Applications of butyric acid in poultry production: the dynamics of gut health, performance, nutrient utilization, egg quality, and osteoporosis

Mohamed T. El-Saadony1,*, Muhammad Umar Yaqoob2,*, Faiz-ul Hassan3, Mahmoud Alagawayn4, Muhammad Arif5, Ayman E. Taha6, Shaaban S. Elnesr7,*, Khaled A. El-Tarabily8,9 and Mohamed E. Abd El-Hack4

1Department of Agricultural Microbiology, Faculty of Agriculture, Zagazig University, Zagazig, 44511, Egypt; 2College of Animal Science, Zhejiang University, Hangzhou, 310058, P. R. China; 3Institute of Animal and Dairy Sciences, University of Agriculture, Faisalabad, Pakistan; 4Poultry Department, Faculty of Agriculture, Zagazig University, Zagazig, 44511, Egypt; 5Department of Animal Sciences, College of Agriculture, University of Sargodha, Sargodha, Punjab, Pakistan; 6Department of Animal Husbandry and Animal Wealth Development, Faculty of Veterinary Medicine, Alexandria University, Edfina, 22758, Egypt; 7Department of Poultry Production, Faculty of Agriculture, Fayoum University, Fayoum, 63514, Egypt; 8Department of Biology, College of Science, United Arab Emirates University, Al-Ain, 15551, United Arab Emirates and 9Harry Butler Institute, Murdoch University, Murdoch, 6150, Western Australia, Australia

Abstract

Due to the increasing demand for antibiotic-free livestock products from the consumer side and the ban on the use of antibiotic growth promoters, the poultry feed industry is increasingly interested in developing more alternatives to cope with this problem. Organic acids (butyric acid) have many beneficial effects on poultry health, performance, and egg quality when used in their diet, thus they can be considered for the replacement of antibiotics in livestock production systems. Butyric acid is most efficacious against pathogenic bacteria such as Salmonella spp. and Escherichia coli, and stimulates the population of beneficial gut bacteria. It is a primary energy source for colonocytes and augments the differentiation and maturation of the intestinal cells. Collectively, butyric acid should be considered as an alternative to antibiotic growth promoters, because it reduces pathogenic bacteria and their toxins, enhancing gut health thereby increasing nutrient digestibility, thus leading to improved growth performance and immunity among birds. The possible pathways and mechanisms through which butyric acid enhances gut health and production performance are discussed in this review. Detailed information about the use of butyric acid in poultry and its possible benefits under different conditions are also provided, and the impacts of butyric acid on egg quality and osteoporosis are noted.

Introduction

Butyric acid is one of the short short-chain fatty acids (SCFAs) generated at millimolar levels in the bird cecum, which is the major site for microbial fermentation of unabsorbed starch (Liu et al., 2017). Butyric acid in its unprotected form is rapidly absorbed in the upper gastrointestinal tract (GIT), suggesting that protection is needed to positively affect the small intestine (Kaczmarek et al., 2016; Elnesr et al., 2020; Silva et al., 2020).

Due to bans on using in-feed antibiotic growth promoters, the poultry industry has been focused on finding new ways to improve performance through improving nutrient and energy utilization while maintaining and potentially improving the health of poultry without using antibiotic growth promoters. The uses of organic acids for improving performance parameters in both layers and broilers have been increasingly explored. Organic acids, including butyric acid and its salts, have shown positive effects on growth performance, egg production, and egg quality due to the source of the acid, diet composition and environment (Soltan, 2008; Elnesr et al., 2019; Maty and Hassan, 2020).

Organic acids, such as butyric acid, improve gut health by providing carbon sources for villi growth, promoting the growth of beneficial bacteria (lactobacilli and Bifidobacteria), and decreasing harmful bacteria (Salmonella, Clostridium, and Escherichia coli) by decreasing luminal pH. Improved gut health is theorized to allow increased absorption, resulting in increased nutrient and energy utilization in poultry, thereby improving performance (Qaisrani et al., 2015; Maty and Hassan, 2020).

In layer farming, egg production and egg quality are of great economic concern. Improved egg quality can be identified as improving eggshell strength while maintaining a good egg size.
Calcium is a major component of the layer diet and is incorporated into both eggshell and bone (Clunies et al., 1992; Makled et al., 2019) by absorption from the small intestine (Saunders-Blades et al., 2009). As the hen ages, its ability to absorb nutrients, including calcium, declines, decreasing eggshell thickness and thus breaking strength. This leads to increased economic losses due to broken eggs (Molnár et al., 2018; Maty and Hassan, 2020).

Organic acids improve the mineral absorption from the intestine by lowering the pH of digesta and inhibiting the formation of calcium-phosphate complexes (Boling et al., 2000; Rafacz-Livingston et al., 2005). It has been found that supplementation of butyric acid and its salts (sodium butyrate) increases serum calcium, phosphorus (Mahdavi and Torki, 2009; Adil et al., 2010; Kamal and Ragaa, 2014), and magnesium levels (Kamal and Ragaa, 2014). This review aims to provide current knowledge about the effects of butyric acid on gut health, performance, nutrient utilization, immunity, osteoporosis, and egg quality in poultry.

**Different formulations of butyric acid**

The efficacy of butyric acid was improved when fed in a coated form, such as encapsulation, suggesting that such protection positively affected the GIT (Kaczmarek et al., 2016; Elness et al., 2020). Previous studies showed variable results, perhaps due to factors such as age, nutrition, diet structure, experimental conditions, flock health, source of butyric acid, and inclusion rate (Taherpour et al., 2009; Levy et al., 2015; Qaisrani et al., 2015; Kaczmarek et al., 2016).

Kaczmarek et al. (2016) found that protected butyrate at various doses significantly improved villi height and apparent metabolizable energy (AME) in broilers, while Levy et al. (2015) found no significant effect of encapsulated butyric acid on villi height compared to controls in broilers. These variations in findings suggest a need for further research to determine the optimal source and inclusion rate of butyric acid, to overcome the variation seen due to other potential factors.

Currently, poultry feed manufacturers tend to produce coated types of butyric acid to overcome its odor and rapid volatility. However, the problem of traditional coated products is the low concentration of butyric acid, as coated salts usually include about 25–30% butyric acid, which is very low; therefore, future research should involve means to coat butyric acid while increasing its concentration to maximize its benefit.

**Butyric acid as an alternative to antibiotics**

In areas of the world such as the European Union and the United States, antibiotics/antibiotic growth promoters are no longer being added to poultry diets (Opinion of the Economic and Social Committee, 1998; Riche, 2003; Deepa et al., 2018), due to the high concentrations of antibiotic residues found in meat and meat products, undesired changes in the microbial communities of the GIT (Kulshreshtha et al., 2014), and increase in antibiotic resistance in pathogenic bacteria (Riche, 2003; Raza et al., 2019).

Ideally, alternative supplements would improve growth performance by acting to improve feed efficiency and nutrient absorption and utilization, as well as to regulate microbial populations in such a way to promote the growth of beneficial microbes and reduce pathogenic microbes in the GIT (Biggs and Parsons, 2008; Deepa et al., 2018). Organic acids, specifically SCFAs, are considered as alternatives. Detailed interactions of butyric acid to enhance the growth performance of poultry through different systems are presented in Fig. 1. Most European Union member states generally regard organic acids and their salts as safe, and they have approved them for use as feed additives for livestock and poultry production (Adil et al., 2011).

SCFAs can also be described as saturated straight-chain monocarboxylic acids, fatty acids, volatile fatty acids, and weak or carboxylic acids. Originally, SCFAs were added to animal feed to prevent fungal growth (Dixon and Hamilton, 1981). Propionate and formic acid (and various combinations) have bactericidal activity in feeds contaminated with foodborne pathogens such as *Salmonella* spp. (Riche, 2003; Raza et al., 2019), and butyric acid is thought to reduce intestinal populations of pathogenic bacteria in different ways (Figs 2 and 3). Butyric acid is now increasingly researched as a feed additive for poultry due to its proposed effectiveness to improve feed conversion efficiency, gut health, and growth performance (Deepa et al., 2018; Imran et al., 2018).
Sources of butyric acid

Butyric acid, along with other SCFAs, is produced in millimolar amounts in the GITs of people and animals, within locations that predominantly contain strictly anaerobic microflora (Ricke, 2003). For poultry, this area is the cecum, which is the major site of microbial fermentation of unabsorbed starch (Liu et al., 2017), non-starch polysaccharides (Levy et al., 2015), and proteins (Kulshreshtha et al., 2014). Butyric acid, propionic acid, and acetic acid are the major byproducts of these processes (Liu et al., 2017).

Butyric acid is most effective in its undissociated (non-ionized, more lipophilic) form (Leeson et al., 2005; Wu et al., 2018), but is often supplemented as butyrate in the diet because of its volatile nature (Liu et al., 2017) and pungent smell (Kaczmarek et al., 2016). Adil et al. (2011) suggested that reduced feed intake can be observed due to reduced palatability of the feed when SCFAs are supplemented in their acid form (properties of butyric acid are presented in Fig. 4).

Another advantage of butyric acid supplemented in salt form is that it is less corrosive and more water-soluble (Khan and Iqbal, 2016; Silva et al., 2020). Butyric acid is quickly absorbed and metabolized by mucosal cells. Absorption and metabolism of butyric acid begin in the mucosa of the crop, and this process continues throughout the GIT. This rapid absorption limits the amount of butyric acid that will arrive in and affect the small intestine. Butyrate can be microencapsulated to reduce rapid absorption, thus helping improve its efficiency by allowing it to stay intact until it arrives in the small intestine. A common
method of encapsulation is stearin or vegetable fat, and it has been found that this method has had positive effects on gut morphology and reduction of pathogen colonization in the intestine (Liu et al., 2017; Makled et al., 2019).

In a study by Liu et al. (2017), researchers created an assay to determine the optimal time for butyric acid release from the GIT for broilers. It was found that encapsulated butyric acid aiming to stimulate epithelial cell development and improve digestibility should release at 30 min to 2.5 h post-ingestion; to focus on hind gut control, and the release should be at 2.5–4 h post-ingestion (Liu et al., 2017; Makled et al., 2019). Butyric acid needs to be in its undissociated form before it arrives at the hind-gut to utilize its antimicrobial effect. Meanwhile, release in the small intestine should affect villi development and nutrient digestibility (Liu et al., 2017).

Butyrate in its free form is used mostly as a feed sanitizer rather than as a supplement because it is quickly absorbed in the crop (Leeson et al., 2005; Maty and Hassan, 2020). Unprotected butyrate is active in the crop, proventriculus, and gizzard. Tributyrin (a triglyceride of butyrate) is active in the small intestine and fat-coated/encapsulated butyrate is active in the ceca and colon (Moquet et al., 2018; Deepa et al., 2018). Butyrate facilitates passage to the lower GIT where butyrate is released by lipase activity (Moquet et al., 2018). Monobutyrin has been used to potentially improve growth performance in broilers (Ahsan et al., 2016; Bedford et al., 2017).

A recent study by Bedford et al. (2017) found that supplementing tributyrin alone had no significant effect on growth performance in broilers, whereas mixtures of mainly monobutyryl and tributyrin, with some dibutyltin, had positive effects on growth performance. Sodium butyrate promotes water absorption and proliferation of epithelial cells, provides energy, stimulates the synthesis of gastrointestinal hormones, and stimulates intestinal blood flow in broiler chicks (Hu and Guo, 2007).

In a study by Moquet et al. (2018), three forms of butyrate were tested in a diet with a poorly digestible protein source, to investigate the effect of butyrate on various parts of the GIT. It was reported that the presence of butyrate beyond the gizzard had an anorexic (appetite-reducing) effect, which was considered unusual for 1 g kg$^{-1}$ of supplemented butyrate (Ahsan et al., 2016; Moquet et al., 2018). Studies have found that this anorexic effect caused by butyrate (and other SCFAs) is modulated by colonic L-cells that produce glucagon-like peptide 1 (GLP-1) and peptide YY (PYY). GLP-1 is released in the presence of digested protein as well as free fatty acids. PYY has an orexigenic (appetite-stimulating) effect in chickens, whereas it has an anorexic effect in rodents. PYY acts directly on the hypothalamus and triggers cholecystokinin (CCK), which promotes the satiety effect via the vagus nerve, reducing rodent appetite. The mechanism by which an orexigenic effect occurs in poultry is unclear (Furness et al., 2013; Maty and Hassan, 2020).

In poultry, L-cells are located all along the distal small intestine, but the colon is the main site of anorexic effects (Moquet et al., 2018). L-cells are enteroendocrine cells that function by stimulating carbohydrate uptake, releasing insulin, and slowing intestine transit (Furness et al., 2013; Wu et al., 2018). Moquet et al. (2018) reported that anorexic effects were reduced when butyrate was delivered to the crop, gizzard, and proventriculus in the unprotected form. It was also found that butyrate in the colon and ceca, in the protected form, increased total tract retention times, allowing more time for absorption and thus improved feed efficiency. Very few studies have demonstrated a link between colon motility and the butyrate effects (Moquet et al., 2018; Makled et al., 2019).

SCFAs have also been found to increase ileal proglucagon mRNA, protein, and glucose transporter (GLUT-2) expression, potentially improving gut epithelial cell proliferation (Adil et al., 2010; Ahsan et al., 2016). In addition to finding which butyrate source is most effective, researchers have begun to examine which diet composition and form is best suited to maximize the effects of butyric acid and its salts when added to different diets. A portion of studies carried out by Zhou et al. (2014) and Qaisrani et al. (2015) looked at how the relationship between diet structure (coarse or fine) and butyric acid supplementation (with or without) affected growth performance and gut morphology in broilers. It was found that feeding a course diet supplemented with butyric acid positively affected performance, decreased crypt depth, and increased villus height to crypt depth ratio when added to a poorly digestible protein source (Qaisrani et al., 2015).

Gut health

The impact of butyric acid on gut health is presented in Fig. 5. Gut health can be affected by nutrition, environment, or infectious disease agents. There is a direct relationship between gut health and animal performance, and many researchers have attempted to create a gut health scoring index that can be applied to poultry diets (Kraieski et al., 2017). Researchers spend more time studying gut health because it is a major factor in the performance of both broilers and layers (Grashorn et al., 2013; Silva et al., 2020). Optimal gut health is characterized in several ways. One of them is the villi height to crypt depth ratio. A high ratio indicates mature and well-functioning villi with a shallow crypt that constantly provides cell renewal (Kaczmarek et al., 2016). Improved gut health has also been attributed to the increased length of the GIT, allowing increased absorption (Adil et al., 2011).

Dietary supplementation with organic acid supports the gut health of poultry species (Alagawany et al., 2021). Butyric acid
can improve epithelial cell development (Levy et al., 2015). Butyric acid is also thought to effectively preserve cell viability and enhance enterocyte turnover, which may improve intestinal recovery. It has been observed that butyrate supplementation can increase villi height and decline crypt depth in poultry and other non-ruminant animals, thereby increasing the absorptive surface (Qaisrani et al., 2015; Wu et al., 2018; Elnesr et al., 2019). SCFAs are theorized to have several mechanisms of antimicrobial activity. One of the most widely accepted mechanisms by which butyric acid can destroy pathogenic bacteria and express its antibacterial activity is that the acid changes the internal pH of the microbe (depolarization) and therefore disrupts nutrient synthesis and transport as well as energy metabolism of that microbe (Figs 2 and 6) (Adil et al., 2011).

Organic acids can penetrate the surrounding membranes of bacteria. Once inside the membrane, they will dissociate, forming H⁺ ions as a result of the neutral pH, releasing excess protons that will lower the pH. The microbe will then attempt to maintain a neutral pH by transporting excess protons outside of cells via ATP synthase, depleting its cellular energy (Fig. 3) (Biggs and Parsons, 2008; Zhou et al., 2014). The microbe is then no longer able to multiply efficiently (Adil et al., 2011). Butyric acid can have antimicrobial effects by decreasing the luminal pH and reducing bacterial colonization in the intestinal wall (Panda et al., 2009; Elnesr et al., 2020), resulting in less damage to epithelial cells (Qaisrani et al., 2015; Wu et al., 2018).

Damaging epithelial cells can disrupt the barrier between the internal and external environment of the lumen, allowing toxins to enter the circulation and increasing the susceptibility of the intestine to colonization by pathogenic bacteria (Abdelqader and Al-Fataftah, 2016). Butyric acid functions by inhibiting Salmonella colonization in the ceca due to the improvement of intestinal barrier function (Abdelqader and Al-Fataftah, 2016) and downregulates Salmonella gene expression (Liu et al., 2017).

Decreasing luminal pH is also beneficial because it stimulates the growth of beneficial bacteria and hampers the growth of pathogenic bacteria (Adil et al., 2010). Commonly, pathogen growth is likely to occur in the GIT when the lumen of the...
small intestine and ceca exceed a pH of 5.8–6.0 and the large intestine exceeds pH 6.2 (Brzóska et al., 2013). In a study by Adil et al. (2010), villus height was significantly different in the duodenum and jejunum when chicks were fed organic acids, with the highest height in chicks consuming the 3% butyric acid diet. It was suggested that the significant growth of the villi was due to a reduction in the growth of pathogenic and non-pathogenic bacteria, decreasing colonization and inflammatory responses of the intestinal mucosa (Adil et al., 2010; Silva et al., 2020).

Inflammation of the intestinal mucosa due to increased pathogenic activity can lead to necrosis of the intestinal epithelium (Brzóska et al., 2013). Crypt depth was not affected compared to broilers fed the control diet (Adil et al., 2010). A study by Hu and Guo (2007) found that supplemented sodium butyrate at 2000 mg kg\(^{-1}\) in broilers had no effect on jejunal villi height and crypt depth and significantly increased the villi height to crypt depth ratio when compared to the control. Table 1 shows the effect of different sources of butyric acid, at varying levels, on different parameters related to gut health.

### Immunity

Butyric acid has a positive impact on bird immunity through the improvement of gut eubiosis, increasing number of beneficial bacteria, limiting the colonization of pathogens, and improving gut pH, and all these factors positively reflected on the birds’ immune responses (Sikandar et al., 2017). It was found that the inclusion of butyric acid in poultry ration was associated with better cell-mediated immune responses in chickens 48 h after phytohemagglutinin-P inoculation, improved humoral immunity, and better antibody production after Newcastle disease vaccine and injection of sheep red blood cells. This resulted in better thymus and spleen weight with better thymus medulla and germinal spleen centers. It also improved the intestinal villi length and depth, and increased goblet cells containing mucins of acidic nature (Sikandar et al., 2017).

### Performance parameters

Increased absorption efficiency due to improved gut health has led to various effects on performance parameters in broilers and laying hens, depending on the forms of butyric acid used and

<table>
<thead>
<tr>
<th>Source</th>
<th>Inclusion levels (%)</th>
<th>Age (days)</th>
<th>Response</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gut morphology</td>
<td>VL CD VL/CD Others effects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blend of acetic acid, butyric acid and formic acid</td>
<td>0.3</td>
<td>49</td>
<td>+* +* +* + Epithelium thickness + Surface area</td>
<td>Maty and Hassan (2020)</td>
</tr>
<tr>
<td>Encapsulated butyric acid</td>
<td>0.05</td>
<td>21</td>
<td>+* +* +* +</td>
<td>Jazi et al. (2018)</td>
</tr>
<tr>
<td>Encapsulated sodium butyrate</td>
<td>0.1</td>
<td>11</td>
<td>+* +* NA</td>
<td>Liu et al. (2017)</td>
</tr>
<tr>
<td>Protected or unprotected butyrate</td>
<td>0.1</td>
<td>21</td>
<td>NA NA NA No effect on gut weight and retention time</td>
<td>Moquet et al. (2018)</td>
</tr>
<tr>
<td>Sodium butyrate</td>
<td>0.1</td>
<td>21/35</td>
<td>+* NA +*</td>
<td>Sikandar et al. (2017)</td>
</tr>
<tr>
<td>Encapsulated butyrate</td>
<td>0.05</td>
<td>42</td>
<td>NA NA NA + Intestinal weight* + Epithelial cell area*</td>
<td>Abdelqader and Al-Fataftah (2016)</td>
</tr>
<tr>
<td>Protected calcium butyrate</td>
<td>0.03</td>
<td>42</td>
<td>+* +* +* +</td>
<td>Kaczmarek et al. (2016)</td>
</tr>
<tr>
<td>Encapsulated butyric acid</td>
<td>0.3</td>
<td>42</td>
<td>NA NA NA No effect on surface area</td>
<td>Levy et al. (2015)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>3</td>
<td>42</td>
<td>− Crop pH + GIT length</td>
<td>Adil et al. (2011)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>3</td>
<td>42</td>
<td>+* NA</td>
<td>Adil et al. (2010)</td>
</tr>
<tr>
<td>Sodium butyrate</td>
<td>0.05</td>
<td>42</td>
<td>+* +*</td>
<td>Hu and Guo (2007)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>0.2</td>
<td>42</td>
<td>NA NA</td>
<td>Leeson et al. (2005)</td>
</tr>
<tr>
<td>Gut bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium butyrate</td>
<td>0.06</td>
<td>21</td>
<td>+ Lactobacilli; - Escherichia coli in ileum</td>
<td>Makled et al. (2019)</td>
</tr>
<tr>
<td>Encapsulated butyric acid</td>
<td>0.05</td>
<td>21</td>
<td>+ Lactobacilli and Bifidobacterium* - Salmonella and Coliform*</td>
<td>Jazi et al. (2018)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>0.1</td>
<td>42</td>
<td>- Salmonella count in caecum</td>
<td>Cerisuelo et al. (2014)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>3</td>
<td>42</td>
<td>- Caecal coliform count*</td>
<td>Adil et al. (2011)</td>
</tr>
<tr>
<td>Free or protected sodium butyrate</td>
<td>0.09</td>
<td>42</td>
<td>- Salmonella enteritidis* in crop, cecum and liver</td>
<td>Fernandez-Rubio et al. (2009)</td>
</tr>
<tr>
<td>Sodium butyrate</td>
<td>0.05</td>
<td>42</td>
<td>- Lactobacilli and Escherichia coli populations*</td>
<td>Hu and Guo (2007)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>0.16</td>
<td>42</td>
<td>- Salmonella in caecum</td>
<td>Van Immerseel et al. (2004)</td>
</tr>
</tbody>
</table>

VL, villus length; CD, crypt depth; VL/CD, villus length/crypt depth; GIT, gastrointestinal tract; NA, not affected; *significant effect (P < 0.05); +, enhanced/improve; −, reduced/lower.

---

141

https://doi.org/10.1017/S1466252321000220 Published online by Cambridge University Press
the inclusion rate. Researchers have found that butyric acid supplementation had positive effects on body weight gain (BWG) and feed conversion rate (FCR) in broilers (Leonel and Alvarez-Leite, 2012; Liu et al., 2017). Detailed data regarding the effects of butyric acid on different growth performances are presented in Table 2.

Several studies have shown that butyric acid does not significantly affect feed consumption. A significant difference in FCR and BWG was seen in favor of organic acids, suggesting better absorption and nutrient utilization than birds on the control diet (Adil et al., 2010). It was also found in this study that there were higher serum calcium and phosphorus concentrations when compared to the control (Adil et al., 2010). When researching butyric acid, there are often contradiction due to the type of diet and the forms of butyrate (calcium salt, sodium salt, glyceride, etc.) (Leonel and Alvarez-Leite, 2012; Kaczmarek et al., 2016).

In a study by Kaczmarek et al. (2016) with broilers, researchers attempted to find a ‘matrix value’ for butyrate in poultry diets to maximize its efficacy. The experiment showed that butyric acid positively affected FCR and BWG, and the addition of 0.2 g kg\(^{-1}\) of butyrate improved FCR, 0.3 g kg\(^{-1}\) improved FCR regardless of the age of birds. In comparison, 0.4 g kg\(^{-1}\) decreased feed intake (FI) and significantly increased FCR. This study indicated that the 0.3 g kg\(^{-1}\) provided produced the most positive effects compared to the control and other butyrate doses. Leeson et al. (2005), found contradictory results, when 0.2 g kg\(^{-1}\) butyrate was supplemented as a glyceride. This addition maintained the performance and carcass quality in vaccinated broilers challenged

### Table 2. Effect of various forms and levels of butyric acid supplementation on growth performance of broiler compared to control group

<table>
<thead>
<tr>
<th>Source</th>
<th>Inclusion levels (%)</th>
<th>Age (days)</th>
<th>Feed intake (%)</th>
<th>Weight gain (%)</th>
<th>FCR Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blend of acetic acid, butyric acid and formic acid*</td>
<td>0.9</td>
<td>49</td>
<td>−34.54*</td>
<td>+0.98</td>
<td>Improved (−1.09)* Maty and Hassan (2020)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>0.2</td>
<td>42</td>
<td>−1.1</td>
<td>−4.57</td>
<td>Improved (−0.08) Nari and Ghasemi (2020)</td>
</tr>
<tr>
<td>Sodium butyrate</td>
<td>0.06</td>
<td>42</td>
<td>+2.38</td>
<td>+1.57</td>
<td>Poor (+0.02) Makled et al. (2019)</td>
</tr>
<tr>
<td>Encapsulated butyric acid</td>
<td>0.05</td>
<td>21</td>
<td>−1.55*</td>
<td>−7.16*</td>
<td>Poor (+0.08) Jazi et al. (2018)</td>
</tr>
<tr>
<td>Monobutyrin</td>
<td>0.3</td>
<td>35</td>
<td>−</td>
<td>+7.17</td>
<td>Improved (−0.07) Bedford et al. (2017)</td>
</tr>
<tr>
<td>Combined monobutyrin/tributyrin</td>
<td>0.05/0.2</td>
<td></td>
<td>+9.27</td>
<td>−</td>
<td>Improved (−0.07)</td>
</tr>
<tr>
<td>Encapsulated sodium butyrate</td>
<td>0.1</td>
<td>11</td>
<td>−</td>
<td>+17.01</td>
<td>Improved (−0.42) Liu et al. (2017)</td>
</tr>
<tr>
<td>Fat-coated butyrate</td>
<td>0.1</td>
<td>21</td>
<td>−6.36</td>
<td>+1.47</td>
<td>Improved (−0.07) Moquet et al. (2018)</td>
</tr>
<tr>
<td>Sodium butyrate</td>
<td>0.1</td>
<td>35</td>
<td>−9.86*</td>
<td>+18.87*</td>
<td>Improved (−0.26) Sikandar et al. (2017)</td>
</tr>
<tr>
<td>Encapsulated butyrate</td>
<td>0.05</td>
<td>42</td>
<td>−1.64</td>
<td>+2.82</td>
<td>Improved (−0.07) Abdelqader and Al-Fataftah (2016)</td>
</tr>
<tr>
<td>Protected calcium butyrate</td>
<td>0.04</td>
<td>42</td>
<td>−2.98</td>
<td>+3.08</td>
<td>Improved (−0.08)* Kaczmarek et al. (2016)</td>
</tr>
<tr>
<td></td>
<td>0.03</td>
<td></td>
<td>+3.13</td>
<td>+9.42*</td>
<td>Improved (−0.09)*</td>
</tr>
<tr>
<td>Encapsulated sodium butyrate</td>
<td>0.025</td>
<td>42</td>
<td>−</td>
<td>+0.7</td>
<td>Poor (+0.06) Abd El-Ghany et al. (2016)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>0.25</td>
<td>42</td>
<td>+2.32</td>
<td>+5.29</td>
<td>Improved (−0.03) Dehghani-Tafti and Jahanian (2016)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>0.3</td>
<td>42</td>
<td>+8.19</td>
<td>+5.90</td>
<td>Improved (−0.09) Lakshmi and Sunder (2015)</td>
</tr>
<tr>
<td>Encapsulated butyric acid</td>
<td>0.03</td>
<td>42</td>
<td>+0.46</td>
<td>+3.15*</td>
<td>Improved (−0.04)* Levy et al. (2015)</td>
</tr>
<tr>
<td></td>
<td>0.05</td>
<td></td>
<td>−</td>
<td>+2.05*</td>
<td>Improved (−0.04)*</td>
</tr>
<tr>
<td>Encapsulated sodium butyrate</td>
<td>0.07</td>
<td>42</td>
<td>−</td>
<td>+5.7</td>
<td>Improved (−0.06) Chamba et al. (2014)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>3</td>
<td>42</td>
<td>−1.05</td>
<td>+9.41*</td>
<td>Improved (−0.21)* Adil et al. (2011)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>3</td>
<td>42</td>
<td>+0.06</td>
<td>+9.26*</td>
<td>Improved (−0.17)* Adil et al. (2010)</td>
</tr>
<tr>
<td>Sodium butyrate</td>
<td>0.2</td>
<td>42</td>
<td>+10.98*</td>
<td>+8.05*</td>
<td>Improved (−0.35)* Taherpour et al. (2009)</td>
</tr>
<tr>
<td>Butyric acid</td>
<td>0.05</td>
<td>42</td>
<td>+1.23</td>
<td>+3.03</td>
<td>Improved (−0.03) Hu and Guo (2007)</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>42</td>
<td>+0.67</td>
<td>+2.32</td>
<td>Improved (−0.03) Leeson et al. (2005)</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>42</td>
<td>−4.44</td>
<td>+0.57</td>
<td>Improved (−0.09)</td>
</tr>
</tbody>
</table>

FCR, feed conversion ratio.
*aExperimental bird was Japanese quail.
*Significant difference (P < 0.05).
with coccidia. It was also found that butyrate in the glyceride form caused FI depression similar to that of 0.4 g kg\(^{-1}\) in the Kaczmarek et al. (2016) experiment. Abdelqader and Al-Fataftah (2016) found that 0.5 g of butyric acid kg\(^{-1}\) diet recovered intestinal epithelia and improved integrity in heat-stressed broilers compared to controls.

A study by Taherpour et al. (2009) showed that broilers supplemented with butyric acid glyceride showed improved BWG compared to the control. In this study, the contradiction of these results compared to other studies was attributed to differences in preparation of the diet composition or particle size and experimental conditions. Like the studies above, FCR improved while FI was increased in favor of butyric acid glyceride. There was no significant difference in mortality in this study. Brzóska et al. (2013) suggested that the use of organic acids in the diet promotes the production of prebiotics and probiotic lactic acid bacteria in young birds.

Brzóska et al. (2013) and Zhou et al. (2014) noted that, in several studies, organic acids, including butyric acid, significantly reduced mortality when compared to controls. Finally, the performance improvement may be attributed to the role of butyric acid in the control of the intestinal barrier, supplying energy to the colonocytes, augmenting the differentiation and maturation of the intestinal cells, thus nutrient utilization, feed efficiency, and the positive immune response of birds. The impacts of adding butyric acid in poultry feed are illustrated in Fig. 7.

**Metabolizable energy and nutrient utilization**

Organic acids have been found to increase the digestibility of calcium, phosphorus, magnesium, zinc, and protein (Adil et al., 2010). Supplementation of organic acids in broiler diets enhanced serum calcium and phosphorus concentrations. These results were credited with the notion that acidic ions form a complex with minerals such as calcium and phosphorus, thereby increasing their digestibility (Table 3). Organic acids also act as substrates for intermediary metabolism (Adil et al., 2011). Butyric acid can increase the feed solubility, digestion, and nutrient absorption (Rahman et al., 2008; Leonel and Alvarez-Leite, 2012).

With fewer pathogenic bacteria, due to organic acids, there is a reduced microbial metabolic need, thereby allowing more nutrients to be available for absorption by the host. The decrease in the toxins produced by harmful bacteria can also cause an increase in energy availability and protein digestibility (Adil et al., 2010; Silva et al., 2020). Adil et al. (2011) suggested that increased protein digestibility because feeding organic acids in the diet reduces gastric pH resulting in increased pepsin activity. Pepsin proteolysis of proteins releases peptides that trigger hormones such as CCK and gastrin to be released. These hormones play a significant role in the digestion and absorption of proteins (Adil et al., 2011).

Goodarzi Boroojeni et al. (2014) noted that the effects of organic acids on digestibility were debatable due to multiple factors affecting the results. There was no significant effect found for nutrient digestibility in this study compared to the control for broilers. Kaczmarek et al. (2016) found that, 0.2, 0.3, and 0.4 g kg\(^{-1}\) of butyrate increased the AME compared to the control diet for broilers, due to the significant increase in villi height and numerically increased mucosal thickness observed in this study.

**Egg quality**

Improved egg quality can be identified as improving eggshell strength while maintaining a good egg size. Laying hens must consume the correct ratio of manganese, vitamin D, calcium, and phosphorus to produce strong eggshells. As the hen ages, mucosal cells in the duodenum have weakened villi, which begin to shorten, and absorption in the small intestine decreases, resulting in reduced eggshell quality (Sengor et al., 2007). Sengor et al. (2007) suggested that butyrate can function in maintaining the mucosa and epithelial cells. In this study, improvements in
eggshell strength and increased egg production were observed and attributed to the healing of damaged epithelial cells in addition to increased villi growth (Sengor et al., 2007; Sikandar et al., 2017).

Maintaining a high eggshell breaking strength is needed to protect the egg from penetration by pathogenic bacteria. Broken shells are a significant source of economic losses for producers (Świątkiewicz et al., 2010). The formation of a normal (not mis-shapen) eggshell requires minerals to be released from the shell gland in the right proportions, at the right time, to ensure good eggshell quality. There must be adequate absorption and metabolism of nutrients to achieve this physiologic state (Sengor et al., 2007). Butyrate has improved calcium metabolism and absorption by increasing villi growth (Rahman et al., 2008).

Sengor et al. (2007) suggested that weakness in the eggshell in older hens can be altered with butyrate, if supplemented at 285 mg kg, resulting in increased eggshell strength and decreased malformed eggs. Świątkiewicz et al. (2010) reported that one of the main concerns is a decrease in eggshell quality as the hen ages due to an increase in egg weight without an increase in the amount of calcium carbonate deposited in the shells. They found a positive effect of the organic acids on some eggshell quality parameters in older hens, probably due to their beneficial effect on calcium absorption.

It was also determined that lowering the pH of the diet can benefit eggshell quality (Świątkiewicz et al., 2010). Butyric acid and its salts have shown different results for egg quality and egg production. This difference has been attributed to the source of butyric acid, the inclusion rate, and the environmental conditions and diet composition (Soltan, 2008; Sikandar et al., 2017). Rahman et al. (2008) reported a significant increase in egg production in 67–74 weeks old hens when fed on a diet supplemented with various concentrations of organic acids, including butyric butyrate, compared to the control diet. They illustrated that the mixture of fumaric acid, salts of butyric, propionic, and lactic acids, did not affect egg weight and eggshell%. In contrast, the egg size and albumen% were increased and yolk% was decreased with dietary supplementation of organic acids.

Also, organic acids significantly increased the eggshell thickness (Rahman et al., 2008; Sunkara et al., 2011). These findings are in agreement with Soltan (2008) but contrary to the study performed by Yesilbag and Colpan (2006), using an organic acid mixture that did not include butyric acid or its salt (Rahman et al., 2008). Work is needed to improve the perception of the effects of butyric acid on egg quality and what can be done in the future to better utilize butyric acid as an antibiotic alternative.

### Osteoporosis

Osteoporosis can be described as an increased porosity and reduced bone thickness, which is a major bone-related disease that can occur when there is an increased demand for calcium from the medullary bone for the eggshell formation and maintenance of eggshell quality. This reduced thickness can result in bone breakage. In hens, osteoporosis manifests as cage layer fatigue (Webster, 2004; Khan and Iqbal, 2016). Cage layer fatigue can be identified by the inability of hen to stand or walk. These hens tend to have a willingness to eat or drink. The hen will die if cage layer fatigue is not treated. Cage layer fatigue can be classified as peracute and acute. Peracute fatigue occurs when the hen dies suddenly with no visible symptoms, and acute fatigue is when the hen experiences leg paralysis and can potentially recover with assistance (Bell and Siller, 1962). Young hens that are in peak production are most likely to develop osteoporosis.

Bell and Siller (1962) also concluded that some genetic lines of layers were more susceptible to osteoporosis than others. Medullary bone development and the end of structural bone remodeling occur simultaneously with the beginning of hen sexual maturity. The medullary bone stores large amounts of calcium, which is released later in the formation of the eggshell when calcium is absent or cannot be readily absorbed from the digestive tract. Osteoporosis will occur if not enough calcium is absorbed from the intestine to remodel the structural bone after it provides calcium to the medullary bone (Webster, 2004; Khan and Iqbal, 2016).

Studies done in ovariectomized rats suggest that organic acids can prevent osteoporosis by reducing the amount of bone turnover due to lowering gut pH and improving calcium absorption, solubility, and utilization, and could further improve osteoporosis and egg quality (Kamal and Ragaa, 2014). It has also been suggested that osteoporosis cannot be avoided in the caged modern hybrid laying hen due to confinement and its high egg production (Webster, 2004). This situation necessitates the use of additives to mitigate adverse effects on birth, health, and production.
Conclusion

Butyric acid has enhanced nutrient/energy utilization, gut health, and production performance in poultry, by improving mineral absorption, immunity, and reducing the populations and products of pathogenic bacteria. Our findings suggest that the high stability of tributyric in the feed and stomach should increase the efficacy of butyric acid, thereby improving the efficiency of gut health and absorption of nutrients, leading to improved performance. However, further investigations are required to explore the effect of butyric acid and its salts on poultry immunity.

Conflict of interest. None.

References


Lakshmi KV and Sunder GS (2015) Supplementation of propionic acid (PA), butyric acid (BA) or antibiotic (AB) in diets and their influence on broiler performance, carcass parameters and immune response. *IJSR* 4, 1002–1006.


Molnár A, Maertens L, Ampe B, Buyse J, Zoons J and Delezie E
Raza M, Biswas A, Mir NA and Mandal AB
Rahman MS, Howlider MAR, Mahiuddin M and Rahman MM
Panda AK, Rao SV, Raju MVLN and Sunder GS
Makled MN, Abouelezz KFM, Gad-Elkareem AEG and Sayed AM
Nari N and Ghasemi HA
Mahdavi R and Torki M