead to enhanced proliferation of enterocytes for improved repair of damaged mucosa and increased height of villi.

Effect of SB on intestinal bacterial populations

The intestines of bird have both beneficial bacteria (like gram-positive lactobacilli or bifidobacteria) for the health and potential pathogenic bacteria (like *Escherichia coli, Clostridium* spp. or *Salmonella*). Generally, good bacteria represent at least 85% of total bacteria (Sun and O'Riordan, 2013; Chamba et al., 2014). The bacterial balance between the number of bad bacteria and beneficial bacteria in the intestine is vital for the host, and any negative influence on intestine health of chicken often comes from the microbial imbalance in the intestine (Choct, 2009). The balance of intestinal microbiota in chicken is essential to get maximum growth performance and the healthy gut (Kabir, 2009). This balance is decisive for the intestinal homeostasis and normal functions (defense and digestive) of the gut of chicken (Sugiharto, 2016). Some dietary supplements can modify the microbial populations in the intestine of chicken, concomitant with the growth of beneficial bacteria (Adil and Magray, 2012). SB possesses antimicrobial property due to its important role in the gut of birds through controlling the population of pathogenic bacteria and inducing beneficial bacteria. The addition of SB in diet can have a favorable effect on poultry health by lessening pathogenic bacteria. BA enhanced the viable counts of *Bifidobacterium* and *Lactobacillus* (Abdelqader and Al-Fataftah, 2016). Makled et al. (2019) stated that the SB displayed beneficial impacts on gut microbiota of meat-type broiler chickens at day 21 through a relative reduction in ileal *E. coli* and an increase in ileal lactobacilli count compared to that of the control.

In birds, butyrate has a direct impact on mucin secretion, mainly for its bactericide action on enteropathogens (Gram positive such as *Clostridium* spp. and Gram negative such as: *Salmonella* spp. and *E. coli*) (Van Immerseel et al., 2006). Timbermont (2010) observed a beneficial effect of SB in the control of necrotic enteritis. Also, supplementing SB in the starting diet of broilers reduced *Salmonella Enteritidis* infections at day 27 (Fernández-Rubio et al., 2009). More investigations have revealed the antimicrobial action of butyrate towards poultry pathogens (*Clostridium perfringens* and *Salmonella typhimurium*) in both *in vivo* trials (Van Immerseel et al., 2005; Fernández-Rubio et al., 2009) and *in vitro* trials (Namkung et al., 2011) and examined its use in poultry diets as a possible alternative to antibiotic growth promoters (Leeson et al., 2005). BA reduces bacterial colonization of the intestine wall (Langhout et al., 1999) and, as a result, the pathogenic microbes produce less toxic compounds, and then cause less damage to the epithelial cells of the intestine (Antongiovanni et al., 2009). When butyrate is present in the lower intestinal tract, it can eliminate colonization of detrimental bacteria, stopping the gene expression responsible for the invasion of the epithelial cells, because its effects are induced via the activation of specific receptors in the epithelial cells (Kulkarni et al., 2007). Gantois et al. (2006) stated that butyrate down-regulates gene expression of *Salmonella* pathogenicity island-1, enlightening one of the mechanisms causing reduced invasion of intestinal epithelial cells. Supplementation of SB lessened intestinal DNA fragmentation prompted by necrotic enteritis (NE) infection (Eshak et al., 2016). The dietary SB supplementation of broilers significantly ameliorated the intestinal microbial community and diversity (Wu et al., 2018). Also, researchers have shown butyrate to boost disease resistance to *Salmonella enteritidis* in chickens by prompting synthesis of various host defense peptides (HDPs) (Sunkara et al., 2011). HDPs are antimicrobial peptides and a critical part of innate immunity (Brogden et al., 2003). Thus, butyrate helps the poultry immune system and exhibits activity against certain gut pathogenic bacteria. We recommended that most common bacteria that affect the intestinal health of birds can be controlled by SB supplementation in the diet. Finally, it turned out that SB regulates the intestinal microecological balance as shown in Figure 3.

Effect of SB on the nutrients digestibility

BA as a feed additive in poultry diets may be an approach to improve ileal protein digestibility of poorly digestible protein sources (Qaisrani et al., 2015). The use of protected butyrate increased the ileal digestibility of thrionine, serine and proline (Kaczmarek et al., 2016). SB improved the ileal digestibility energy on d 42 compared to the control (Liu et al., 2017 a). This improvement could be attributed to a good health status of GIT or larger villi surface area. Also, these positive impacts of BA supplementation may be due to improved nutrient digestion and absorption (Mansoub, 2011), as a consequence of augmented pancreatic enzyme secretion, and because of their impacts on the intestinal mucosa and their antimicrobial action (Adil et al., 2010).

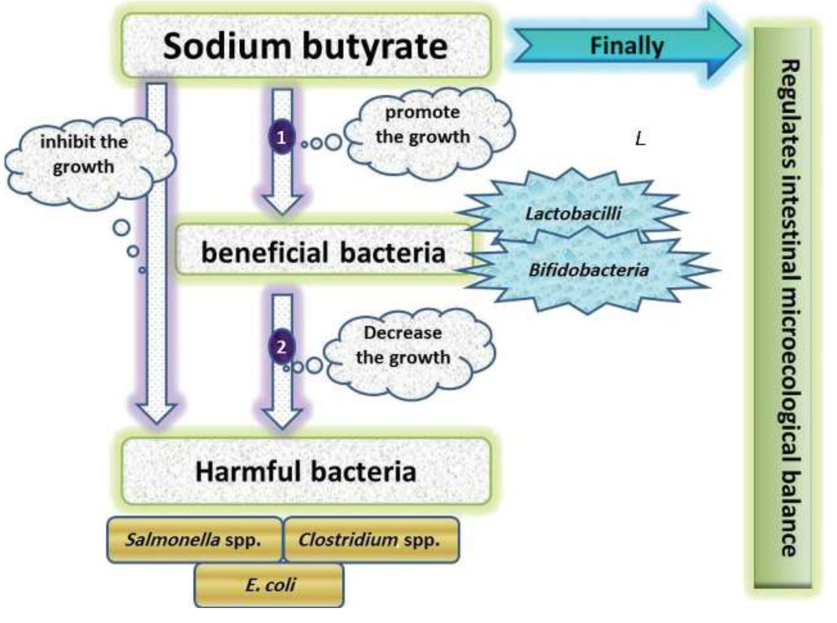

Figure 3. Role SB regulation of the intestinal microecological balance; (1) SB depresses the pH of intestine, causing growth of bacteria that produce lactic acid (LA) (*Lactobacilli* and *Bifidobacteria* spp.) (Vogt et al., 1982). (2) The LA producing bacteria compete within the intestine on nutrients and space with pathogenic bacteria (Furuse and Okumura, 1994; Rolfe, 2000). *Lactobacilli* spp. produces bacteriocins (Joerger, 2003), and *Bifidobacteria* spp. secrete some organic acids (LA and acetic acid) and bactericidal constituents (Gibson and Wang, 1994) which moderate the pathogenic bacterial count, and also causing the inhibition of pathogenic bacteria such as *Salmonella* spp. and *E. coli*

Conclusion

Thus, SB could be a potential alternative to improve intestinal health and replace antibiotics in the poultry industry. The gastrointestinal tract health contributes the overall performance and health of poultry. SB plays an important role in maintaining the integrity of the intestinal mucosa as evidenced by the improvement in the intestine histomorphometery. The SB ameliorated the intestinal microbial community. Therefore, SB is a bactericidal and a stimulant of intestinal epithelium development. Thus, we believe that this approach will help us to develop the poultry industry by producing a bird with good intestinal health.

References

Abdelnour S., Alagawany M., El-Hack M.E.A., Sheiha A.M., Saadeldin I.M., Swelum A.A. (2018). Growth, carcass traits, blood hematology, serum metabolites, immunity, and oxidative indices of growing rabbits fed diets supplemented with red or black pepper oils. Animals, 8: 168.

Abdelqader A., Al-Fataftah A.R. (2016). Effect of dietary butyric acid on performance, intestinal morphology, microflora composition and intestinal recovery of heat-stressed broilers. Livest. Sci., 183: 78–83.

Adil S., Banday T., Bhat G.A., Mir M.S., Rehman M. (2010). Effect of dietary supplementation of organic acids on performance, intestinal histomorphology, and serum biochemistry of broiler chicken. Vet. Med Int., 2010: 479–485.

Adil S., Banday T., Ahmad Bhat G., Salahuddin M., Raquib M., Shanaz S. (2011). Response of broiler chicken to dietary supplementation of organic acids. J. Central Eur. Agric., 12: 498–508.

Adil S., Magray S.N. (2012). Impact and manipulation of gut microflora in poultry: a review. J. Anim. Vet. Adv., 11: 873– 877.

Aghazadeh A.M., Tahayazdi M. (2012). Effect of butyric acid supplementation and whole wheat inclusion on the performance and carcass traits of broilers. South Afr. J. Anim. Sci., 42: 241–248.

Alagawany M., Abd El-Hack M.E., Al-Sagheer A.A., Naiel M.A., Saadeldin I.M., Swelum A.A. (2018 a). Dietary cold pressed watercress and coconut oil mixture enhances growth performance, intestinal microbiota, antioxidant status, and immunity of growing rabbits. Animals, 8: 212.

Alagawany M., Abd El-Hack M.E., Farag M.R., Sachan S., Karthik K., Khama K. (2018 b). The use of probiotics as eco-friendly alternatives for antibiotics in poultry nutrition. Environ. Sci. Poll. Res., 25: 10611–10618.

Alagawany M., Elnesr S.S. Farag M.R. (2019). Use of liquorice (*Glycyrrhiza glabra*) in poultry nutrition: Global impacts on performance, carcass and meat quality. World. Poult. Sci. J., 75: 293–303.

Al-Sagheer A.A., Abd El-Hack M.E., Alagawany M., Naiel M.A., Mahgoub S.A., Badr M.M., Hussein E.O.S., Alowaimer A.N., Swelum A.A. (2019). Paulownia leaves as a new feed resource: chemical composition and effects on growth, carcasses, digestibility, blood biochemistry, and intestinal bacterial populations of growing rabbits. Animals, 9: 95.

Antongiovanni M., Buccioni A., Petacchi F., Leeson S., Minieri S., Martini A., Cecchi R. (2009). Butyric acid glycerides in the diet of broiler chickens: Effects on gut histology and carcass composition. It. J. Anim. Sci., 6: 19–25.

Awaad M.H.H., Abd El-Ghany W.A., Nasef S.A., El-Halawany M.S., Mohamed F.F., Gaber A.F. (2016). Effect of Na-butyrate supplementation on electromicroscopy, virulence gene expression analysis and gut integrity of experimentally induced Salmonella enteritidis in broiler chickens. Asian J. Poult. Sci., 10: 126–133.

Awad W.A., Molnar A., Aschenbach J.R., Ghareeb K., Khayal B., Hess C., Liebhart D., Dublecz K., Hess M. (2015). *Campylobacter* infection in chickens modulates the intestinal epithelial barrier function. Innate Imm., 21: 151–60.

Brogden K.A., Ackermann M., Mccray Jr. P.B., Tack B.F. (2003). Antimicrobial peptides in animals and their role in host defenses. Int. J. Antimicrob. Agent., 22: 465–478.

Chamba F., Puyalto M., Ortiz A., Torrealba H., Mallo J.J., Riboty R. (2014). Effect of partially protected sodium butyrate on performance, digestive organs, intestinal villi and *E. coli* development in broilers chickens. Int. J. Poult. Sci., 13: 390–396.

Chiang G., Lu W.Q., Piao X.S., Hu J.K., Gong L.M., Thacker P.A. (2010). Effects of feeding solid-state fermented rapeseed meal on performance, nutrient digestibility, intestinal ecology and intestinal morphology of broiler chickens. Asian- Austral. Anim. Sci., 23: 263–271.

Choct M. (2009). Managing gut health through nutrition. Brit. Poultry Sci., 50: 9–15.

Czerwiński J., Højberg O., Smulikowska S., Engberg R.M., Mieczkowska A. (2012). Effects of sodium butyrate and salinomycin upon intestinal microbiota, mucosal morphology and performance of broiler chickens. Arch. Anim. Nutr., 66: 102–116.

Elnesr S.S., Ropy A., Abdel-Razik A.H. (2019). Effect of dietary sodium butyrate supplementation on growth, blood biochemistry, haematology and histomorphometry of intestine and immune organs of Japanese quail. Animal, 13: 1234–1244.

Eshak M.G., Elmenawey M.A., Atta A., Gharib H.B., Shalaby B., Awaad M.H.H. (2016). The efficacy of Na-butyrate encapsulated in palm fat on performance of broilers infected with necrotic enteritis with gene expression analysis. Vet. World, 9: 450.

Farag M.R., Alagawany M. (2019). The role of *Astragalus membranaceus* as immunomodulator in poultry. World. Poultry Sci. J., 75: 43–54.

Fernández-Rubio C., Ordóñez C., Abad-González J., Garcia-Gallego A., Pilar Honrubia M., Jose Mallo J., Balaña-Fouce R. (2009). Butyric acid-based feed additives help protect broiler chickens from *Salmonella* Enteritidis infection. Poultry Sci., 88: 943–948.

Furuse M., Okumura J. (1994). Nutritional and physiological characteristics in germ-free chickens. Comp. Biochem. Physiol. A: Physiol., 109: 547–556.

Gálfi P., Neogrády S. (2002). The pH-dependent inhibitory action of n-butyrate on gastrointestinal epithelial cell division. Food Res. Int., 34: 581–586.

Gantois I., Ducatelle R., Pasmans F., Haesebrouck F., Hautefort I., Thompson A., Hinton J.C., Van Immerseel F. (2006). Butyrate specifically down-regulates *Salmonella* pathogenicity island 1 gene expression. Appl. Environ. Microbiol., 72: 946–949.

Geetha V., Chakravarthula S.N. (2018). Chemical composition and anti-inflammatory activity of *Boswellia ovalifoliolata* essential oils from leaf and bark. J. Forest. Res., 29: 373–381.

Gibson G.R., Wang X. (1994). Regulatory effects of bifidobacteria on the growth of other colonic bacteria. J. Appl. Bacteriol., 77: 412–420.

González-Ortiz G., Dos Santos T.T., Vienola K., Vartiainen S., Apajalahti J., Bedford M.R. (2019). Response of broiler chickens to xylanase and butyrate supplementation. Poultry Sci., 98: 3914–3925.

Guilloteau P., Martin L., Eeckhaut V., Ducatelle R., Zabielski R., Van Immerseel F. (2010). From the gut to the peripheral tissues: The multiple effects of butyrate. Nutr. Res. Rev., 23: 366–384.

Hassanin A., Tony M.A., Sawiress F.A.R., Abdl-Rahman M.A., Saleh S.Y. (2015). Influence of dietary supplementation of coated sodium butyrate and/or synbiotic on growth performances, caecal fermentation, intestinal morphometry and metabolic profile of growing rabbits. J. Agri. Sci., 7: 180.

Hodin R. (2000). Maintaining gut homeostasis: The butyrate-NF-kappaB connection. Gastroenterology, 118: 798–801.

Hu Z., Guo Y. (2007). Effects of dietary sodium butyrate supplementation on the intestinal morphological structure, absorptive function and gut flora in chickens. Anim. Feed Sci. Technol., 132: 240–249.

Jankowski J., Juśkiewicz J., Lichtorowicz K., Zdunczyk Z. (2012). Effects of the dietary level and source of sodium on growth performance, gastrointestinal digestion and meat characteristics in turkeys. Anim. Feed Sci. Technol., 178: 74–83.

Jiang Y., Zhang W., Gao F., Zhou G. (2015). Effect of sodium butyrate on intestinal inflammatory response to lipopolysaccharide in broiler chickens. Can. J. Anim. Sci., 95: 389–395.

Joerger R.D. (2003). Alternatives to antibiotics: bacteriocins, antimicrobial peptides and bacteriophages. Poultry Sci., 82: 640–647.

Kabir S.M.L. (2009). The role of probiotics in the poultry industry. Int. J. Mol. Sci., 10: 3531–3546.

Kaczmarek S.A., Barri A., Hejdysz M., Rutkowski A. (2016). Effect of different doses of coated butyric acid on growth performance and energy utilization in broilers. Poultry Sci., 95: 851–859.

Kirchgessner M., Roth F.X. (1982). Fumaric acid as a feed additive in pig nutrition. Pig News Info., 3: 259–264.

Kulkarni R., Parreira V., Sharif S., Prescott J. (2007). Immunization of broiler chickens against *Clostridium perfringens* – Induced necrotic enteritis. Clin. Vaccins Immunol., 14: 1070–1077.

Langhout D.J., Schutte J.B., Van Leeuwen P., Wiebenga J., Tamminga S. (1999). Effect of dietary high and low methylated citrus pectin on the activity of the ileal microflora and morphology of the small intestinal wall of broiler chicks. Brit. Poultry Sci., 40: 340–347.

Leeson S., Namkung H., Antongiovanni M., Lee E.H. (2005). Effect of butyric acid on the performance and carcass yield of broiler chickens. Poultry Sci., 84: 1418–1422.

Leu R., Hu Y., Brown I., Young G. (2009). Effect of high amylase maize starches on colonic fermentation and apoptotic response to DNA-damage in the colon of rats. Nutr. Metab., 6: 11.

Liu J.D., Bayir H.O., Cosby D.E., Cox N.A., Williams S.M., Fowler J. (2017 a). Evaluation of encapsulated sodium butyrate on growth performance, energy digestibility, gut development, and *Salmonella* colonization in broilers. Poultry Sci., 96: 3638–3644.

Liu J.D., Secrest S.A., Fowler J. (2017 b). Computed tomographic precision rate-of-passage assay without a fasting period in broilers: more precise foundation for targeting the releasing time of encapsulated products. Livest. Sci., 200: 60–63.

Mahdavi R., Torki M. (2009). Study on usage period of dietary protected butyric acid on performance, carcass characteristics, serum metabolite levels and humoral immune response of broiler chickens. J. Anim. Vet. Adv., 8: 1702–1709.

Makled M.N., Abouelezz K.F.M., Gad-Elkareem A.E.G., Sayed A.M. (2019). Comparative influence of dietary probiotic, yoghurt, and sodium butyrate on growth performance, intestinal microbiota, blood hematology, and immune response of meat-type chickens. Trop. Anim. Health Prod., 51: 2333–2342.

Mallo J.J., Puyalto M., Rama Rao S.V. (2012). Evaluation of the effect of sodium butyrate addition to broilers diet on energy and protein digestibility, productive parameters and size of intestinal villi of animals. Feed Livest., 8: 26–30.

Mansoub N.H. (2011). Comparative effect of butyric acid, probiotic and garlic on performance and serum composition of broiler chickens. Am. Eur. J. Agri. Environ. Sci., 11: 507–511.

Namkung H., Yu H., Gong J., Leeson S. (2011). Antimicrobial activity of butyrate glycerides toward *Salmonella* Typhimurium and *Clostridium perfringens*. Poultry Sci., 90: 2217–2222.

Panda A.K., Rama Rao S.V., Raju M.V.L.N., Sunder G.S. (2009). Effect of butyric acid on performance, gastrointestinal tract health and carcass characteristics in broiler chickens. Asian-Austral. J. Anim. Sci., 22: 1026–103.

Qaisrani S.N., Van Krimpen M.M., Kwakkel R.P., Verstegen M.W.A., Hendriks W.H. (2015). Diet structure, butyric acid, and fermentable carbohydrates influence growth performance, gut morphology, and cecal fermentation characteristics in broilers. Poultry Sci., 94: 2152–2164.

Reilly K.J., Frankel W.L., Bain A.M., Rombeau J.L. (1995). Colonic short-chain fatty-acids mediate jejunal growth by increasing gastrin. Gut, 37: 81–86.

Rinttila T., Apajalahti J. (2013). Intestinal microbiota and metabolites – implications for broiler chicken health and performance. J. Appl. Poult. Res., 22: 647–658.

Roediger W.E. (1982). Utilization of nutrients by isolated epithelial cells of the rat colon. Gastroenterology, 83: 424–429.

Rolfe R.D. (2000). The role of probiotic cultures in the control of gastrointestinal health. J. Nutr., 130: 396S–402S.

Saeed M., Alagawany M., Fazlani S.A., Kalhoro S.A., Naveed M., Ali N., Arain M.A., Chao S. (2019). Health promoting and pharmaceutical potential of ferulic acid for the poultry industry. World. Poultry Sci. J., 75: 83–92.

Sánchez Herrera I., Posadas Hernández E., Sánchez Ramírez E., Fuente Martinez B., Hernández Espinoza J., Laparra Vega J.L., Ávila González E. (2009). Effect of sodium butyrate on diets for laying hens on the productive performance, egg quality and intestinal villi. Vet. México, 40: 397–403.

Schenk M., Mueller C. (2008). The mucosal immune system at the gastrointestinal barrier. Best. Pract. Res. Clin. Gastroenterol., 22: 391–409.

Shahir M.H., Moradi S., Afsarian O., Esmaeilipour O. (2013). Effects of cereal type, enzyme and sodium butyrate addition on growth performance, carcass traits and intestinal morphology of broilers. Rev. Bras. Ciên. Aví., 15: 181–189.

Sikandar A., Zaneb H., Younus M., Masood S., Aslam A., Ashraf S., Adil M. Rehman H. (2017 a). Protective effect of sodium butyrate on growth performance, immune responses and gut mucosal morphometry in salmonella-challenged broiler chickens. Int. J. Agri. Biol., 19: 1387–1393.

Sikandar A., Zaneb H., Younus M., Masood S., Aslam A., Khattak F., Ashraf S., Yousaf M.S., Rehman H. (2017 b). Effect of sodium butyrate on performance, immune status, microarchitecture of small intestinal mucosa and lymphoid organs in broiler chickens. Asian-Austral. J. Anim. Sci., 30: 690–699.

Smith D.J., Barri A., Herges G., Hahn J., Yersin A.G., Jourdan A. (2012). *In vitro* dissolution and *in vivo* absorption of calcium [1–14C] butyrate in free or protected forms. J. Agri. Food Chem., 60: 3151–3157.

Söderholm J.D., Perdue M.H. (2006). Effect of stress on intestinal mucosal function. In: Physiology of the gastrointestinal tract, Johnson L.R., Barret K.E., Gishan F.K., Merchant J.L., Said H.M., Wood J.D. (eds.). 4th ed. Elsevier Academic Press, Amsterdam, pp. 763–780.

Sugiharto S. (2016). Role of nutraceuticals in gut health and growth performance of poultry. J. Saudi Soc. Agri. Sci., 15: 99–111.

Sun Y., O'Riordan M.X.D. (2013). Regulation of bacterial pathogenesis by intestinal short-chain fatty acids. Adv. Appl. Microbiol., 85: 93–118.

Sunkara L.T., Achanta M., Schreiber N.B., Bommineni Y.R., Gan D., Jiang W., Lamont S., Lillehoj S.H., Beker A., Teeter R.G., Zhang G. (2011). Butyrate enhances disease resistance of chickens by inducing antimicrobial host defense peptide gene expression. PLoS ONE, 6:e27225.

Svihus B. (2014). Function of the digestive system. J. Appl. Poult. Res., 23: 306–314.

Svihus B., Choct M., Classen H.L. (2013). Function and nutritional roles of the avian caeca: A review. World Poultry Sci. J., 69: 249–263.

Timbermont L., Lanckriet A., Dewulf J., Nollet N., Schwarzer K., Haesebrouck F., Ducatelle R., Van Immerseel F. (2010). Control of *Clostridium perfringens*-induced necrotic enteritis in broilers by target-released butyric acid, fatty acids, and essential oils. Avian Pathol., 39: 117–121.

Van der Wielen P. (2002). Dietary strategies to influence the gastrointestinal microflora of young animals and its potential to improve intestinal health. In: Nutrition and health of the gastrointestinal tract, M.C. Blok, H.A. Vahl, L. de Lange, A.E. van de Braak, G. Hemke, and M. Hessing (eds.). Wageningen Academic Publishers, Wageningen, the Netherlands, pp. 37–60.

Van Immerseel F., Boyen F., Gantois I., Timbermont L., Bohez L., Pasmans F., Haesebrouck F., Ducatelle R. (2005). Supplementation of coated butyric acid in the feed reduces colonization and shedding of *Salmonella* in poultry. Poultry Sci., 84: 1851–1856.

Van Immerseel F., Russell J.B., Flythe M.D., Gantois I., Timbermont L., Pasmans F., Haesebrouck F., Ducatelle R. (2006). The use of organic acids to combat Salmonella in poultry: A mechanistic explanation of the efficacy. Avian Pathol., 35: 182–188.

Vogt H., Matthes S., Harnisch S. (1982). The effect of organic acids on productivity of broilers. Arch. Geflugelkd., 46: 223–227.

Warnecke T., Gill R.T. (2005). Organic acid toxicity, tolerance, and production in *Escherichia coli* biorefining applications. Microb. Cell Fact., 4: 25.

Wu W., Xiao Z., An W., Dong Y., Zhang B. (2018). Dietary sodium butyrate improves intestinal development and function by modulating the microbial community in broilers. PloS ONE, 13: e0197762.

Youn B.S., Nam K.T., Chang K.M., Hwang S.G., Choe I.S. (2005). Effects of wood vinegar addition for meat quality improvement of old layer. Korea J. Poult. Sci., 32: 101–106.

Received: 27 VI 2019
Accepted: 24 X 2019