

Effect of protected sodium butyrate on growth performance, carcass traits, relative weight of digestive organs and intestinal histomorphology of broilers

C. Hanim^{1,*}, N.D. Dono¹, B. Ariyadi², M.F. Habibi², M. Al Anas¹ and M.F. Hanif²

¹ Universitas Gadjah Mada, Faculty of Animal Science, Department of Animal Nutrition and Feed Science, 55281 Yogyakarta, Indonesia

² Universitas Gadjah Mada, Faculty of Animal Science, Department of Animal Production, 55281 Yogyakarta, Indonesia

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* Corresponding author:
e-mail: c.hanim@ugm.ac.id

ABSTRACT. Protected sodium butyrate (PSB) is considered an alternative to antibiotics in broiler diets. The present study investigated the effect of PSB supplementation on growth performance, carcass traits, relative weight of internal organs and intestinal morphology in broilers. A total of 1200 one-day-old New Lohman male broilers were randomly allocated to two dietary treatment groups (6 replicates, 100 birds per treatment) and fed a basal diet (CON) or a diet supplemented with 1 g of PSB per kg of diet for 5 weeks of the rearing period. On days 21 and 35, one bird per replicate was randomly selected and slaughtered to determine carcass traits, relative weight of internal organs, and measurements of intestinal histomorphological parameters. The results showed that dietary treatment with PSB increased body weight and average daily gain, but it also led to increased mortality rate ($P < 0.05$) on day 35 compared to the control group. Furthermore, PSB supplementation increased liver weight, jejunum length and colon length, while decreasing heart weight ($P < 0.05$) on day 21. In the PSB group, there was a decrease in the number of crypts in the jejunum and an increase in the height of the villi in the ileum ($P < 0.05$). In conclusion, on day 21, PSB supplementation resulted in an increase in broiler digestive organ parameters, especially liver weight and intestinal morphology. Furthermore, improved growth performance of broilers was recorded on day 35.

Introduction

Several years ago, antibiotics were commonly used as feed additives in broiler diets to prevent diseases and maximise chicken growth, with the aim of improving feed utilisation, and reducing mortality caused by pathogens (Muaz et al., 2018). However, the emergence of multidrug-resistant pathogens has led to a ban on the use of antibiotics as feed additives (Kalia et al., 2022). This situation has prompted the poultry sector and industry to seek safe alternatives to antibiotics growth promoter (AGP) and to develop

more sustainable feed management strategies to improve poultry growth performance (Adhikari et al., 2020). Sodium butyrate (SB) is one such feed additive that is being considered as a potential substitute for antibiotic growth promoters due to its positive effects on poultry production (Lan et al., 2020).

The small intestine plays a critical role in nutrient digestion and absorption. Maintaining a healthy small intestine is essential for optimal feed efficiency and enhanced growth performance (Elnesr et al., 2020). SB is preferred over BA due to its solid and stable form, as well as its reduced odour.

It serves as a source of BA, which is known for its beneficial effects on gut health (Ahsan et al., 2016). In the digestive tract, SB is readily converted to BA, which helps improve intestinal health by reducing the intestinal inflammatory response, increasing villi height, and decreasing crypt depth (Zou et al., 2019). SB is available in coated and enteric-coated forms, which can be either fat or fatty acid salt-protected (Ahsan et al., 2016). Protected sodium butyrate (PSB) is a specific type of SB that is safeguarded by a physical and chemical matrix of buffer salts. This protection prevents premature dissociation at low pH in the stomach or gizzard, ensuring sufficient release of butyrate in the small intestine (Zhao et al., 2022). The effects of PSB on digestive organs, small intestine development and carcass traits have not been extensively investigated. Therefore, the objective of this study was to examine the influence of PSB supplementation on growth performance, carcass traits, and the development of digestive organs in broilers at different stages. We hypothesized that including PSB in the diet could improve broiler performance and carcass traits by promoting the development of gastrointestinal tract morphology.

Material and methods

The experiment was conducted in a research barn (closed house), at the Faculty of Animal Science, Universitas Gadjah Mada, Indonesia. Prior approval was obtained from the Ethics Committee of the Faculty of Veterinary Medicine, Universitas Gadjah Mada, Indonesia with No: 0009/EC-FKH/Eks./2021.

Birds, diets and housing

A total of 1 200 one-day-old male New Lohmann broiler chickens (\pm 40–45 g) were used in the current study. The birds were divided into 2 dietary treatment groups: a control group (CON) fed a basal diet and an experimental group fed a basal diet supplemented with 1 g/kg PSB (Gustor N'RGY[®]; Norel S.A., Madrid, Spain). The experimental design followed a t-test design, and the feeding dose was determined based on a previous research scheme (Mallo et al., 2021). Each treatment was repeated 6 times, with each replicate consisting of 12 pens measuring 5 m \times 2 m, 100 birds in each replicate per pen. The basal diet was a maize-soybean-based diet with a metabolizable energy (ME) content of 3 000–3 200 kcal and crude protein of 20–23%. The composition and formulation of the starter (1–12 days), grower (13–23 days), and finisher (24–35 days) feeds are listed in Table 1. Drink-

Table 1. Ingredients and nutrient composition of experimental broiler starter, grower, and finisher diets

Ingredient, %	Starter		Grower		Finisher	
	CON	PSB	CON	PSB	CON	PSB
Maize	55.00	55.00	58.12	58.08	63.24	63.21
Soybean meal	33.46	33.17	27.54	27.30	19.88	19.66
Corn gluten meal	2.19	2.39	2.70	2.87	3.71	3.85
Meat bone meal	2.50	2.50	3.50	3.50	4.00	4.00
Palm kernel meal	1.00	1.00	1.50	1.50	2.00	2.00
Bran pollard	-	-	1.00	1.00	1.50	1.50
Palm oil	2.15	2.13	3.00	3.00	3.50	3.50
L-Lysine	0.30	0.31	0.23	0.24	0.24	0.24
DL-Methionine	0.32	0.32	0.22	0.22	0.17	0.17
L-Threonine	0.18	0.18	0.11	0.11	0.08	0.08
Limestone	1.07	1.07	0.82	0.82	0.60	0.60
Sodium chloride	0.22	0.22	0.20	0.20	0.19	0.19
Sodium bicarbonate	0.18	0.18	0.18	0.18	0.18	0.19
Sodium huminate	0.10	0.10	0.10	0.10	0.10	0.10
Calcium propionate	0.05	0.05	0.05	0.05	0.05	0.05
Choline chloride	0.10	0.10	0.10	0.10	0.10	0.10
Premix ¹	0.16	0.16	0.16	0.16	0.16	0.16
Enzyme	0.10	0.10	0.10	0.10	0.10	0.10
Toxin binder	0.10	0.10	0.10	0.10	0.10	0.10
Additive	0.81	0.81	0.26	0.26	0.11	0.11
Protected sodium butyrate	-	0.10	-	0.10	-	0.10
Total	100	100	100	100	100	100
Nutrient composition, %						
ME, kcal/kg	3355	3359	3466	3469	3580	3583
crude protein	25.59	25.62	23.87	23.89	21.59	21.61
lysine	1.62	1.62	1.48	1.48	1.33	1.33
Met	0.75	0.75	0.65	0.65	0.58	0.58
Met + Cys	1.17	1.17	1.09	1.09	1.00	1.00
threonine	1.13	1.13	1.03	1.03	0.93	0.93
calcium	1.09	1.09	0.99	0.99	0.90	0.90
available phosphorus	0.51	0.51	0.42	0.42	0.39	0.39

CON – control, PSB – protected sodium butyrate treatment, ME – metabolizable energy, Met – methionine, Cys – cysteine; ¹contained per kg of complete diet: mg: Cu 132.0, Zn 403.6, P 1.7 g, S 131.8, Mn 772.3, Co 6.0, K 185.7; g: Ca 258.0, Mg 2.0, Na 18.2, Fe 16.3; μ g: Se 93.0

ing water was provided *ad libitum* throughout the 5-week rearing period. The starter, grower, and finisher diets were given on days 0–10, 11–21, and 22–35, respectively. Room lighting, relative humidity, and temperature were controlled during the experiment. The animal care practices employed in this study were conducted in accordance with the guidelines outlined in the Guide for the Care and Use of Agricultural Animals in Research and Teaching (Federation of Animal Science Societies, 2010).

Growth performance and carcass trait

Data on body weight, feed intake, weight gain, feed conversion ratio (FCR), and performance index

were collected on days 0, 7, 14, 21, and 35 of the study. Mortality of broiler chickens was monitored daily. On days 21 and 35, one bird per replicate per treatment was randomly selected and weighed. These birds were then slaughtered in a professional slaughterhouse by cutting the jugular vein. The carcass weight of the samples was obtained by weighing the whole body of broilers after removing blood, feathers, neck, head, claws, and internal organs, excluding the kidneys and lungs. Intestinal segments (small and large intestines), as well as internal organs were removed for further inspection. Relative carcass weight was obtained by dividing carcass weight by live weight multiplied by 100%. The weights of the digestive organs, including the crop, proventriculus, gizzard, liver, and caecum were excised and measured on days 21 and 35. The relative weight of the internal organs was determined by dividing the weight of internal organs by bird's live weight.

Digestive tract and intestinal histomorphology

The length of the digestive tract of broiler chickens was measured after separating each part (duodenum, jejunum, ileum, caecum, and colon). On day 35, intestinal segments (2 cm) from the midpoint of the duodenum (duodenum), the midpoint between the bile duct entry and Meckel's diverticulum (jejunum), and the distal end of the lower ileum were dissected and fixed in 10% buffered formalin (100 ml 40% formaldehyde, 4 g phosphate, 6.5 g dibasic sodium phosphate, and 900 ml distilled water) and soaked for 24–48 h. The samples were prepared quickly by dehydrating them (soaking in a gradual series of alcohol – 70, 80, 90, and 100%). The small intestine samples were then cleared by soaking them in xylol and then embedded in paraffin (Leica Biosystems, Wetzlar, Germany). The samples were sectioned into 5- μ m pieces using a rotary microtome (Yamato Kohki Industrial Co., Ltd., Saitama, Japan) and stained with haematoxylin and eosin. Finally, the samples were examined under a light microscope. The sections were observed at 4 \times magnification under a microscope with Optilab Viewer software version 2.2 (PT. Miconos Transdata Nusantara, Yogyakarta, Indonesia) connected to a device monitor. The resulting photographs of the histomorphological samples was measured using the Image Raster software version 4.0.5 (PT. Miconos Transdata Nusantara, Yogyakarta, Indonesia).

Statistical analysis

The pen was considered an experimental unit for conducting statistical analyses of various parameters,

including growth performance (initial weight, body weight gain, final weight, feed intake, feed conversion ratio, mortality and index performance), carcass weight, internal organ weight, histomorphology of the small and large intestine (absolute, relative, and total weight), and histomorphology of the small intestine (villus height, villus width, crypt depth, and villus height-to-crypt ratio). The statistical analysis was performed using the t-test implemented in the SPSS software version 26 (SPSS Inc., Chicago, IL, USA).

Results

Growth performance and carcass traits

The result showed that feed intake, FCR, and performance index were not significantly different between the two groups. However, the PSB group exhibited a significant improvement in body weight, weight gain, and mortality compared to the CON group on day 35 ($P < 0.05$; Table 2, Figure 1). Additionally, the PSB group showed a significant enhancement in weight gain on day 35. The results presented in Table 3 indicated that dietary PSB did not have a significant effect ($P > 0.05$) on the percentages of carcass traits.

Table 2. Effect of protected sodium butyrate on growth performance of male broilers, measured on days 21 and 35

Parameters	Group		SEM	P-value
	CON	PSB		
Day 21				
weight gain, g/bird/day	45.3	46.3	0.264	0.082
feed intake, g/bird/day	64.7	62.2	1.163	0.312
feed conversion ratio	1.4	1.3	0.026	0.128
mortality, %	1.0	1.8	0.322	0.231
performance index	310	339	9.014	0.134
Day 35				
weight gain, g/bird/day	59.5	61.2	0.425	0.047
feed intake, g/bird/day	89.4	87.5	1.655	0.597
feed conversion ratio	1.5	1.4	0.003	0.266
mortality, %	4.0	6.0	0.471	0.034
performance index	243	282	12.346	0.139

CON – animals fed basal diet, PSB – animals fed basal diet mixed with 1 g/kg protected sodium butyrate; SEM – standard error of the mean; $P < 0.05$ indicates that the values are significantly different

Relative weight of digestive organs

Table 4 shows the relative weight of the digestive organs of broilers on days 21 and 35. On day 21, broilers fed PSB had higher relative liver weight and lower relative heart weight compared to the control group ($P < 0.05$). However, the dietary treatments

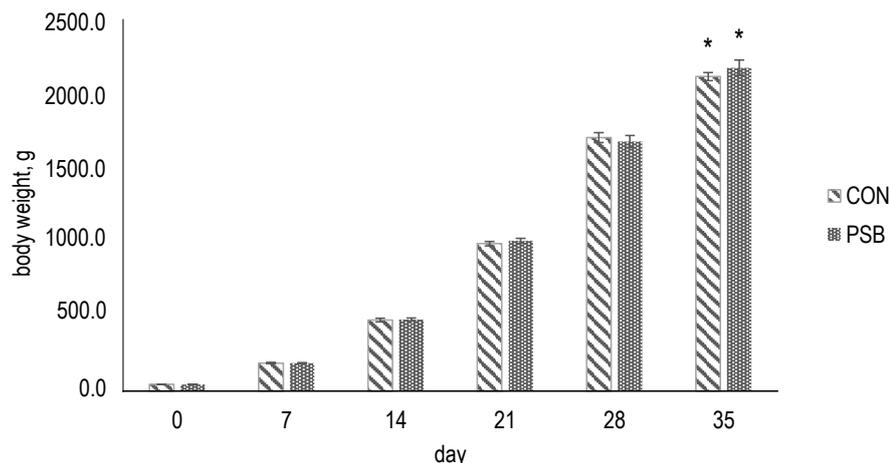


Figure 1. Effect of protected sodium butyrate on body weight of male broilers from days 7 to 35

CON – basal diet, PSB – basal diet mixed with 1 g/kg protected sodium butyrate; data are presented as mean value \pm SEM; * indicate significant differences at $P < 0.05$

Table 3. Effect of protected sodium butyrate on carcass trait of male broilers, measured on days 21 and 35

Parameters	Group		SEM	P-value
	CON	PSB		
Day 21				
live weight, g/bird	997	1017	5.39	0.080
carcass weight, g	738	749	13.6	0.708
carcass, %	73.9	73.7	1.31	0.925
Day 35				
live weight, g/bird	2128	2188	14.8	0.048
carcass weight, g	1531	1495	29.0	0.579
carcass, %	72.0	68.5	1.68	0.340

CON – animals fed basal diet, PSB – animals fed basal diet mixed with 1 g/kg protected sodium butyrate; SEM – standard error of the mean; $P < 0.05$ indicates that the values are significantly different

Table 4. Effect of protected sodium butyrate on relative weights of internal organs in male broilers, measured on days 21 and 35

Parameters, %	Group		SEM	P-value
	CON	PSB		
Day 21				
crop	0.28	0.27	0.010	0.671
proventriculus	0.69	0.55	0.052	0.189
gizzard	2.25	2.14	0.084	0.566
liver	2.11	2.60	0.117	0.038
heart	0.61	0.48	0.026	0.007
cecum	0.51	0.57	0.052	0.580
Day 35				
crop	0.35	0.31	0.041	0.653
proventriculus	0.60	0.62	0.077	0.923
gizzard	1.15	1.01	0.039	0.083
liver	2.37	2.23	0.130	0.633
heart	0.46	0.38	0.019	0.052
cecum	0.62	0.64	0.044	0.859

CON – animals fed basal diet, PSB – animals fed basal diet mixed with 1 g/kg protected sodium butyrate; SEM – standard error of the mean; $P < 0.05$ indicates that the values are significantly different

had no effect on the relative weight of the broilers' digestive organs at 35 days of age.

Digestive tract length and intestinal morphology

PSB inclusion improved the length of the jejunum and colon in broilers on day 21 ($P < 0.05$; Table 5). In contrast, the length of the gastrointestinal tract of broilers was not affected by the dietary treatments on day 35. In the jejunum, the PSB group exhibited significantly lower crypt depth compared to the CON group ($P < 0.05$; Table 6). Additionally, the PSB group had the highest ratio of villi to crypts in the jejunum ($P = 0.007$). PSB administration also increased the height of villi in the ileum ($P < 0.05$, Table 6).

Table 5. Effect of protected sodium butyrate on length of the intestinal tracts of male broilers, measured on days 21 and 35

Parameters, cm	Group		SEM	P-value
	CON	PSB		
Day 21				
duodenum	24.7	25.5	0.682	0.583
jejunum	54.0	66.8	2.409	0.004
ileum	55.8	59.9	2.188	0.403
cecum	25.5	27.8	1.056	0.312
colon	6.3	9.5	0.499	0.000
Day 35				
duodenum	28.3	30.0	1.046	0.472
jejunum	75.0	79.8	1.511	0.131
ileum	72.3	73.7	1.882	0.752
cecum	36.0	36.7	1.076	0.782
colon	9.5	10.3	0.571	0.511

CON – animals fed basal diet, PSB – animals fed basal diet mixed with 1 g/kg protected sodium butyrate; SEM – standard error of the mean; $P < 0.05$ indicates that the values are significantly different

Table 6. Effect of protected sodium butyrate on intestinal histomorphology in male broilers, measured on day 35

Parameters, μm	Group		SEM	P-value
	CON	PSB		
Duodenum				
villus height	1014	1084	27.62	0.302
villus width	117.0	113.9	8.28	0.881
crypt	193.1	174.6	7.53	0.314
villus: crypt	5.3	6.4	0.31	0.159
Jejunum				
villus height	681	654	40.07	0.794
villus width	107.6	110.3	5.46	0.846
crypt	252.5	149.1	19.95	0.013
villus: crypt	2.7	4.5	0.32	0.007
Ileum				
villus height	594	406.2	36.47	0.013
villus width	104.9	138.2	9.13	0.117
crypt	187.9	126.3	16.99	0.121
villus: crypt	3.3	3.7	0.31	0.542

CON – animals fed basal diet, PSB – animals fed basal diet mixed with 1 g/kg protected sodium butyrate; SEM – standard error of the mean; $P < 0.05$ indicates that the values are significantly different

Discussion

The aim of this study was to investigate the effect of dietary PSB as a potential antibiotic alternative on growth performance, carcass traits and digestive organ development in broilers at different growth stages. The findings suggest that the supplementation of PSB may improve broiler performance and carcass traits by promoting the development of gastrointestinal villi.

The supplementation of PSB increased body weight gain and final body weight, but had no effect on FCR on day 35. These findings were consistent with previous studies by Wan et al. (2022) and Chamba et al. (2014), which reported improvements in body weight and body weight gain on day 42, respectively, when administering protected sodium butyrate to broiler chickens. However, PSB supplementation in the latter studies also improved FCR.

The improvement in broiler performance may be attributed to various functions performed by sodium butyrate. Butyric acid and its derivative have been shown to enhance gut health (Wu et al., 2018; Zou et al., 2019), stimulate the pancreatic exocrine function (Mallo et al., 2021; Miao et al., 2021), and increase the secretion of digestive enzymes, such as amylase and lipase. These effects ultimately lead to improved feed digestion and nutrient absorption in broilers.

In our study, the supplementation of protected sodium butyrate increased the length of the jejunum

and colon, which was consistent with previous research conducted by Chamba et al. (2014). The elongation of the jejunum is beneficial for optimizing nutrient digestion and absorption, which ultimately contributes to improved bird growth performance (Aderibigbe et al., 2020). Butyrate, apart from providing energy to epithelial cells, has been shown to significantly increase epithelial cell proliferation, differentiation, and enhance colonic barrier function (Guilloteau et al., 2010). When infused into the colon, butyrate exerted a trophic effect on ileal and jejunal epithelial cells, promoting their proliferation, differentiation, and maturation. Additionally, it reduced apoptosis in the small intestine by influencing gene expression and protein synthesis (Sengupta et al., 2006). These mechanisms likely contribute to the observed increase in both relative weight and length of the small intestine with PSB supplementation.

The addition of protected sodium butyrate result in the delivery of a portion of butyrate to more distal sections of the gastrointestinal tract due to its slow release during digestion, leading to mucosal modulation in the gut (Sikandar et al., 2017). This improvement is related to the ability of sodium butyrate to lower intestinal pH (Lan et al., 2020). As a result, PSB has been shown to increase the diversity of the ileal microbial community and affect gut morphology (Zhao et al., 2022), ultimately supporting nutrient absorption in the small intestine (Liu et al., 2014). Moreover, butyrate, the active ingredient in sodium butyrate, is readily absorbed by enterocytes as an energy source, which stimulates proper intestinal development and function, and thus overall health (Mahdavi and Toriki, 2009; Wu et al., 2018). The current study demonstrated that sodium butyrate supplementation increased the height of villi in the small intestine, which was consistent with previous findings by Chamba et al. (2014) and Sikandar et al. (2017). The increased height of the villi, along with appropriate crypt depth, provides a larger surface area for enhanced nutrient absorption capacity and supports healthy intestinal development. Additionally, this architectural feature promotes faster tissue turnover, thereby contributing to the optimal health status of the gut (Marchewka et al., 2021).

The supplementation of protected sodium butyrate (PSB) in broiler diets has been observed to increase liver weight and decrease heart weight. This finding is consistent with the study conducted by Aghazadeh and TahaYazdi (2012), where sodium butyrate supplementation resulted in increased liver weight. The liver plays a crucial role in various metabolic

processes, including synthesis, metabolism, excretion, and detoxification. Therefore, an increase in liver mass is generally considered a positive indicator associated with higher metabolic activity (Zaefarian et al., 2019). Supplemented butyrate has also been found to impact the chromatin structure of hepatocytes in chickens. Regardless of the dose, butyrate caused hyperacetylation of histones (Mátis et al., 2013; Terova et al., 2016). Furthermore, the application of butyrate has been shown to mitigate the stimulatory effect of concurrently administered phenobarbital, an enzyme inducer, on cytochrome P450 2H and cytochrome P450 3A37 activity in chicken liver (Mátis et al., 2015). Cytochrome P450 (CYP) enzymes are primarily expressed in cell types such as hepatocytes in the endoplasmic reticulum, but they are also found in the intestinal mucosa, where they serve as a primary metabolic barrier against orally ingested xenobiotics (Obach et al., 2001).

Conclusions

Overall, our findings suggest that dietary supplementation with PSB can positively impact growth performance, digestive organs, and intestinal morphology in broilers. The administration of PSB until day 21 increased the weight of chicken liver and improved intestinal morphology, while treatment up to day 35 enhanced broiler performance.

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Conflict of interest

The Authors declare that there is no conflict of interest.

References

- Aderibigbe A., Cowieson A., Sorbara J.O., Adeola O., 2020. Intestinal starch and energy digestibility in broiler chickens fed diets supplemented with α -amylase. *Poult. Sci.* 99, 5907–5914, <https://doi.org/10.1016/j.psj.2020.08.036>
- Adhikari P., Kiess A., Adhikari R., Jha R., 2020. An approach to alternative strategies to control avian coccidiosis and necrotic enteritis. *J. Appl. Poult. Res.* 29, 515–534, <https://doi.org/10.1016/j.japr.2019.11.005>
- 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, <https://doi.org/10.4314/sajas.v42i3.5>
- Ahsan U., Cengiz O., Raza I., Kuter E., Chacher M.F.A., Iqbal Z., Umar S., Çakir S., 2016. Sodium butyrate in chicken nutrition: The dynamics of performance, gut microbiota, gut morphology, and immunity. *Worlds Poult. Sci. J.* 72, 265–275, <https://doi.org/10.1017/S0043933916000210>
- 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, <https://doi.org/10.3923/ijps.2014.390.396>
- Elnesr S.S., Alagawany M., Elwan H.A.M., Fathi M.A., Farag, M.R., 2020. Effect of sodium butyrate on intestinal health of poultry – a review. *Ann. Anim. Sci.* 20, 29–41, <https://doi.org/10.2478/aoas-2019-0077>
- Federation of Animal Science Societies, 2010. Guide for the care and use of agricultural animals in research and teaching. Champaign (IL): Federation of Animal Science Societies, Champaign (IL, USA)
- 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, <https://doi.org/10.1017/S0954422410000247>
- Kalia V.C., Shim W.Y., Patel S.K.S., Gong C., Lee J.K., 2022. Recent developments in antimicrobial growth promoters in chicken health: Opportunities and challenges. *Sci. Total Environ.* 834, 155300, <https://doi.org/10.1016/j.scitotenv.2022.155300>
- Lan R., Zhao Z., Li S., An L., 2020. Sodium butyrate as an effective feed additive to improve performance, liver function, and meat quality in broilers under hot climatic conditions. *Poult. Sci.* 99, 5491–5500, <https://doi.org/10.1016/j.psj.2020.06.042>
- Liu H., Zhang J., Zhang S., Yang F., Thacker P.A., Zhang G., Qiao S., Ma X., 2014. Oral administration of *Lactobacillus fermentum* I5007 favors intestinal development and alters the intestinal microbiota in formula-fed piglets. *J. Agric. Food Chem.* 62, 860–866, <https://doi.org/10.1021/jf403288r>
- 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
- Mallo J.J., Sol C., Puyalto M., Bortoluzzi C., Applegate T.J., Villamide M.J., 2021. Evaluation of sodium butyrate and nutrient concentration for broiler chickens. *Poult. Sci.* 100, 101456, <https://doi.org/10.1016/j.psj.2021.101456>
- Marchewka J., Sztandarski P., Zdanowska-Sąsiadek Ż., Adamek-Urbańska D., Damaziak K., Wojciechowski F., Riber A.B., Gunnarsson S., 2021. Gastrointestinal tract morphometrics and content of commercial and indigenous chicken breeds with differing ranging profiles. *Animals* 11, 1881, <https://doi.org/10.3390/ani11071881>
- Mátis G., Kulcsár A., Turowski V., Fébel H., Neogrády Z., Huber K., 2015. Effects of oral butyrate application on insulin signaling in various tissues of chickens. *Domest. Anim. Endocrinol.* 50, 26–31, <https://doi.org/10.1016/j.domaniend.2014.07.004>
- Mátis G., Neogrády Z., Csikó G., Kulcsár A., Kenéz Á., Huber K., 2013. Effects of orally applied butyrate bolus on histone acetylation and cytochrome P450 enzyme activity in the liver of chicken—a randomized controlled trial. *Nutr. Met.* 10, 12, <https://doi.org/10.1186/1743-7075-10-12>

- Miao S., Zhou W., Li H., Zhu M., Dong X., Zou X., 2021. Effects of coated sodium butyrate on production performance, egg quality, serum biochemistry, digestive enzyme activity, and intestinal health of laying hens. *Ital. J. Anim. Sci.* 20, 1452–1461, <https://doi.org/10.1080/1828051X.2021.1960209>
- Muaz K., Riaz M., Akhtar S., Park S., Ismail A., 2018. Antibiotic residues in chicken meat: global prevalence, threats, and decontamination strategies: a review. *J. Food Prot.* 81, 619–627, <https://doi.org/10.4315/0362-028X.JFP-17-086>
- Obach R.S., Zhang Q.-Y., Dunbar D., Kaminsky L.S., 2001. Metabolic characterization of the major human small intestinal cytochrome P450S. *Drug Met. Dispos.* 29, 347–352
- Sengupta S., Muir J.G., Gibson P.R., 2006. Does butyrate protect from colorectal cancer? *J. Gastroenterol. Hepatol.* 21, 209–218, <https://doi.org/10.1111/j.1440-1746.2006.04213.x>
- Sikandar A., Zaneb H., Younus M., Masood S., Aslam A., Khattak F., Ashraf S., Yousaf M.S., Rehman H., 2017. Effect of sodium butyrate on performance, immune status, microarchitecture of small intestinal mucosa and lymphoid organs in broiler chickens. *Asian-Australas. J. Anim. Sci.* 30, 690–699, <https://doi.org/10.5713/ajas.16.0824>
- Terova G., Díaz N., Rimoldi S., Ceccotti C., Gliozheni E., Piferri F., 2016. Effects of sodium butyrate treatment on histone modifications and the expression of genes related to epigenetic regulatory mechanisms and immune response in European sea bass (*Dicentrarchus labrax*) fed a plant-based diet. *PLoS One* 11, e0160332, <https://doi.org/10.1371/journal.pone.0160332>
- Wan F., Deng F.L., Chen L., Zhong R.Q., Wang M.Y., Yi B., Liu L., Zhao H.B., Zhang H.F., 2022. Long-term chemically protected sodium butyrate supplementation in broilers as an antibiotic alternative to dynamically modulate gut microbiota. *Poult. Sci.* 101, 102221, <https://doi.org/10.1016/j.psj.2022.102221>
- 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, <https://doi.org/10.1371/journal.pone.0197762>
- Zaefarian F., Abdollahi M.R., Cowieson A., Ravindran V., 2019. Avian liver: The forgotten organ. *Animals* 9, 63, <https://doi.org/10.3390/ani9020063>
- Zhao H., Bai H., Deng F., Zhong R., Liu L., Chen L., Zhang H., 2022. Chemically protected sodium butyrate improves growth performance and early development and function of small intestine in broilers as one effective substitute for antibiotics. *Antibiotics* 11, 132, <https://doi.org/10.3390/antibiotics11020132>
- Zou X., Ji J., Qu H., Wang J., Shu D.M., Wang Y., Liu T.F., Li Y., Luo C.L., 2019. Effects of sodium butyrate on intestinal health and gut microbiota composition during intestinal inflammation progression in broilers. *Poult. Sci.* 98, 4449–4456, <https://doi.org/10.3382/ps/pez279>