



A Meta-Analysis of the Effect of Antimicrobial Peptide Purity on the Growth Performance, Dry Matter Digestibility, and Intestinal Morphology of Broiler

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Abstract | This meta-analysis aimed to systematically evaluate the effect of the administration of antimicrobial (AMP) both in form of single AMP (SAP) and composite AMP (CAP) on the growth performance, dry matter digestibility, and intestinal morphology of broiler. Data tabulation only involved credible international journals as indicated by Scopus indexed, equipped with doi number, and ranked in the scientific journal rankings cluster. There were 68 experiments with 210 datum collected from 33 literatures. The data were analyzed using a linear mixed model. The differences between the experiments were noted as random effects, while the purity of AMP was determined as fixed effects. The AMP purity significantly ($P < 0.05$) improved the several observed variables, such as body weight, average daily gain, feed conversion ratio, and dry matter digestibility both in the starter period, finisher period, and total period of broiler. It also significantly improved intestinal morphology in the duodenum (alike villus height), jejunum (alike crypt depth), and ileum (like villus height and crypt depth). Compared to CAP, SAP supported better performance on most of observed variables. In short, the AMP could bring positive effect on the growth performance, dry matter digestibility, and intestinal morphology of broiler not only in starter, finisher but also in total of period of broiler. Compared to CAP, the administration of SAP showed a greater performance on broiler.

Keywords | Broiler, Dry matter digestibility, Meta-analysis, Intestinal morphology, Antimicrobial peptide

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INTRODUCTION

The limitation or even prohibition of the use of the antibiotic growth promoter (AGP) has been implemented in the European Union (FAO and IFIF, 2010; Anom, 2019). In similar, Indonesia government have made certain regulation to ban the use of several antibiotic growth promoters. Based on the Minister of Agriculture regulation number 14 on 2017, several AGPs such as avoparcin, beta

1-adrenergic agonist, beta 2-adrenergic agonist, carbadox, carbon tetrachloride, flavomycin, ipronidazole, and roxarsone have been banned as feed additives because of resistant effect (Ministry of Agriculture, 2017). *Escherichia coli* and *Salmonella* spp. reported to resistance to certain antibiotics, namely ciprofloxacin, cephalosporins, ampicillin, and trimoxazole during the period 2004 to 2014 in Tanzania (Gasparly et al., 2017). However, this prohibition caused the disruption on the broiler growth performance usage.

Previous study by Crisol-Martínez et al. (2017) reported that the use of the antibiotic growth promoter, such zinc bacitracin, significantly improved the feed conversion ratio. Therefore, an alternative antibiotic growth promoter is needed especially those with resistant effect, no residues in broiler-derived products and highly effective to kill certain pathogenic microbes that have been resistant to common antibiotics (Yi et al., 2014; Park et al., 2015; Xiao et al., 2015; Gadde et al., 2017).

Antimicrobial peptide (AMP) is a peptide derived from natural materials (vertebrate animal tissue, plants, prokaryotic organisms, and insects) and recombinant products. AMP has a broad spectrum of microbial inhibitory activity (Mylonakis et al., 2016). Based on *in vitro* studies, AMP show various characteristics i.e. resistance to high temperatures (100° C for 15 minutes), show antioxidant, anticancer and germicides activity against various types of pathogenic microbes including gram positive and gram negative bacteria, fungi, yeasts, parasites, and virus (Li et al., 2012; Bahar and Ren, 2013). As a natural product that can synthesize from organic materials, AMP has easily degraded and has not resistant effect (Hassan et al., 2012).

The biological function of AMP as an antimicrobial compound is to inhibit pathogenic microbial activity through the membrane transport system and intercellular activity (Yeaman and Yount, 2003). Inhibition of the membrane transport system is the mechanism of inhibiting cell nutrient transport through the model of barrel-stave, toroidal, carpet, and aggregate channel (Xiao et al., 2015). Inhibition of intercellular activity can be varied in form of the inhibition of DNA, RNA, and protein synthesis, and inducing the formation of reactive oxygen species (ROS). ROS can remove the electron transport mechanism from the mitochondria so that pathogenic bacteria will decrease their growth rate due to lack of energy (Tang et al., 2012). Based on its purity level, AMP is divided into two groups, namely single AMP (SAP) and composite AMP (CAP). The SAP is derived from purification of natural ingredients or recombinant products with a purity level for more than 90 or 95% (Wang et al., 2006; Cao et al., 2012). The SAPs, such as cecropin and lysozyme were reported to have positive effects, such as (i) the improvement of broiler growth performances, (ii) the reduction of the number of pathogenic bacteria (coliform and *Escherichia coli*) in the ileum and cecum, and (iii) the increase of mucosal immunity at starter and finisher period (Zhang et al., 2010; Wen and He, 2012; Choi et al., 2013a; Choi et al., 2013b). In addition, other types of SAP (such as cecropin, defensin, and scorpion toxin) show germicidal properties against antibiotic-resistant bacteria such as *Staphylococcus aureus*, *Salmonella* spp. and *Escherichia coli* (Yeaman and Yount, 2003; Cao et al., 2012; Park and Yoe, 2017a; Park and Yoe,

2017b). In opposite, the CAP is the mixture of several SAPs or derivative products of functional proteins (Karimzadeh et al., 2016). The CAP itself has a purity of less than 50% and sometime its AMP component is not clearly identified. The mixed AMP, such as soybean bioactive peptide and porcine mucosa peptide show a positive effect on broiler growth performance, immunity and gastrointestinal health of broiler (Mateos et al., 2014; Beski et al., 2016; Abdollahi et al., 2017).

Other studies, however, no report to systematically compared the used of SAP and CAP on broiler. Thus, this meta-analysis aimed to comprehensively evaluate the effect of antimicrobial peptide purity on growth performance, dry matter digestibility, and intestinal morphology at starter, finisher and total period of broiler chickens.

MATERIALS AND METHODS

REFERENCE CHARACTERISTICS

This meta-analysis article used data sources from various regions of the world. Therefore, the regional difference factor was used as a weighting factor in the mathematical model. The condition (e.g., temperature, light, and humidity) of the rearing cage was controlled. The temperature was regulated based on the growing period. Warmer was used in the first week. The references reported that (i) the rearing cage had met the code of conduct for research with animal subjects, (ii) AMP was given to broilers by mixing it into the feed, and (iii) the use of other AGPs in feed was not carried out.

DATA TABULATION

Literatures that contained information on the effect of addition of antimicrobial peptide (mg per Kg of feed) on growth performance, dry matter digestibility, and broiler intestinal morphology were determined as targeted literatures. The collection of literature was carried out using the search engines namely “google scholar” and “science direct”. The keywords used during the literature searching were “antimicrobial peptide”, “cecropin”, “lactoferrin”, “lysozyme”, “broiler”, “growth performance”, “dry matter digestibility”, and “intestinal morphology”. Initially, there were 43 literatures that met the criteria to be further evaluated. The criteria used was the abstract of paper should include the AMP dosage and the results in form of broiler growth performance, dry matter digestibility, and intestinal morphology. The evaluation was continued to the entire paper content. Finally, there were 68 experiments that consisted of 210 datums had been collected from 41 literatures.

The result of data collection could be seen in Table 1. Broiler maintenance categories were divided into three periods,

Table 1: Literature involved in the meta-analysis of the effect of antimicrobial peptide purity on the growth performance, dry matter digestibility, and intestinal morphology of broiler

| No. | Reference | AMP | Purity | Level ¹⁾ | Breed | Sex | Starter | Finisher | Region | Cage ²⁾ |
|-----|---------------------------|----------------------------|--------|---------------------|-------------|--------|---------|----------|-----------|--------------------|
| 1. | Abdel-Latif et al. (2017) | Lisozyme | SAP | 0 - 120 | ROSS 308 | Both | 1-21 | 22-35 | Africa | Controlled |
| 2. | Abdollahi et al. (2017) | Soybean bioactive peptide | CAP | 0 - 6000 | ROSS 308 | Male | 1-21 | - | Australia | Controlled |
| 3. | Abdollahi et al. (2018) | Soybean bioactive peptide | CAP | 0 - 6000 | ROSS 308 | Male | 1-21 | 22-42 | Australia | Controlled |
| 4. | Aguirre et al. (2015) | Bovine lactoferrin | SAP | 0 - 520 | Cobb 500 | Both | 8-28 | 29-42 | Asia | Controlled |
| 5. | Ali and Mohnanny (2014) | Bee venom | SAP | 0 - 1.5 | ROSS 308 | Both | 1-21 | 22-42 | Africa | - |
| 6. | Bai et al. (2019) | Cecropin | SAP | 0 - 600 | Arbor Acres | Both | 1-21 | 22-42 | Asia | Controlled |
| 7. | Bao et al. (2009) | Porcine intestinal peptide | CAP | 0 - 200 | Arbor Acres | Male | 1-21 | 22-42 | Asia | Controlled |
| 8. | Beski et al. (2016) | Porcine plasma | CAP | 0 - 20000 | ROSS 308 | Male | 1-24 | 25-35 | Australia | Controlled |
| 9. | Choi et al. (2013a) | AMP – A3 | SAP | 0 - 90 | ROSS 308 | Both | 1-21 | 22-35 | Asia | Controlled |
| 10. | Choi et al. (2013b) | AMP – P5 | SAP | 0 - 60 | ROSS 308 | Both | 1-21 | 22-35 | Asia | Controlled |
| 11. | Daneshmand et al. (2019) | Lactoferrin | SAP | 0 - 20 | Cobb 500 | Male | 1-10 | 11-24 | Asia | Controlled |
| 12. | Daneshmand et al. (2019) | Camel lactoferrin | SAP | 0 - 20 | Cobb 500 | Male | 1-22 | - | Asia | Controlled |
| 13. | Enany et al. (2017) | Lactoferrin | SAP | 0 - 250 | Hubbard | Both | - | - | Africa | - |
| 14. | Frikha et al. (2014) | Porcine mucosa peptide | CAP | 0 - 75000 | ROSS 308 | Male | 1-15 | 16-22 | Europe | Controlled |
| 15. | Geier et al. (2011) | Bovine lactoferrin | SAP | 0 - 500 | Cobb 500 | Male | 1-24 | 25-32 | Australia | Controlled |
| 16. | Gong et al. (2017) | Lisozyme | SAP | 0 - 100 | ROSS 308 | Male | 1-24 | 25-35 | America | Controlled |
| 17. | Han et al. (2010) | Bee venom | SAP | 0 - 1 | Arbor Acres | Both | 1-28 | - | Asia | Controlled |
| 18. | Hu et al. (2010) | Glucagon-like peptide | SAP | 0 - 0.33 | Arbor Acres | Both | 1-21 | - | Asia | Controlled |
| 19. | Humphrey et al. (2002) | Lactoferrin | SAP | 0 - 5000 | Cobb 500 | Male | 1-19 | - | America | Controlled |
| 20. | Jiang et al. (2009) | Soybean bioactive peptide | SAP | 0 - 200 | Arbor Acres | Both | 1-28 | 29-49 | Asia | Controlled |
| 21. | Józefiak et al. (2018) | Insect peptide | CAP | 0 - 2000 | ROSS 308 | Female | 1-21 | 22-41 | Europe | Controlled |
| 22. | Karimzadeh et al. (2016) | Canola bioactive peptide | CAP | 0 - 250 | ROSS 308 | Male | 1-28 | 29-42 | Asia | Controlled |
| 23. | Karimzadeh et al. (2017b) | Antimicrobial peptide | CAP | 0 - 250 | Unknown | Both | 1-10 | 11-28 | Asia | Controlled |
| 24. | Karimzadeh et al. (2017b) | Canola bioactive peptide | CAP | 0 - 250 | ROSS 308 | Male | 1-28 | 29-42 | Asia | Controlled |

| | | | | | | | | | | |
|-----|-------------------------|----------------------------|-----|-----------|-------------|------|-------|-------|-----------|------------|
| 25. | Kim et al. (2018) | Bee venom | SAP | 0 - 0.5 | ROSS 308 | Male | 1-21 | - | Asia | Controlled |
| 26. | King et al. (2005) | Bovine colostrum | CAP | 0 - 50000 | ROSS 308 | Male | 1-14 | 14-35 | Australia | Controlled |
| 27. | Liu et al. (2010) | Lisozyme | SAP | 0 - 40 | Arbor Acres | Male | 1-14 | 15-28 | Asia | Controlled |
| 28. | Ma et al. (2020) | Plectasin | SAP | 0 - 200 | Arbor Acres | Male | 1-21 | 22-42 | Asia | Controlled |
| 29. | Mateos et al. (2014) | Porcine mucosa peptide | CAP | 0 - 25000 | ROSS 308 | Both | 1-21 | 22-32 | Europe | Controlled |
| 30. | Oblakova et al. (2015) | Natsim | SAP | 0 - 300 | ROSS 308 | Male | 1-21 | 22-49 | Europe | Controlled |
| 31. | Ohh et al. (2009) | Potato protein | CAP | 0 - 7500 | ROSS 308 | Male | 1-21 | 22-42 | Asia | Controlled |
| 32. | Ohh et al. (2010) | Potato protein | CAP | 0 - 7500 | ROSS 308 | Both | 1-21 | 22-42 | Asia | Controlled |
| 33. | Osho et al. (2019) | Soybean bioactive peptide | CAP | 0 - 5000 | Cobb 500 | Male | 1-22 | - | America | Controlled |
| 34. | Salavati et al. (2020) | Sesame bioactive peptide | SAP | 0 - 150 | ROSS 308 | Both | 1-24 | 25-35 | Asia | Controlled |
| 35. | Torki et al. (2018) | Lisozyme | SAP | 0 - 40 | ROSS 308 | Male | 14-28 | 29-33 | Europe | Controlled |
| 36. | Wallace and Yang (2010) | Soybean bioactive peptide | CAP | 0 - 5000 | Unknown | Male | 1-21 | - | Asia | Controlled |
| 37. | Wang et al. (2009) | Porcine intestinal peptide | CAP | 0 - 0.1 | Lohman | Both | - | - | Asia | Controlled |
| 38. | Wang et al. (2015) | Sublancin | SAP | 0 - 11.52 | Arbor Acres | Both | 1-21 | 22-28 | Asia | Controlled |
| 39. | Wang et al. (2020) | Microcin J28 | SAP | 0 - 1 | Arbor Acres | Male | 1-21 | 22-42 | Asia | Controlled |
| 40. | Wen and He (2012) | Cecropin A | SAP | 0 - 8 | Lingnan | Male | 14-28 | 29-42 | Asia | Controlled |
| 41. | Zhang et al. (2010) | Lisozyme | SAP | 0 - 200 | Cobb 500 | Male | 1-28 | - | America | Controlled |

AMP, Antimicrobial peptide; No., Number of studys; ¹Unit of antimicrobial peptide is mg per kg of feed; ²Controlled environment (e.g., temperature, light, and humidity) of rearing period.

namely: starter period (from the 1st to 21st days) and finisher period (from 21st to 42nd days) and the total period (from the 1st to 42nd days). The observed variables were broiler growth performance, including body weight (g), average daily gain or ADG (g per head per day), average daily feed intake or ADI (g per head per day), feed conversion ratio or FCR, and dry matter digestibility (%). Also, intestinal morphology in the duodenum, jejunum, and ileum such as villus height and crypt depth (µm).

MODELLING AND DATA ANALYSIS

The R software version 3.6.3 with the addition of the “nlme” and “tidyverse” packages was used for modeling and analysis (Pinheiro et al., 2020; R Core Team, 2020). The method used for present meta-analysis was the maxim likelihood model (LMM). The difference in the experiment was determined as random effects and the purity of antimicrobial

peptide was noted as fixed effects (St-Pierre, 2001). The statistical model had a P-value and whenever the P-value was less than or equal to 0.05, it meant significant. Also, Akaike information criteria (AIC) and root mean square error (RMSE) were used to evaluate the statistical model (Chai and Draxler, 2014).

$$Y_{ij} = \beta_0 + \beta_1 AMP_{ij} + Experiment_i + Experiment_i AMP_{ij} + e_{ij}$$

Notes: linear mixed model, fixed effect = $\beta_0 + \beta_1 AMP_{ij}$, random effect = $Experiment_i + Experiment_i AMP_{ij}$, Y_{ij} = fixed variable, β_0 = the value when the difference in AMP purity intersects the Y-axis for all combinations of random effect, β_1 = specific coefficient of AMP, AMP_{ij} = the differences of AMP purity on random effect, $Experiment_i$ = experiment number-i, e_{ij} = error model.

Table 2: The effect of antimicrobial peptide purity on the growth performance, dry matter digestibility, and intestinal morphology of broiler

| No. | Variable | N | Antimicrobial peptide | | | P-value |
|-----------------|------------------------------|-----|-----------------------|---------------------|---------------------|---------|
| | | | Control | SAP | CAP | |
| 1. | Level ¹⁾ | | 0 | 249 | 17,879 | |
| Starter period | | | | | | |
| 2. | Body weight (gram) | 155 | 782 ^a | 792.33 ^a | 884 ^b | <0.001 |
| 3. | ADG (gram/head/day) | 155 | 36.2 ^a | 38.06 ^b | 36.6 ^b | <0.001 |
| 4. | ADI (gram/head/day) | 159 | 52.5 | 51.69 | 53 | 0.172 |
| 5. | Feed conversion ratio | 159 | 1.47 ^b | 1.39 ^a | 1.48 ^b | <0.001 |
| 6. | Dry matter digestibility (%) | 31 | 71.6 ^a | 72.81 ^{ab} | 77.8 ^b | 0.002 |
| Finisher period | | | | | | |
| 7. | Body weight (gram) | 123 | 2,221 ^a | 2,535 ^b | 2,093 ^a | <0.001 |
| 8. | ADG (gram/head/day) | 123 | 77 ^{ab} | 86.3 ^b | 73.9 ^a | <0.001 |
| 9. | ADI (gram/head/day) | 123 | 146 ^a | 151.7 ^b | 149 ^{ab} | 0.004 |
| 10. | Feed conversion ratio | 123 | 1.9 ^a | 1.76 ^a | 2.02 ^b | <0.001 |
| 11. | Dry matter digestibility (%) | 19 | 73.6 | 75.9 | 73.6 | 0.334 |
| Total period | | | | | | |
| 12. | Body weight (gram) | 174 | 1,816 ^a | 2,019 ^b | 1,867 ^{ab} | <0.001 |
| 13. | ADG (gram/head/day) | 174 | 55.1 ^a | 58.8 ^b | 56.2 ^a | <0.001 |
| 14. | ADI (gram/head/day) | 174 | 95.6 ^b | 93.3 ^a | 99.1 ^b | 0.001 |
| 15. | Feed conversion ratio | 174 | 1.77 ^b | 1.58 ^a | 1.77 ^b | <0.001 |
| 16. | Mortality (%) | 23 | 4.38 ^b | 3.21 ^{ab} | 2.95 ^a | 0.008 |
| Duodenum | | | | | | |
| 17. | Villus height (µm) | 60 | 1,120 ^a | 1,504 ^b | 1,137 ^{ab} | <0.001 |
| 18. | Crypt depth (µm) | 51 | 215 | 181 | 211 | 0.249 |
| Jejunum | | | | | | |
| 19. | Villus height (µm) | 54 | 938 | 1,005 | 1,519 | 0.224 |
| 20. | Crypt depth (µm) | 49 | 197 ^{ab} | 120 ^a | 234 ^b | 0.036 |
| Ileum | | | | | | |
| 21. | Villus height (µm) | 38 | 600 ^a | 612 ^a | 846 ^b | 0.007 |
| 22. | Crypt depth (µm) | 34 | 159 ^b | 111 ^a | 150 ^{ab} | 0.002 |

Feed conversion ratio is the ratio between ADI and ADG; ADI, average daily intake; N, number of data; ADG, average daily gain; Superscript in the same row means a significant difference (P<0.05). ¹⁾Average antimicrobial peptide level added (mg per kg of feed).

RESULT AND DISCUSSION

Although there was difference in term of purity level, both SAP and CAP were able to improve broiler growth performance and dry matter digestibility in all periods as compared to controls (Table 2). In starter period, AMP purity level significantly (P <0.05) improved broiler body weight, ADG, FCR, and dry matter digestibility. During starter period, the broiler body weight, FCR, and dry matter digestibility on SAP treatment were significantly (P <0.05) lower than those treated with CAP. In finisher period, AMP purity level also significantly (P <0.05) improved body weight, ADG, ADI, and FCR. However, dry matter digestibility of SAP and CAP were not significant-

ly different (P> 0.05) than control. In the finisher period, the broiler body weight, ADG, and ADI after treated with SAP tended to be higher than that of CAP and the opposite result found in FCR variables, i.e significantly (P <0.05) lower. In the total period, the AMP purity level significantly (P <0.05) increase broiler body weight, ADG, ADI, and FCR, while the mortality was significantly reduced rather than controls. The broiler body weight and ADG was higher in SAP, while ADI and FCR were significantly lower (P <0.05) in SAP than CAP. Broiler intestinal morphology treated with SAP and CAP were better than controls. In duodenum, the SAP treatment produced a higher villus height than controls (P <0.05) and CAP. In the jejunum, the crypt depth of SAP treatment was signif-

Table 3: The regression equation of the effect of antimicrobial peptide purity on the growth performance, dry matter digestibility, and intestinal morphology of broiler

| No. | Variable | N | Variable estimates | | | | Model estimates | |
|-----------------|------------------------------|-----|--------------------|---------|-------|----------|-----------------|-------------------|
| | | | Int. | SE Int. | Slope | SE Slope | RMSE | AIC ¹⁾ |
| Starter period | | | | | | | | |
| 1. | Body weight (gram) | 155 | 782 | 41.4 | 50.2 | 12.3 | 0.834 | 1988 |
| 2. | ADG (gram/head/day) | 155 | 36.4 | 1.51 | 2.25 | 0.62 | 0.835 | 898 |
| 3. | ADI (gram/head/day) | 159 | 52.5 | 1.99 | -0.86 | 0.59 | 0.831 | 943 |
| 4. | Feed conversion ratio | 159 | 1.47 | 0.02 | -0.11 | 0.02 | 0.836 | -370 |
| 5. | Dry matter digestibility (%) | 31 | 71.6 | 1.45 | 4.28 | 1.59 | 0.866 | 196 |
| Finisher period | | | | | | | | |
| 6. | Body weight (gram) | 123 | 2213 | 67.4 | 134.3 | 27.2 | 0.834 | 1703 |
| 7. | ADG (gram/head/day) | 123 | 76.6 | 2.32 | 5.44 | 1.07 | 0.834 | 805 |
| 8. | ADI (gram/head/day) | 123 | 146 | 4.24 | 2.47 | 1.52 | 0.833 | 922 |
| 9. | Feed conversion ratio | 123 | 1.97 | 0.05 | -0.15 | 0.04 | 0.835 | -161 |
| 10. | Dry matter digestibility (%) | 19 | 74.2 | 0.95 | 1.97 | 1.82 | 0.882 | 104 |
| Total period | | | | | | | | |
| 11. | Body weight (gram) | 174 | 1817 | 92 | 138 | 24.2 | 0.829 | 2403 |
| 12. | ADG (gram/head/day) | 174 | 55.3 | 3.01 | 4.29 | 0.66 | 0.830 | 1099 |
| 13. | ADI (gram/head/day) | 174 | 97.8 | 5.75 | 1.1 | 0.71 | 0.831 | 1179 |
| 14. | Feed conversion ratio | 174 | 1.79 | 0.04 | -0.13 | 0.02 | 0.833 | -298 |
| 15. | Mortality (%) | 23 | 4.38 | 2.85 | -8.2 | 3.87 | 0.862 | 211 |
| Duodenum | | | | | | | | |
| 16. | Villus height (µm) | 60 | 1120 | 95.5 | 192 | 64 | 0.833 | 890 |
| 17. | Crypt depth (µm) | 51 | 216 | 34.6 | -9.63 | 16.7 | 0.842 | 599 |
| Jejunum | | | | | | | | |
| 18. | Villus height (µm) | 54 | 938 | 294 | 720 | 788 | 0.988 | 906 |
| 19. | Crypt depth (µm) | 49 | 198 | 28.1 | -14.5 | 10.3 | 0.851 | 439 |
| Ileum | | | | | | | | |
| 20. | Villus height (µm) | 38 | 600 | 92.8 | 105 | 64.9 | 0.856 | 609 |
| 21. | Crypt depth (µm) | 34 | 159 | 16.9 | -18.7 | 17.5 | 0.870 | 424 |

ADG, average daily gain; ADI, average daily intake; AIC, akaike information criterion; Int., intercept; N, number of data; RMSE, root mean square errors; SE, standard error; ¹⁾AIC is an estimator of the accuracy of mathematical model.

icantly ($P < 0.05$) lower than control and CAP. The AMP purity level did not affect the villus height in the jejunum. In the ileum, the villus height and crypt depth on CAP treatment were significantly ($P < 0.05$) better rather than controls. Meanwhile, the SAP treatment had a significantly lower crypt depth ($P < 0.05$) than control.

AMP was reported to have germicidal activity against pathogens originating from bacteria (both gram positive and gram negative bacteria), fungi, yeast, endoparasites, and viruses (Yi et al., 2014; Xiao et al., 2015; Wang et al., 2016; Gadde et al., 2017). Previous study by Choi et al. (2013b) reported that the AMP-P5 (SAP) could increase the ADG and FCR of broiler either in starter and finisher period. Other positive effects were the improvement of

broiler growth performance and the decline of pathogenic bacteria in digestive tract as the effect of AMP-A3 (SAP) administration (Choi et al., 2013a). The best dosage of AMP-P5 and AMP-A3 to improve growth performance, nutrient digestibility, intestinal morphology, and coliform reduction were 60 and 90 mg per Kg of feed, respectively. Other studies by Abdel-Latif et al. (2017) and Gong et al. (2017) also displayed similar pattern of finding.

The addition of CAP into the broiler feed could bring positive effect on growth performance and intestinal morphology (King et al., 2005; Wallace and Yang, 2010). Previous study by Ohh et al. (2009) stated that CAP derived from potato contained protein for about 7500 mg per Kg of feed and it resulted the best effect on growth perfor-

CONCLUSION

mance and nutrient digestibility at starter and finisher period of broiler. In addition, the CAP derived from porcine mucosa peptide as much as 2500 up to 5000 mg per Kg of feed could increase broiler growth performance during starter period (Frikha et al., 2014).

Based on AMP levels added (Table 2), SAP was lower (e.g., 249 mg per Kg of feed) compared to CAP (e.g., 17,879 mg per Kg of feed). Consequently, SAP was better than CAP and it was highly recommended as an alternative to antibiotic growth promoter. The addition of a low levels of AMP would not affect the nutrient composition of the feed. The finding of this meta-analysis highlighted that the capability of SAP was 50 to 100 times greater than CAP. It might be related to the purity level of AMP used. The purity of SAP was 95% or more (Haeberli et al., 2000; Cao et al., 2012; Wei et al., 2015), while the purity of CAP was only 54.9% (Karimzadeh et al., 2016). Those finding confirmed that the SAP was purer than CAP. Moreover, the CAP also displayed a low antimicrobial activity (Karimzadeh et al., 2016) so that there was a need to increase the CAP dosage to compete with SAP.

There were special techniques required to obtain SAP, such as DNA recombinant, cloning, and staggered isolation using a specific instrument (Park et al., 2015; Park and Yoe, 2017a). Meanwhile, CAP could be produced through hydrolysis process by using protease (Karimzadeh et al., 2017a; Osho et al., 2019). Both SAP and CAP displayed positive effect on growth performance and dry matter digestibility of broiler at starter, finisher and total period. Previous studies confirmed that pure AMP in form of AMP-A3 and AMP-P5 (90 and 60 mg per Kg of feed, respectively) resulted the highest value of villus height and villus height to crypt depth ratio in the duodenum, jejunum and ileum (Choi et al., 2013a; Choi et al., 2013b). In addition, Abdollahi et al. (2017) mixed AMP derived from soybeans as much as 300 mg per Kg of feed also significantly increased the villus height.

Therefore, there was better composition of microbes in the digestive tract, as indicated by the proportion of *Lactobacillus* spp. in the ileum of healthy broilers for about 83% (Apajalahti and Vienola, 2016). In addition, these microbes also produced certain organic acids that could trigger the energy availability to epithelial cells (Krajmalnik-Brown et al., 2012; Shang et al., 2018). Energy availability increased cell metabolism so that intestinal morphology could be maintained (Aliakbarpour et al., 2012). Additionally, the lactic acid bacteria was reported to be able to increase mucosa thickness (Aliakbarpour et al., 2012). Therefore, it was proven that SAP and CAP improved the intestinal morphology of broilers.

This meta-analysis concluded that the addition of AMP could improve the growth performance of broiler chickens as indicated by body weight, average daily gain, dry matter digestibility and intestinal morphology both in the starter period, finisher period, and total period of broiler. AMP constantly reduced FCR value in starter and finisher periods. Compared to CAP, the administration of SAP showed a greater performance on broiler.

CONFLICT OF INTEREST

We declare no competing interests.

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AUTHORS CONTRIBUTION

Conceptualization: N and JN. Data curation: MMS. Perform meta-analysis and interpretation data: MMS and AJ. Writing manuscript: MMS and ATW. Review and editing: AJ and ATW.

(Note: N as Nahrowi, JN as Jun Nomura, MMS as Mohammad Miftakhus Sholikin, AJ as Anuraga Jayanegara, and ATW as Aris Tri Wahyudi)

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