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Effect of bile acid supplementation on growth performance, carcass trait, fat digestibility, and blood lipid profile of broiler: A meta-analysis

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ABSTRACT

Bile acid (BA) is a feed additive that can increase fat digestibility in poultry. The objectives of this meta-analysis were to assess the effectiveness of supplementation with bile acid on growth performance, carcass trait, fat digestibility, and blood lipid profile of broiler by meta-analysis evidence. Peer-reviewed randomized controlled trials (RCTs) published in English were found using databases such as PubMed, and Scopus. The meta-analysis required information on moderators (inclusion level, and treatment duration), a sufficient description of randomization, performance data, and associated measures of variance such as standard deviation (SD) or standard error (SE). All analyses were carried out using the Open Meta-analyst for Ecology and Evolution (OpenMEE) program. Data from the 10 studies included in the meta-analysis were pooled and presented as standardized mean differences (SMDs) at a 95% confidence interval (CI) using a random-effects model. Results indicate that dietary BA supplementation decreases FCR (SMD = –0.50, 95% CI: –0.76 to -0.23, p<0.001), and tends to decrease abdominal fat (SMD = SMD = -0.39; 95% CI = -0.78 to 0.01; p=0.055). Contrastingly, BA supplementation increases fat digestibility (SMD = 1.67; 95% CI 0.73 to 0.26; p<0.001) and dressing carcass (0.44; 95% CI -0.08 to 0.8; p=0.016) compared with the controls The meta-analysis explains that bile acid is an ingredient that could be used as a feed additive in broiler.

Introduction

The energy component accounts for 70% of the overall feed cost in chicken feed. This economic importance and the effects of energy on animal performance have led to the development of different systems to make energy in animal feeds more efficient (Noblet *et al*., 2022; Noblet *et al*., 2024). Corn is the most widely used energy source in commercial animal diets, particularly in the United States, Southern Europe, and Asia, where corn is the primary ingredient for all poultry feed (Dei, 2017; Melo-Duran *et al*., 2024). However, the availability of corn in the field is very limited due to fluctuating production caused by unfavorable seasons. This will have an impact on reducing the quality of carbohydrates which results in lowering energy content. On the other side, the use of maize in feed competes with human consumption (Gatrell *et al*., 2014; Pantaya *et al*., 2020).

Oil and fat are added to diet as additional ingredients to help resolve this issue (Pantaya *et al*., 2020). However, their inclusion with fats and oils can lead to excessive accumulation of fat in the carcass of broiler chickens, especially in abdominal and visceral areas, which are one of the undesirable consequences of selection for increased growth of broiler chickens (Sudharsan *et al*., 2020). Obese broiler chickens reduce the purchase intention of consumers who are concerned about nutritional and healthy aspects of meat and decrease the net return for producers as abdominal fat is non-profitable. Under these circumstances, producers of modern broiler chickens have taken many strategies, including an increase in the proportion of unsaturated fatty acids (UFAs) in dietary fat (Skřivan *et al*., 2018), and the supplementation of exogenous enzymes (Shoaib *et al*., 2021) and emulsifiers such as bile acid (Geng *et al*., 2022).

Bile acid (BA) is a series of compounds composed of a hydrophobic face, a concave hydrophilic face, and a lateral chain (di Gregorio *et al*., 2021). They are constituted by primary BAs such as cholic acid (CA) and chenodeoxycholic acid (CDCA), as well as secondary BAs such as s deoxycholic acid (DCA) and lithocholic acid (LCA) and tertiary BAs such as ursodeoxycholic acid (UDCA), with diverse numbers and positions of hydroxyl groups (di Ciaula *et al*., 2017). Due to this amphipathic nature, BAs can work as emulsifiers to promote the utilization of fat and fat-soluble vitamins (Saeed *et al*., 2017). Studies have indicated that supplementary BAs in animal diets can elevate nutrient digestibility (Alzawqari *et al*., 2016; Maisonnier *et al*., 2003), growth performance (Maisonnier *et al*., 2003; Parsaie *et al*., 2007), and decrease abdominal fat deposition (Ge *et al*., 2019; Lai *et al*., 2018a).

Inconsistencies between empirical research may result in subjective prejudice and conclusions that lack support. For a more comprehensive and statistically supported conclusion regarding bile acid as a growth enhancer, an objective and quantitative testing methodology is required (Sadarman *et al*., 2021; Adli *et al*., 2022). Meta-analysis establishes the main summary or broad summary and verifies the efficacy of a treatment (Hanif *et al*., 2023a; Hanif *et al*., 2023b; Hanif *et al*., 2024). This meta-analysis attempted to evaluate effect of bile acid supplementation on growth performance, carcass trait, fat digestibility, and blood lipid profile of broiler.

Materials and methods

Literature search and study selection

A comprehensive search was conducted on several scientific web databases for studies discussing the effects of bile acid supplementation on laying hen productivity characteristics, including PubMed (pubmed.ncbi.nlm.nih.gov), and Scopus (www.scopus.com). The literature search was not restricted by date and the search terms used were "bile acid" and "broiler". Inclusion criteria for this meta-analysis research were a randomized trial design with treatment and control groups, average data from the treatment and control groups and their variability (standard deviation

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and standard error), and sample size. The papers in this meta-analysis must include data on feed intake, weight gain, feed conversion ratio, fat digestibility, dressing carcass, abdominal fat, serum cholesterol, serum triglyceride, serum HDL and serum LDL. In this study, the explanatory factors the amount of bile acid used, and the duration of administration. Exclusion criteria were a lack of knowledge of the study design and its variability. Based on the searches conducted, 10 studies were obtained that met the criteria as shown in Fig. 1.

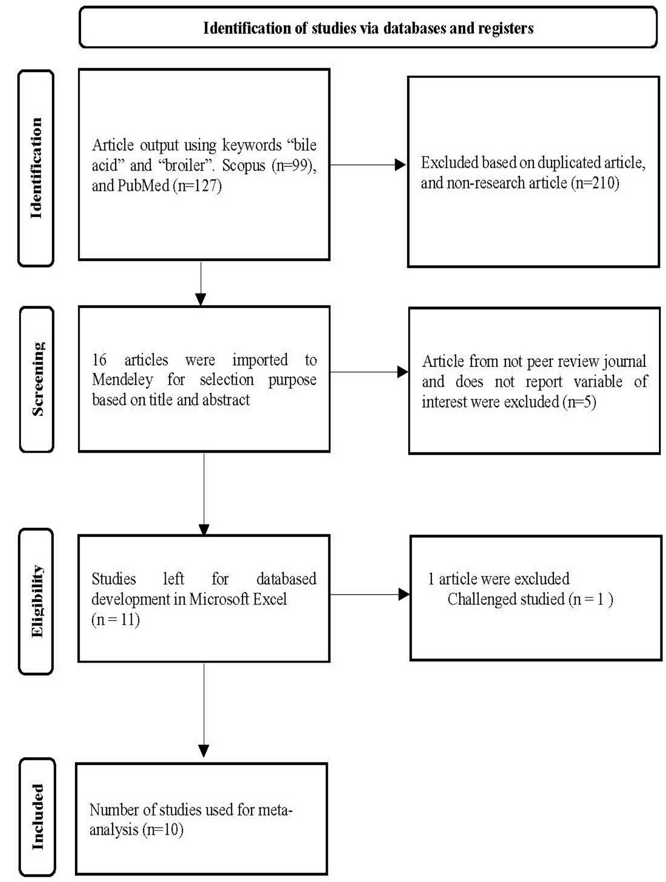

Fig. 1. Flow charts of the articles selection process utilized for the meta-analysis.

Data extraction

The bile acid supplementation rate and duration of bile acid supplementation were obtained from each publication that met the inclusion criteria. The mean and standard deviations (SD or SE) of the outcome variables of interest for the treatment and control groups, as well as the surname of the first author and the year of publication, were retrieved. In studies where SE was utilized instead of SD, the SE values were converted to SD (Higgins and Deeks, 2008). The data from the 10 papers that satisfied the selection criteria were converted to a comma-separated value (CSV) file format of Microsoft Excel 2021, which is the enabled file format for the analysis using Brown University's OpenMEE (Open meta-analyst for ecology and evolution) software.

Statistical Analysis

Data collected from each article was put into an Excel sheet, transformed into Comma-Separated Value (CSV) files, and then analyzed using OpenMEE, an open-source software (Wallace *et al*., 2017). The continuous variable results were presented as a 95% confidence interval (CI) standardized mean difference (SMD) between the bile acid treatment and controls. To assess heterogeneity, the DerSimonian and Lard test (Chi-square (Q) - statistic) and the Inconsistency index (I2) – statistic were used (Higgins *et al*., 2003). The I2 statistic denotes the proportion of variance in a meta-analysis attributed to study heterogeneity. The random-effects model (REM) was chosen for the meta-analysis because heterogeneity occurs at varying levels in each pooled analysis. Meta-regression was performed to determine the origins of heterogeneity. The moderator factors employed in the subgroup analysis were also utilized to predict the study effects in the meta-regression. $p<0.050$ was regarded statistically significant in the current investigation. Variables that had a comparison count below 20 were not subjected to sub-group analysis.

Results

Study characteristic

A total of 10 studies conducted in 6 countries worldwide were aggregated, mainly shown in China (4/10), Pakistan (2/10), Egypt (1/10), Indonesia (1/10), Thailand (1/10) and Saudi Arabia (1/10). Inclusion levels of BA varied among studies, from 0.1 g/kg diet to 1.5 g/kg diet. The duration of BA treatment varies from among others to the grower and finisher phases (Table 1).

Growth performance and fat digestibility

Meta-analysis of the effect of BA on feed intake of broiler was performed using 31 articles where the pooled mean effect estimate was -0.01 (95% CI = -0.25 to 0.22; p=0.923). The pooled SMD estimates indicated that BA supplementation did not affect BWG of broiler (SMD=0.23; 95% CI = -0.21 to 0.67; P=0.306). Grand estimates obtained from SMD suggested that BA decreased on FCR of broiler (SMD = –0.50, 95% CI: –0.76 to -0.23, p<0.001). Interestingly, restricted subgroup analysis showed BA decreases FCR in broilers fed bile acid to finisher (p<0.001). In addition, the Grand mean estimate revealed an increase of treatment effect on fat

Table 1. Studies included in the meta-analysis of bile acid supplementation on growth performance, carcass trait, fat digestibility, and blood lipid profile of broiler.

Study	Reference	Country	Breed	Sex	Dose (g/kg)	Duration (d)	Variables
1	Alzawqari *et al*. (2016)	Saudi Arabia	Ross 308	Male	0-5	42	FI, BWG, FCR, FD, DC, AF, CL, TG, HDL, LDL
2	Lammasak *et al*. (2019)	Thailand	Arbor Arcer	Male	0-5	21	FI, BWG, FCR,
3	Lai *et al*. (2018b)	China	Arbor Arcer	Male	0-0.08	42	FI, BWG, FCR, DC, AF, TG, HDL, LDL
4	Lai *et al*. (2018a)	China	Arbor Arcer	Male	0-0.4	42	FI, BWG, FCR,
5	Ge *et al*. (2019)	China	Arbor Arcer	Male	0-0.08	42	FI, BWG, FCR, AF, CL, TG
6	Arshad *et al*. (2020)	Pakistan	-	mix	0-0.3	35	FI, BWG, FCR, FD, AF, CL, TG, HDL, LDL
7	Pantaya *et al*. (2020)	Indonesia	Cobb	-	0-1.5	35	FI, BWG, FCR, DC, AF
8	Shoaib *et al*. (2021)	Pakistan	Ross 308	-	0-0.5	35	FI, BWG, FCR, FD, DC, AF
9	Geng *et al*. (2022)	China	Arbor Arcer	Male	0-0.08	42	FI, BWG, FCR, FD, DC, AF, CL, TG, HDL, LDL
10	Hussien *et al*. (2022)	Egypt	Ross 308	-	0-0.2	31	FI, BWG, FCR, FD, DC, AF, CL, TG, HDL, LDL

FI: feed intake; BWG: body weight gain; FCR: feed conversion ratio; FD: fat digestibility; DC: dressing carcass; AF: abdominal fat; CL: Serum cholesterol level; TG: serum triglycerides levels; HDL: high density lipid level; LDL: low density lipid level.

digestibility (SMD = 1.67; 95% CI 0.73 to 0.26; p <0.001).

Carcass trait

Assessing the effect of BA supplementation on carcass trait of broiler, 13 comparisons that met the eligibility rule for inclusion in the meta-analysis were used. The Grand mean estimate revealed increased of treatment effect on dressing carcass (SMD = 0.44; 95% CI -0.08 to 0.8; p =0.016). The pooled effect estimates from SMD revealed that BA supplementation tends to decrease abdominal fat (SMD = -0.39; 95% CI = -0.78 to 0.01; p =0.055).

Blood lipid profile

Grand estimates obtained from SMD suggested that BA did not affect cholesterol (SMD = 0.23; 95% CI = -0.60 to 1.05; p =0.582), triglyceride (SMD = -0.01; 95% CI = -0.37 to 0.35; p =0.958), HDL (SMD = 0.04; 95% CI = -0.36 to 0.43; p =0.862), and LDL (SMD = -0.05; 95% CI = -0.41 to 0.31; p =0.789).

Publication bias

The funnel plots evaluating the effects of bile acid supplementation on all parameters in broiler indicate that the funnel plots were almost symmetrical (Fig. 2, Fig. 3 and Fig. 4). Because a substantial number of unpublished papers would be required to change the statistically significant results, the presence of publication bias was not a problem in this meta-analysis.

Discussion

This study aimed to determine the effect of bile acid supplementation in broiler diets on growth performance, carcass quality, fat digestibility and blood profile at different growth stages by meta-analysis evidence. The findings suggest that bile acid supplementation may improve broiler growth performance by increasing the digestibility of feed fat in the digestive tract of broiler.

The current study showed that bile acid supplementation did not af

Table 2. Meta-analysis of the effect of bile acid supplementation on growth performance, carcass trait, fat digestibility, and blood lipid profile of broiler.

Variables	N	SMD	CI 95%		SE	*p* -value	Heterogeneity	
			Lower	Upper			I²	p-value
Feed intake	31	-0.01	-0.25	0.22	0.12	0.92	13.3	0.26
Body weight gain	31	0.23	-0.21	0.67	0.23	0.31	71.4	<0.001
Feed conversion ratio	31	-0.5	-0.76	-0.23	0.14	<0.001	29.4	0.07
Fat digestibility	12	1.7	0.73	2.6	0.48	<0.001	75.6	<0.001
Dressing carcass	13	0.44	0.08	0.8	0.18	0.02	0.4	5.0
Abdominal fat	15	-0.39	-0.78	0.01	0.2	0.06	0.1	33.1
Serum cholesterol	12	0.23	-0.6	1.1	0.42	0.58	77.1	< 0.001
Serum triglyceride	18	-0.01	-0.37	0.35	0.19	0.96	38	0.05
Serum HDL	18	0.04	-0.36	0.43	0.2	0.86	45.2	0.02
Serum LDL	18	-0.05	-0.41	0.31	0.19	0.79	37.7	0.05

SMD and I2 were considered significant at p< 0.05, N: number of comparisons, SMD: standardized mean differences between the bile acid supplementation and controls, CI: confidence interval, SE: standard error, p: probability value

Table 3. Subgroup-analysis of the effect of bile acid supplementation on broiler performance.

Variable	Subgroup	N	SMD	CI 95%		SE	*p*-value	Heterogeneity	
				Lower	Upper			I²	p-value
Feed intake	Treatment duration								
	21 d (Until Grower)	14	-0.16	-0.47	0.16	0.16	0.33	0	0.92
	28-42 d (Until Finisher)	17	0.15	-0.23	0.54	0.2	0.44	39.8	0.05
	Dose								
	<1 g/kg	22	0.06	-0.21	0.34	0.14	0.65	18.6	0.21
	1 – 10 g/kg	9	-0.24	-0.68	0.21	0.23	0.30	0	0.48
Body weight gain	Treatment duration								
	21 d (Until Grower)	14	0.01	-0.31	0.32	0.16	0.98	0	0.97
	28-42 d (Until Finisher)	17	0.5	-0.35	1.4	0.44	0.25	83.4	<0.001
	Dose								
	<1 g/kg	22	0.31	-0.14	0.76	0.23	0.18	65.6	<0.001
	1 – 10 g/kg	9	-0.01	-1.2	1.2	0.61	0.98	81.1	<0.001
Feed conversion ratio	Treatment duration								
	21 d (Until Grower)	14	-0.22	-0.59	0.16	0.19	0.26	0.2	24.00
	28-42 d (Until Finisher)	17	-0.74	-1.1	-0.39	0.18	<0.001	21.1	0.21
	Dose								
	<1 g/kg	22	-0.46	-0.8	-0.12	0.17	0.01	43.5	0.02
	1 – 10 g/kg	9	-0.62	-1.1	-0.17	0.23	0.01	0	0.78

SMD and I2 were considered significant at p< 0.05, N: number of comparisons, SMD: standardized mean differences between the bile acid supplementation and controls, CI: confidence interval, SE: standard error, p: probability value

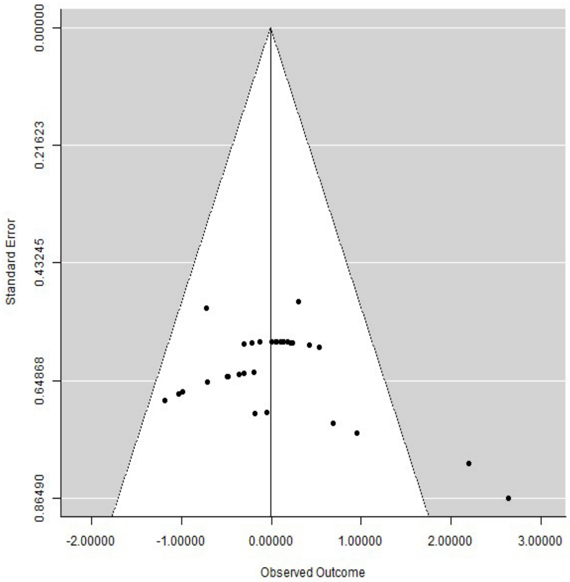

Fig. 2. Funnel plots analysis on feed intake to detect publication bias between studies.

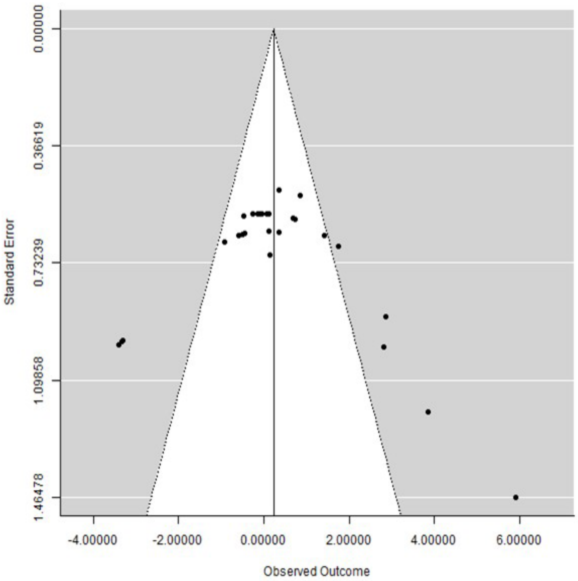

Fig. 3. Funnel plots analysis on body weight gain to detect publication bias between studies.

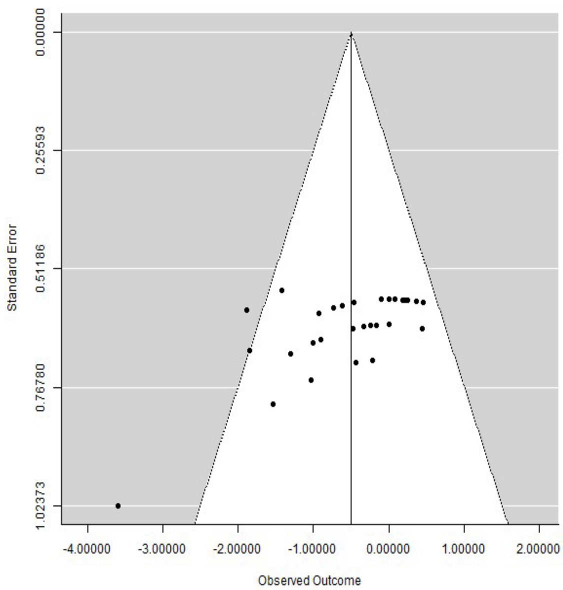

Fig. 4. Funnel plots analysis on feed conversion ratio to detect publication bias between studies.

fect feed intake and weight gain of broiler. In contrast, bile acid decreased broiler feed conversion ratio (FCR) values. Previous studies have demonstrated that exogenous emulsifier inclusion could promote the growth performance of broilers (Mart´ınez, 2013; Wang *et al.*, 2016). Emulsifiers as a kind of amphiphilic molecules can increase the absorption of fat-soluble nutrients (Zou *et al.*, 2015). Ge *et al.* (2019) finding also showed that dietary BAs could increase lipid digestibility in broiler. As an essential emulsifier, exogenous BAs not only increased the digestibility of extract ether (EE) in broiler chickens in this study, but also increased the utilization rate of gross energy in diets (Alzawqari *et al.*, 2011). Bile acids activate the mitogen-activated protein kinase pathway, are ligands for the G-protein-coupled receptor Takeda G-protein-coupled receptor 5 (TGR5) (Kawamata *et al.*, 2003), and activate nuclear hormone receptors such as farnesoid X receptor α (Wang *et al.*, 1999). Through this mechanism, BAs regulate glucose metabolism, and they are closely related to glucose and lipid homeostasis. Therefore, BAs are implicated not only in the hepatic regulation of cholesterol metabolism but also in that of glucose (Nguyen and Bouscarel, 2008).

Further research has shown that BAs can activate the nuclear receptor farsenoid X receptor (FXR), which can impede the production of fas cell surface death receptor (FAS), acetyl-CoA carboxylase (ACC), and sterol regulatory element-binding factor 1 (SREBF1) in the liver (Noel *et al.*, 2016; Schonewille *et al.*, 2016). SREBP-1a and SREBP-1c, which are both capable of regulating the expression of genes linked to lipid metabolism, particularly the lipogenic genes like ACC and FAS, are encoded by SREBF1, a transcription factor that is a member of the basic helix-loop-helixleucine zipper family (Le Hellard *et al.*, 2010; Watanabe *et al.*, 2006). Piekarski *et al.* (2016) findings also reported that ACC and FAS expression levels were lowered by chenodeoxycholic acid. Peroxisome proliferator-activated receptor alpha (PPARα) and Carnitine palmitoyltransferase I (CPT1) are the genes involved in lipolysis. A rate-limiting fatty acid oxidation enzyme that CPT1 encodes aids in the movement of activated fatty acids towards the mitochondria for β-oxidation (Schreurs *et al.*, 2010; Zhao *et al.*, 2018). PPARα belongs to a nuclear receptor superfamily that controls the transcription of genes encoding lipolytic enzymes for the oxidation of fatty acids (Bremer, 2001; Cattley, 2003).

One of the biggest issues facing the chicken business is excessive fat deposition, which lowers carcass production and results in significant waste in the abattoir. High energy diets typically cause chickens to accumulate more fat on their bodies (Fouad and El-Senousey, 2014; Xie *et al.*, 2010). The two main factors determining the carcass yield of poultry are thought to be subcutaneous and abdominal fat (Tumová and Teimouri, 2010). Emulsifiers have been shown to have beneficial benefits on lowering fat deposition and enhancing carcass quality in grill chickens by numerous researchers (Xu *et al.*, 2003; Zhao and Kim 2017). Lai *et al.* (2018b) also verified these results, and this simultaneous increase in the breast muscle percentage but decrease in the abdominal fat may also suggest that BAs could promote broilers to use more nutrients for muscle growth than fat deposition. In chickens, the principal location for fatty acid production is the liver (Xu *et al.*, 2003). Moreover, it has been suggested that a high energy diet may result in an increased buildup of triglycerides in the liver (Zaman *et al.*, 2008).

Conclusion

From meta-analysis studies, it can be concluded that bile acid supplementation can decrease FCR value and abdominal fat. Contrastingly, bile acid increases fat digestibility, and dressing carcass. Supplementation of bile acid from starter to finisher showed better results than supplementation to grower.

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Conflict of interest

The Authors declare that there is no conflict of interest

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