3. Review 3:

The study investigated effects of additive antimicrobial peptides on broiler chicken performance, nutrient digestibility, and serum metabolites using a meta-analysis on. The study is very interesting, but there are the following comment and concern.

(1) Please re-analyze the effectiveness of AMPs in terms of i) each feeding stage, such as, starter, grower, and finisher, ii) with or without synthetic AGPs, or iii) sex, if theoretically possible.
- control 0 mg Kg^{-1} of feed
- antibiotic 40.9 mg Kg^{-1} of feed
- antimicrobial peptide 145 mg Kg^{-1} of feed

(2) Is it possible to suggest optimal dose of AMPs although the titer and MIC?

(3) Introduction
- Add what meta-analysis is and introduce the previous investigation using this method.

(4) Methods
- Line 62-65; Add "peer-reviewed publications" somewhere in terms of scientific/academic reliability and accuracy.

B. Rivewer response:

3. Response of reviewer 3:

Thank you for the suggestions given by reviewer 3. Here we attach the improvements according to the suggestions from reviewer 3.

(1) We have done a re-analysis by adding the ratio of AGPs and AMPs in each growth phase according to points one (i) and two (ii) (Table 5). Meanwhile, the third point (iii) cannot be done because of the sufficiency of the data that does not fulfill the analysis.

Table 5. Effect of antibiotic growth promoters and antimicrobial peptides on growth performance, digestibility and metabolizable energy, blood serum, and small intestine morphology of broilers

Response variables	Unit	Antibiotic vs AMP			p-value
		Control	AGPs	AMPs	
Average dosage	mg Kg^{-1} of diet	0	40.9	145	
Growth performance in starter phases					
Body weight	gram	905^{a}	$1,069^{b}$	895^{ab}	0.005
Average daily gain	$gh^{-1}d^{-1}$	38.2^{a}	44.5^{b}	37.3^{a}	0.003
Daily feed intake	$gh^{-1}d^{-1}$	57.7^{a}	65.7^{b}	54.9^{a}	0.011
Feed conversion ratio	no unit	1.55^{b}	1.55^{ab}	1.5^{a}	0.000
Digestibility and metabolizable energy in starter phases					
Dry matter	%	76.5^{a}	79.4^{b}	77.7^{a}	0.002
Crude protein	%	64.7	72.2	63.8	0.061
Apparent metabolizable energy	kcal kg^{-1}	2,741	2,776	2,919	0.180
Blood serum in starter phases					
Total protein	g dL^{-1}	4.54	-	4.53	0.705
Albumin	g dL^{-1}	3.4	-	3.09	0.062

Response variables	Unit	Antibiotic vs AMP			p-value
		Control	AGPs	AMPs	
Globulin	g dL^{-1}	1.69	-	1.95	0.283
AGR	no unit	2.65	-	1.73	0.047
Cholesterol	mg dL^{-1}	124	-	112	0.132
Triacylglycerol	mg dL^{-1}	88	-	74.6	0.224
Growth performance in finisher phases					
Body weight	gram	$2,092^{a}$	$2,076^{ab}$	$2,096^{b}$	<0.001
Average daily gain	$gh^{-1}d^{-1}$	70^{a}	71.5^{b}	72.4^{b}	<0.001
Daily feed intake	$gh^{-1}d^{-1}$	150	146	148	0.99
Feed conversion ratio	no unit	2.18^{b}	2.07^{a}	2.05^{a}	<0.001
Digestibility and metabolizable energy in finisher phases					
Dry matter	%	73.9	76.6	74.5	0.312
Crude fat	%	79.2	-	80.4	0.737
Blood serum in finisher phases					
Total protein	g dL^{-1}	21.4	-	18.6	0.677
Albumin	g dL^{-1}	8.13	-	7.04	0.114
Globulin	g dL^{-1}	2.95	-	2.90	0.62
AGR	no unit	2.15	-	1.81	0.153
Cholesterol	mg dL^{-1}	106	-	97.1	0.187
Triacylglycerol	mg dL^{-1}	87.6	-	81.4	0.555
Creatinine	mg dL^{-1}	0.37^{b}	-	0.33^{a}	0.016
Uric acid	mg dL^{-1}	7.34^{b}	-	6.19^{a}	0.02
Growth performance in all phases					
Body weight	gram	$1,738^{a}$	$1,802^{b}$	$1,913^{b}$	<0.001
Average daily gain	$gh^{-1}d^{-1}$	53.9^{a}	49.7^{b}	57.2^{b}	<0.001
Daily feed intake	$gh^{-1}d^{-1}$	102	$85.^{3}$	103	0.638
Feed conversion ratio	no unit	1.92^{b}	1.81^{a}	1.82^{a}	<0.001
Mortality rate	%	16.6^{b}	9.40^{a}	5.07^{a}	0.001
Small intestine morphology in duodenum					
Mucosa thickness	µm	620^{a}	-	780^{b}	0.003
Villus height	µm	$1,000^{a}$	$1,425^{ab}$	$1,107^{b}$	<0.001
Crypt depth	µm	234	345	212	0.074

Response variables	Unit	Antibiotic vs AMP			p-value
		Control	AGPs	AMPs	
RVCD	no unit	5.58[a]	4.93[ab]	6.30[ab]	0.003
Small intestine morphology in jejunum					
Villus height	µm	804	1,138	1,406	0.508
Crypt depth	µm	210	282	209	0.09
RVCD	no unit	4.71	4.13	8.06	0.492
Small intestine morphology in ileum					
Villus height	µm	643	665	780	0.054
Crypt depth	µm	159	210	143	0.386
RVCD	no unit	4.12	3.05	5.37	0.116

Note : AGPs = antibiotic growth promoters; AGR = albumin-globulin ratio; AMPs = antimicrobial peptides; RVCD = ratio of villus height to crypt depth.
[a,b] Different superscript letters in the same row are significantly different with a level of $p < 0.05$.

(2) Dosage recommendations of AMPs can be assessed from antibody titers and MIC (minimal inhibitory concentration), but this meta-analysis focuses on the findings from in vivo trials. Therefore, the appropriate recommendation is the growth performance parameter. Despite that, based on literature compilation, we found no MIC-related data and restricted data of antibody titer in broilers.

(3) Introduction

- "Meta-analysis is a statistical analysis by combining results from scientific reports. Meta-analysis produces a weighted average of the output, and the uncertainty value of the estimated equation can also be calculated (St-Pierre, 2001; Sauvant et al., 2008). Meta-analyzes can compare differences in research results and identify patterns between them, sources of differences among these results, or other interesting relationships. A recent meta-analysis of antimicrobial additives has been reported by (Vanrolleghem et al., 2019; Xu et al., 2021) in swine feed. However, studies of AMPs in broilers are still not available".

(4) Methods

- Searching and collection of literature were carried out on Google Scholar (https://scholar.google.com/) and Science Direct (https://www.sciencedirect.com/), by using various keywords such as "antimicrobial peptide," "digestibility," "growth performance," "small intestine morphology," "blood serum," and or "broiler.". Literature search based on Hidayat et al., (2020) and Prihambodo et al., (2021) work flow.

4. References

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C. Other response:

1. Change of contract number:

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