p-ISSN 2615-787X e-ISSN 2615-790X
Accredited by Directorate General of Higher Education, Research, and Technology, Republic of Indonesia, No. 225/E/KPT/2022

Tropical Animal Science Journal, September 2024, 47(3):321-332
DOI: https://doi.org/10.5398/tasj.2024.47.3.321
Available online at https://journal.ipb.ac.id/index.php/tasj

Egg Production, Blood Profile, and Histopathology in Japanese Quail with Phytogenic Additives

R. Murwani[a,b,*], R. Anggraeni[a,b], M. H. Muslih[a], A. O. Yogantara[a], & Mulyono[c]
[a]Laboratory of Physiology and Biochemistry, Department of Animal Science, Faculty of Animal and Agricultural Sciences, Universitas Diponegoro, Semarang
[b]Natural Product Laboratory, UPT Laboratorium Terpadu, Universitas Diponegoro, Semarang
[c]Laboratory of Animal Nutrition and Feed Science, Department of Animal Science, Faculty of Animal and Agricultural Sciences, Universitas Diponegoro, Semarang
Jl. Prof Soedarto Tembalang, Semarang 50275, Indonesia
*Corresponding author: rmurwani.undip@gmail.com
(Received 08-01-2024; Revised 19-03-2024; Accepted 05-04-2024)

ABSTRACT

This study aimed to determine the effect of combining phytogenic *Curcuma aeruginosa* Roxb powder with *C. xanthorizza* standardized extract or with *Anredera cordifolia* leaf powder in an antibiotic-free diet on the egg production, red and white blood cell profile, fecal endoparasite, serum biochemistry, and intestinal and liver histopathology of Japanese quails. Four hundred eight-month-old Japanese quails were raised in 5-tier cages, randomly allocated into four treatments, namely: T0 (standard diet), T1 (standard diet plus 1% *C. aeruginosa* Roxb rhizome powder), T2 (standard diet plus 1% *C. aeruginosa* Roxb rhizome powder and *C. aeruginosa* extract (equal to 200 ppm standardized curcumin), and T3 (standard diet plus 1% *C. aeruginosa* Roxb powder and 1% *A. cordifolia* leaf powder). The data were analyzed using variance analysis (ANOVA). Duncan's test was carried out at a 5% significant level when a significant effect was found. The results showed that weekly egg production was not affected by phytogenic addition, but egg production significantly increased on the last day of treatment ($p<0.05$). Combining 1% *C. aeruginosa* Roxb and 1% *A. cordifolia* significantly increased ($p<0.05$) erythrocytes, hemoglobin, hematocrit, leukocytes, lymphocytes, serum glucose, uric acid, creatinine, and AST. However, their values remained within the normal range of Japanese quails. No endoparasites were found in the fecal samples. The addition of phytogenic did not affect the height of intestinal villi and crypt depth ($p>0.05$). Interestingly, intestinal inflammation levels were reduced significantly in T1 and T2 compared to the control, while T3 was the same as the control ($p<0.05$). An elevated liver score was found (1 score higher) in T2 ($p<0.05$). This study suggests that phytogenic additives can help reduce normal intestinal inflammation (due to harsh intestinal environment) and improve the performance of laying Japanese quail, especially in the absence of endoparasites or infection.

Keywords: Anredera cordifolia; Curcuma aeruginosa; Curcuma xanthorrhiza; health indices; laying potential; quail

INTRODUCTION

Japanese quail is a dual-purpose livestock, producing animal protein from meat and eggs, and is widely raised by the local community globally. In Indonesia, the most commonly raised strain of quail is *Coturnix coturnix japonica*. Increased population and nutrition knowledge led to the growth demand for quail eggs. Egg consumption from quails in Indonesia was 9,177 eggs/unit in 2018 (Livestock and Animal Health, 2019). Environmental challenges, such as sudden climate change, viral and parasite infections in egg-producing birds, can lower their productivity, and many phytogenic additives have replaced antibiotic growth promotors (AGP). Furthermore, many studies showed the negative consequences of AGP (Murwani & Bayuardhi, 2007; Murwani, 2008a). Therefore, a search for natural substitutes of AGP and natural phytogenic that benefit poultry production is continuously being developed and studied, and many products have reached the market to maintain livestock productivity.

The phytogenic include the use of naturally occurring phytochemicals of feed ingredients such as sorghum seeds (Murwani, 2008b); from botanical such as stem extract of *Scrulla oortiana* (Murtini *et al.*, 2010), the fruit extracts of *Annacardium occidentale* (Tanod *et al.*, 2015), ethanol extract of *Ficus carica* (Sukowati *et al.*, 2019), and *Aegle marmelos (L)* (Sumardi *et al.*, 2021), *Arecha catechu L* seed powder and the leaf of *Anredera cordifolia* (Marlani *et al.*, 2017; Kusumanti & Murwani, 2018; Murwani *et al.*, 2022), and there are many more of other reported studies. One of the phytogenic additives

actively still being researched is *Curcuma aeruginosa,* locally named "Temu hitam" or black curcuma. It has an antibacterial, antiparasitic, and anticancer (Akarchariya *et al.,* 2017; Aziz *et al.,* 2021; Fitria *et al.,* 2019; Sari & Supratman, 2022). The tannin components can kill and break the life cycle of larvae and eggs of parasitic intestinal worms of laying hens (Vanda *et al.,* 2020). The curcumenol, isocurcumenol, germacrone, curcumin, demethothoxycurcumin, phenols, tannins, and saponins can weaken the liver worm's muscle and lead to its death. The ethanol extract of *C. aeruginosa* Roxb contains essential oils, flavonoids, tannin, polyphenols, and curcumin (Jose & Thomas, 2014). The antioxidant of phenolic compounds, flavanols, and proanthocyanidins can prevent cell damage from free radicals (Septaningsih *et al.,* 2018; Burapan *et al.,* 2020; Simoh *et al.,* 2018; Nurcholis *et al.,* 2017). A 1.25% and 1.5 % black ginger flour given to Peking ducks reduced feed consumption and conversion, increased weight gain, and serum HDL cholesterol (Syaefudin *et al.,* 2016). *C. aeruginosa* juice extract at 0.5%-1.5% can increase total leukocytes, phagocytosis activity, reduce mortality due to pathogenic *V. alginolyticus* and *V. parahaemolyticus* in tiger grouper (Setyati *et al.,* 2019). In contrast, several studies showed the toxicity of *C. aeruginosa*. Increased *C. aeruginosa* dosages (10 ppm, 100 ppm, and 1000 ppm) produced higher toxicity in shrimp larvae (Fitria *et al.,* 2019; Mustariani *et al.,* 2017). The toxic effect was due to the alkaloids, saponins, and flavonoids on the stomach and feed recognition receptors (Zulfiah *et al.,* 2020). The polyphenol content can also reduce protein synthesis in the liver (Maksudi *et al.,* 2018). The administration of *C. aeruginosa* extract at a dose of 32.5 mg/kg body weight showed the presence of central vein congestion, degeneration, and necrosis of liver cells, interfering with liver function in detoxification (Hestianah *et al.,* 2014).

C. xanthorrhiza rhizome, locally named "Temulawak," has been a medicinal herbal supplement since ancient times (Rahmat *et al.,* 2021). The administration of fresh decoction of *C. xanthorrhiza* in rats given paracetamol showed no changes in liver color compared to the control group with paracetamol, only having changes in liver color and necrosis (Pramono *et al.,* 2018). Meanwhile, the administration of the extract increases the antioxidant status essential in the detoxification process in the liver and kidneys (Devaraj *et al.,* 2014). The extract contains xanthorizol, which stimulates liver cells to produce bile fluid and maintain liver function in protein synthesis (Rahmat *et al.,* 2021). Tetrahydro curcuminoid is one of the metabolites of curcumin and has the most potent antioxidants (Zhang *et al.,* 2019). Curcumin can improve cellular redox status and activate NF-E2-related factor 2 (NrF2), vital in suppressing oxidative stress (Zhang *et al.,* 2019). Related to the potential benefit of *C. aeruginosa* as a feed additive, but on the other hand, it is also potentially toxic, it is hypothesized that when combined with hepatoprotective curcumin from a commercial standardized *C. xanthorrhiza* extract, it could offset the potential toxicity of *C. aeruginosa*.

Anredera cordifolia leaves, locally named "Binahong," contain flavonoids, saponins, and tannins with antibacterial and anti-fungal activity (Indarto *et al.,* 2019). The bioactive can disrupt pathogenic *Vibrio cholerae* growth (Sari *et al.,* 2020), inhibiting *Escherichia coli* and *Staphylococcus aureus* mediated by cell wall permeability damage (Maryana *et al.,* 2019). The antibacterial function of *A. cordifolia* leaf can increase carcass percentage by reducing pathogenic bacteria in the gastrointestinal tract, improving its function and resistance to infection (Alba *et al.,* 2020; Leliqia *et al.,* 2017). Administration of *A. cordifolia* extract showed no segmentation of glomerular cells, reducing alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels (Leliqia *et al.,* 2017). At 150 mg/Kg BW, *A. cordifolia* extract can repair cell damage (Sukandar *et al.,* 2016). Furthermore, *A. cordifolia* has a "wound healing" activity and protects liver function (Marlani *et al.,* 2017; Murwani *et al.,* 2022; Yuniarti & Lukiswanto, 2017). This study was conducted by considering both the beneficial *C. aeruginosa* as an anti-bacterial and anti-parasite and its potential toxicity, combined with the hepatoprotective curcumin from *C. xanthorrhiza* extract or with *A. cordifolia* leaves. Therefore, the effect of combining phytogenic *Curcuma aeruginosa* Roxb with standardized *C. xanthorrhiza* extract (200 ppm curcumin) or with *A. cordifolia* into an antibiotic-free diet was investigated on the blood cell profile, fecal endoparasite, serum biochemistry, intestinal and liver histopathology of eight-month-old laying quails, along with its impact on egg production.

MATERIALS AND METHODS

This research protocol has received ethical commission approval with Ethical Approval Number 036/EA/KEPK-FKM/2023.

Phytogenic Materials

All fresh phytogenic samples were identified at the Faculty of Sciences and Mathematics, Universitas Diponegoro (UNDIP). *Curcuma aeruginosa* obtained from local markets was washed, drained, and skin peeled. The clean rhizome was sliced thinly, air-dried, and ground into a fine powder. The *C. xanthorizza* extract was purchased from an official pharmacy store. It contains standardized curcumin 20 mg/tablet (Curcuma Force, SOHO Global Health from *C. xanthorizza* extract). The extract is in tablet form and ground into a fine powder before use. Meanwhile, *A. cordifolia* leaves were obtained from a horticulture center in Magelang Regency. They were washed, drained, cut into small pieces, dried, and ground into fine powder. For phytogenic addition to the standard quail diet, the ready-to-use phytogenic additives were mixed with the diet until homogeneous, and the mix was molded into a pellet. Each treatment additive was mixed into the commercial quail feed according to experimental designs.

Experimental Design

This study was carried out at one of the quail farms in Semarang City, which has a capacity of 3,000 birds.

From the 3,000 birds, 400 eight-month-old Japanese quails with an initial weight of ±202.5 g were randomly placed in eight 5-tier wood cages. Each tier cage is 64 x 46 cm and can house ten birds. It is equipped with free access to feed and drinking water. The diet was a quail layer PP3 from PT. Cargill and its composition and nutritional content are presented in Table 1 (antibiotic-free feed). A completely randomized design with four treatments, namely T0: Control (antibiotic-free feed with no additives), T1: antibiotic-free feed + 1% *C. aeruginosa* powder; T2: antibiotic-free feed + 1% *C. aeruginosa* powder + *C. xanthorizza* extract (equal to 200 ppm standardized curcumin); T3: antibiotic-free feed + 1% *C. aeruginosa* powder + 1% *A. cordifolia* leaf powder was carried out. Each treatment consisted of ten replicates, with ten birds in each replicate. The treatment was given for four weeks. Sanitation of the quail housing was done twice daily, in the morning and afternoon.

Egg Production and Feed Conversion Ratio

Egg production was recorded daily from each replicate (10 birds) of each group, and the average weekly egg production was calculated. The egg production on the final day of phytogenic treatment was also presented in the Results. The feed conversion ratio (FCR) is obtained from the feed consumed divided by the egg's weight.

Red and White Blood Cell Profile and Serum Biochemical Determination

One bird from each group's replicate was taken for blood profile determination; blood was drawn via the jugular vein. Blood was directly placed in a vacutainer containing EDTA. Determination of erythrocytes, hematocrit, hemoglobin, leukocytes, lymphocytes, eosinophils, and neutrophils was carried out using the electrical impedance method using PRIMA© (Fully Auto Hematology Analyzer), which works automatically with a dilution process and hemolyzing (diluting the sample with 26 mL diluent and 0.35 mL lyse reagent). All data were processed by a microprocessor and displayed on the monitor screen. The Analyzer can count the Red Blood Cell, Hemoglobin, Hematocrit, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), and Mean Corpuscular Hemoglobin Concentration (MCHC) and differentiate leukocytes into lymphocytes, eosinophils, and neutrophils.

For serum biochemical determination, another bird from each replicate of each group was taken, and blood was placed in a vacutainer without EDTA. The serum was separated by centrifugation at 4000 rpm for 10 minutes, collected in an Eppendorf tube, and stored frozen until analyses. The serum samples were determined by photometric method (Microlab 300 Photometer at a wavelength (λ) 516 nm) (Sukowati *et al.*, 2019; Murwani *et al.*, 2022).

Table 1. Composition and nutrient content of quail layer rations – PP3*

Nutrients	Nutrient content (Feed label)[a]	Proximate analysis
Moisture	12%	8.99%
Crude protein	19%–22%	19.88%
Ash	14%	12.30%
Crude fat	7%	7.66%
Energy from fat	-	68.94 Kcal/100g
Carbohydrate	-	51.40%
Total energy	-	354.02 Kcal/100g
Crude fiber	7%	-
Calcium	2.5%–3.5%	-
Phosphorus	0.6%–1.0%	-
Aflatoxin	40 ppb	-

Note: [a]PT. Cargill New Zealand, 2020.
Proximate analyses by an accredited laboratory, 2020.
Feed ingredient composition: Yellow corn, rice bran, soybean meal, meat and bone meal, vegetable oil, vitamins, minerals, and antioxidant premix.

Histopathology

After sacrificing the bird, the liver and small intestine were removed and stored in 10% NBF (Neutral Buffer Formalin). The histopathological slides were prepared using the paraffin method (4–5 μm thickness) with Hematoxylin – Eosin staining (Murtini *et al.*, 2010; Murwani *et al.*, 2022). A histopathologist analyzed the samples. Intestines were observed for villus and crypt height and inflammation level (the level of infiltrating inflammatory cells). The intestinal inflammation was scored as "1" (inflammatory cell infiltration 0–25% of the entire visual field), "2" (inflammatory cell infiltration 26–50% of the entire visual field), "3" (inflammatory cell infiltration 51–75% of the entire visual field) and "4" (inflammatory cell infiltration >75% of the entire visual field). Liver histopathology was scored "1" normal (polygonal cells appear, homogeneous red cytoplasm, clearly defined cell walls), "2" parenchymatous degeneration (cell swelling accompanied by cloudy and granular cytoplasm), "3" hydropic degeneration (swollen cells, fluid accumulation and there are many vacuoles) and "4" necrosis (permanent cell damage or cell death).

Collection of Fecal Samples, Parasite Identification, and Enumeration

At the end of the experiment, fresh feces were collected from each replicate (10 birds per replicate) of each treatment. Each replicates fecal sample was mixed thoroughly, sampled approximately 25 grams with a sterile spoon, and preserved in 10% formalin for endoparasite determination (Murwani *et al.*, 2022). The parasite identification and enumeration were made by experienced staff at the Laboratory of Animal Health Semarang City, Regional Office of Animal Husbandry and Health.

Statistical Analyses

The data were analyzed using variance analysis (ANOVA) to determine the effect of the phytogenic ad-

ditives. When a significant effect was found, Duncan's test was carried out. A p-value < 0.05 was used to determine statistical significance.

RESULTS

The effects of phytogenic addition on egg production, feed consumption, and feed conversion ratio (FCR) of Japanese quail are presented in Table 2. Of phytogenic addition, combined 1% *C. aeruginosa* with 1% *A. cordifolia* (T3) significantly increased (p<0.05) feed consumption and feed conversion ratio but not egg production. However, on the last day of the experiment, egg production significantly increased (p<0.05) with the combined additives.

The effects of phytogenic additives on the erythrocytes and leukocyte profiles are presented in Table 3. It showed that both of the combined phytogenic additives significantly increased (p<0.05) the erythrocytes, hemoglobin, hematocrit, leucocytes, lymphocytes, eosinophils, and neutrophils, while MCV, MCH, and MCHC were not affected. No endoparasites were found in the fecal samples.

The effect of phytogenic additives on serum biochemistry is presented in Table 4. It showed that the phytogenic significantly affected (p<0.05) glucose, uric

Table 2. Feed consumption, feed conversion ratio, and egg production of eight-month-old Japanese quail during phytogenic supplementation for 4-weeks

Variables	Treatments				*p*
	T0	T1	T2	T3	
Feed consumption (g)					
Week 1	20.95 ± 1.91	21.00 ± 1.32	20.93 ± 2.14	20.88 ± 1.15	0.99
Week 2	22.89 ± 1.56	21.96 ± 1.53	22.22 ± 2.34	22.13 ± 1.37	0.65
Week 3	23.25 ± 2.87	23.64 ± 1.37	23.66 ± 1.86	24.08 ± 0.71	0.81
Week 4	21.49 ± 2.72 ^{a}	21.41 ± 2.28 ^{a}	21.91 ± 1.74 ^{ab}	23.71 ± 0.72 ^{b}	0.05*
FCR					
Week 1	1.95 ± 0.16	1.92 ± 0.38	1.94 ± 0.16	1.97 ± 0.12	0.97
Week 2	2.11 ± 0.12	2.11 ± 0.12	2.07 ± 0.18	2.09 ± 0.12	0.89
Week 3	2.13 ± 0.23	2.26 ± 0.14	2.19 ± 0.19	2.24 ± 0.06	0.32
Week 4	1.97 ± 0.25^{a}	2.03 ± 0.22^{a}	2.04 ± 0.18^{a}	2.23 ± 0.07^{b}	0.03*
Egg production (%)					
Week 1	77.65 ± 11.91	76.66 ± 7.72	79.43 ± 10.42	79.57 ± 9.09	0.89
Week 2	80.46 ± 11.99	80.63 ± 8.15	78.29 ± 9.71	81.38 ± 10.36	0.92
Week 3	77.69 ± 6.72	81.30 ± 8.55	78.87 ± 9.14	80.74 ± 8.50	0.75
Week 4	75.92 ± 8.79	76.24 ± 5.18	81.05 ± 7.02	81.83 ± 7.02	0.17
Last day of the experiment	63 ± 14.94^{a}	64 ± 10.75^{a}	71 ± 9.94^{ab}	79 ± 8.76^{b}	0.01*

Note: Each value is the average of ten replicate birds. Means in the same row with different superscripts differ significantly (p<0.05).
T0= Control (antibiotic-free feed with no additives), T1= antibiotic-free feed + 1% *Curcuma aeruginosa* powder; T2= antibiotic-free feed + 1% *C. aeruginosa* powder + 200 ppm curcumin, T3= antibiotic-free feed + 1% *C. aeruginosa* powder + 1% *Anredera cordifolia* leaf powder.

Table 3. The erythrocyte, leucocyte profile, and endoparasites of eight-month-old Japanese quails after phytogenic addition for 4-weeks

Variables	Treatments				*p*
	T0	T1	T2	T3	
Erythrocyte profile					
Erythrocytes (10^6/μL)	3.68 ± 0.40^{bc}	3.52 ± 0.68^{c}	4.31 ± 0.76^{a}	4.60 ± 1.02^{a}	0.00*
Hemoglobin (g/dL)	14.00 ± 1.89^{b}	13.85 ± 2.36^{b}	16.63 ± 3.17^{a}	16.95 ± 2.62^{a}	0.01*
Hematocrit (%)	50.50 ± 5.31^{bc}	47.93 ± 8.89^{c}	58.55 ± 10.96^{b}	62.30 ± 12.87^{a}	0.00*
MCV (fl)	138.08 ± 2.63	136.94 ± 6.44	137.38 ± 4.49	136.57 ± 7.11	0.94
MCH (pg)	36.15 ± 5.64	38.92 ± 2.20	38.82 ± 3.25	37.74 ± 3.58	0.36
MCHC (g/dL)	27.62 ± 1.50	28.55 ± 1.57	28.41 ± 2.41	27.77 ± 2.75	0.71
Leukocyte profile					
Leukocytes (x10^3/mm^3)	138.03 ± 43.65^{c}	128.70 ± 36.18^{c}	190.80 ± 65.65^{b}	241.20 ± 34.56^{a}	0.00*
Lymphocytes (x10^3/mm^3)	135.95 ± 43.00^{b}	127.40 ± 35.72^{b}	188.83 ± 64.63^{a}	373.75 ± 418.99^{a}	0.00*
Neutrophils (thousand/mm^3)	2.08 ± 1.20	1.30 ± 0.54	1.98 ± 1.13	2.45 ± 0.72	0.06*
Eosinophils (%)	0	0	0	0	-
Endoparasites	Not found	Not found	Not found	Not found	-

Note: Each value is the average of ten replicate birds. Means in the same row with different superscripts differ significantly (p<0.05).
T0= Control (antibiotic-free feed with no additives), T1= antibiotic-free feed + 1% *Curcuma aeruginosa* powder; T2= antibiotic-free feed + 1% *C. aeruginosa* powder + 200 ppm curcumin, T3= antibiotic-free feed + 1% *C. aeruginosa* powder + 1% *Anredera cordifolia* leaf powder. MCV= mean corpuscular volume; MCH= mean corpuscular hemoglobin; MCHC= mean corpuscular hemoglobin concentration.

acid, creatinine, and AST. Glucose levels increased in T1 and T2 and were significantly (p<0.05) higher than control. Uric acid levels increased in T2 and T3, and T3 was significantly (p<0.05) higher than control. However, T2 was similar to T1 and T0 (p<0,05). Creatinine and AST levels in T1, T2, and T3 were significantly (p<0.05) higher than in control.

Table 5 and Figure 1a show that the intestinal villi height and crypt depth were not affected by phytogenic additives (p>0.05). Interestingly, inflammation levels in T1 and T2 were reduced compared to the control, while T3 was the same as the control (Figure 1b). An elevated liver scoring was found (1 score higher) in T2 (p<0.05) and illustrated in Figure 2.

DISCUSSION

Feed Consumption, Feed Conversion Ratio, and Egg Production

In the fourth week, the combined 1% *C. aeruginosa* with 1% *A. cordifolia* significantly increased (p<0.05) feed consumption and feed conversion ratio in T3 (2.23 compared to T0 1.97) but not egg production. Other studies in laying quails (Ashour *et al*., 2020; Herve *et al*., 2019; Mat *et al*., 2021; Özbilgin & Kara, 2023) have shown that a good feed conversion ratio ranges from 2.8 to 4.6. Therefore, the increase in FCR in T3 was still lower than 2.8, which signifies a good FCR. Interestingly, egg production was significantly increased in T3 on the last day of the experiment (p<0.05). The possible mechanism of increased egg production was discussed in the erythrocyte profile.

Erythrocyte Profile

Combined *C. aeruginosa* powder with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) or with *A. cordifolia* leaf powder significantly increased total erythrocytes count (p<0.05) (Table 2). The possible mechanism of action of the combined phytogenic additive on erythrocytes may be explained by the absorption of the bioactive components (phenolic and flavonoid) of the combined phytogenic in the small intestine, which then carried by circulation and reach the bone marrow in adult birds. In the bone marrow, the bioactive component might stimulate the erythropoietin hormone (Zheng *et al*., 2011), triggering the production of erythrocytes (Zhang *et al*., 2017). Additionally, the phenolic and flavonoid contents could increase the antioxidant status of the erythropoiesis-associated organs (liver, kidney, and bone marrow) and help protect those organs by

Table 4. Serum biochemistry of eight-month-old Japanese quail after phytogenic supplementation for 4-weeks

Variables	Treatments				*p*
	T0	T1	T2	T3	
Triglyceride (mg/dL)	1315.61 ± 478.54	1150.65 ± 553.18	1215.64 ± 432.65	1169.52 ± 370.78	0.86
HDL (mg/dL)	31.43 ± 7.15	32.19 ± 7.90	36.82 ± 11.04	31.13 ± 6.92	0.41
LDL (mg/dL)	67.83 ± 25.48	77.78 ± 18.49	80.61 ± 37.24	69.15 ± 16.32	0.62
Cholesterol (mg/dL)	174.12 ± 46.93	162.27 ± 34.40	192.30 ± 36.29	171.67 ± 51.43	0.47
Glucose (mg/dL)	153.81 ± 25.44^{a}	278.34 ± 81.26^{b}	327.61 ± 54.54^{c}	190.90 ± 26.43^{a}	0.00*
Uric acid (mg/dL)	4.14 ± 1.18^{a}	4.36 ± 1.48^{a}	5.47 ± 1.81^{ab}	6.66 ± 2.81^{b}	0.02*
Bilirubin (mg/dL)	0.16 ± 0.08	0.11 ± 0.07	0.14 ± 0.06	0.24 ± 0.22	0.12
Creatinine (mg/dL)	0.29 ± 0.04^{a}	0.35 ± 0.08^{b}	0.36 ± 0.03^{b}	0.37 ± 0.05^{b}	0.00*
ALT (U/L)	14.16 ± 10.69	15.92 ± 12.03	11.46 ± 5.87	12.50 ± 8.38	0.73
AST (U/L)	197.32 ± 104.55^{a}	295.66 ± 47.99^{b}	278.10 ± 99.89^{b}	283.82 ± 31.07^{b}	0.03*

Note: Each value is the average of ten replicate birds. Means in the same row with different superscripts differ significantly (p<0.05).
T0= Control (antibiotic-free feed with no additives), T1= antibiotic-free feed + 1% *Curcuma aeruginosa* powder; T2= antibiotic-free feed + 1% *C. aeruginosa* powder + 200 ppm curcumin, T3= antibiotic-free feed + 1% *C. aeruginosa* powder + 1% *Anredera cordifolia* leaf powder. ALT= alanine aminotransferase, AST= aspartate aminotransferase, HDL= high density lipoprotein, LDL= low density lipoprotein.

Table 5. Intestinal and liver histopathology of eight-month-old Japanese quail after phytogenic supplementation for 4-weeks

Variables	Treatments				*p*
	T0	T1	T2	T3	
Crypt depth (μm)	63.65 ± 10.67	61.44 ± 10.71	72.74 ± 15.54	74.30 ± 19.34	0.14
Height of villi (μm)	777.87 ± 180.38	766.03 ± 181.43	711.95 ± 119.98	767.64 ± 184.48	0.81
Intestinal inflammation	2.23 ± 0.32^{a}	1.30 ± 0.40^{b}	1.13 ± 0.28^{b}	2.23 ± 0.32^{a}	0.00*
Liver scoring	1.10 ± 0.23^{a}	1.00 ± 0.00^{a}	2.73 ± 0.34^{b}	1.10 ± 0.23^{a}	0.00*

Note: Each value is the average of ten replicate birds. Means in the same row with different superscripts differ significantly (p<0.05).
T0= Control (antibiotic-free feed with no additives), T1= antibiotic-free feed + 1% *Curcuma aeruginosa* powder; T2= antibiotic-free feed + 1% *C. aeruginosa* powder + 200 ppm curcumin, T3= antibiotic-free feed + 1% *C. aeruginosa* powder + 1% *Anredera cordifolia* leaf powder.
Intestinal inflammation Level: "1" Inflammatory cell infiltration 0%–25% of the entire visual field, "2" Inflammatory cell infiltration 26%–50% of the entire visual field, "3" Inflammatory cell infiltration 51%–75% of the entire visual field and "4" Inflammatory cell infiltration >75% of the entire visual field.
Liver Scoring: "1" Normal (polygonal cells appear, homogeneous red cytoplasm, clearly defined cell walls), "2" Parenchymatous degeneration (cell swelling accompanied by cloudy and granular cytoplasm), "3" Hydropic degeneration (swollen cells, fluid accumulation and there are many vacuoles) and "4" Necrosis (Permanent cell damage or cell death).

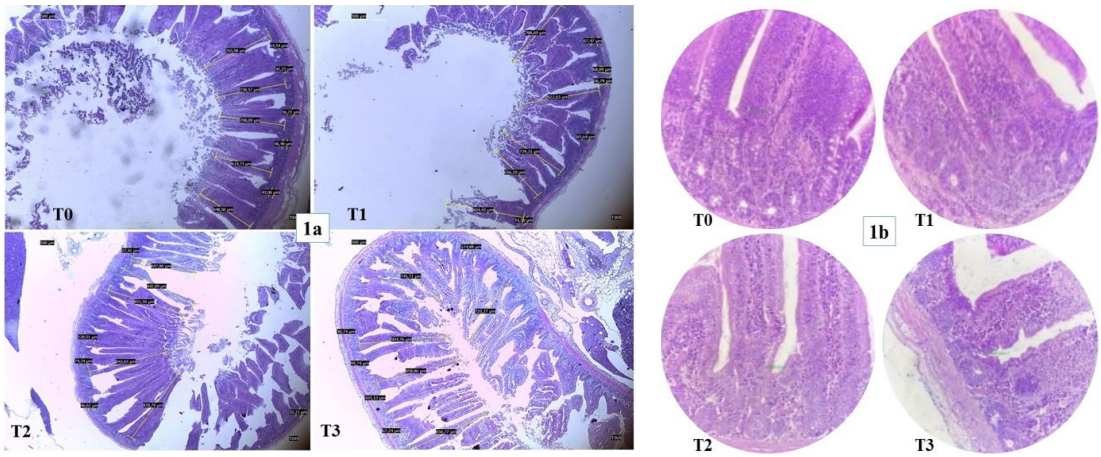

Figure 1. Intestinal histopathology of eight-month-old Japanese quails after phytogenic supplementation for 4-weeks (1a. Crypt depth and villi height with their values in Table 5, 1b. The intestinal inflammation level with the scoring in Table 5). T0= Control (antibiotic-free feed with no additives), T1= antibiotic-free feed + 1% *Curcuma aeruginosa* powder; T2= antibiotic-free feed + 1% *C. aeruginosa* powder + 200 ppm curcumin, T3= antibiotic-free feed + 1% *C. aeruginosa* powder + 1% *Anredera cordifolia* leaf powder.

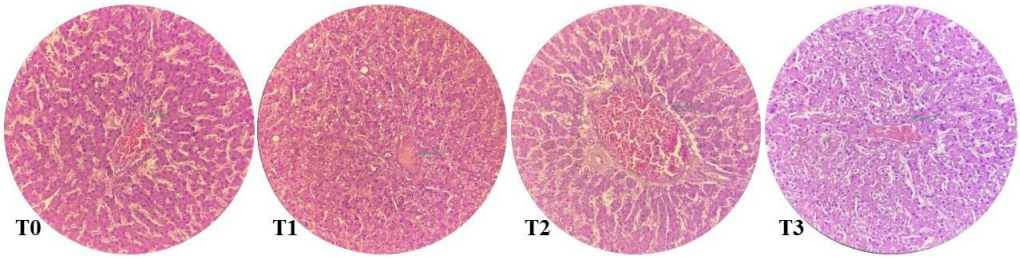

Figure 2. Liver histopathology of eight-month-old Japanese quails after phytogenic supplementation for 4-weeks. Liver scoring was given in Table 5. T0= Control (antibiotic-free feed with no additives), T1= antibiotic-free feed + 1% *Curcuma aeruginosa* powder; T2= antibiotic-free feed + 1% *C. aeruginosa* powder + 200 ppm curcumin, T3= antibiotic-free feed + 1% *C. aeruginosa* powder + 1% *Anredera cordifolia* leaf powder.

suppressing lipid peroxidation, scavenging free radicals, and subduing proinflammatory cytokines (Al-Khayri *et al.*, 2022; Farzaei *et al.*, 2018; Vargas *et al.*, 2018; Wang *et al.*, 2021; Zhang *et al.*, 2019). Although the bioactive components of the other studies, flavonoids formononetin, ononin, calycosin, and calycosin-7-O-b-Dglucoside (Zhang *et al.*, 2017; Zheng *et al.*, 2011) were different from the combined phytogenic additives used in this study, it may exert the same effect. Further studies are needed to test this possibility.

The lifespan of avian erythrocytes is 28–45 days, after which they grow old and are recycled (Matos & Morrisey, 2021). In the Japanese quail *Coturnix coturnix*, the mean survival of erythrocytes is 34 days (Scanes, 2022). The liver, lymph, bone marrow, and macrophages will take these circulating old erythrocytes and break them down into their components. An overhaul of old erythrocytes occurs with the decomposition of hemoglobin into globin and heme, which would become amino acids and iron, respectively. The iron is stored in the liver as ferritin, while iron in transferrin form is transported through the circulation for reuse in synthesizing red blood cells in the bone marrow (Scanes, 2022). The hemoglobin binds and transports oxygen and carbon dioxide. Erythrocyte count is aligned with hemoglobin level, as shown in Table 2, and hence, O_2 content (Scanes, 2022). Increased erythrocytes and hemoglobin are within the normal range, which improves oxygen supply to fulfill quail metabolism required during laying. Metabolism for egg synthesis or production is therefore supported, followed by an increase in egg production due to the combined supplementation of phytogenic additives shown in T2 and T3 (Table 4) at the end of the experiment.

Hematocrit is the percentage of red blood cells in the blood. Its level indicates the blood's ability to transport oxygen. When the level reaches above average, it may indicate a state of dehydration. This is due to decreased blood volume and increased erythrocytes, causing plasma leakage while the solid remains in the blood vessels (Edi *et al.*, 2020). However, if the number is below average, it may indicate anemia. Hematocrit is related to the viscosity of blood. Higher viscosity can increase blood flow resistance, increasing the liver's workload in pumping blood and interfering with perfusion (Lenz *et al.*, 2007). The hematocrit range in other Japanese quail studies was 22.75–51.33% (Agina *et al.*, 2017; Alagawany *et al.*, 2020; Anggraeni *et al.*, 2016; Olgun *et al.*, 2020; Wardiny *et al.*, 2012). The results that combining *C. aeruginosa* with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin), or *A. cordifolia*, increased the erythrocytes

number, hemoglobin, and hematocrit significantly without affecting the erythrocyte index (MCV, MCH, MCHC) is somewhat a novel and unique discovery. The erythrocyte index is used to determine anemia; therefore, as it is not affected and is within the normal range, it indicates that the quail's oxygen requirement is fulfilled and in good condition.

Leukocyte Profile

Birds have five types of leukocytes: lymphocytes, neutrophils, eosinophils, monocytes, and basophils. Their circulating concentrations can shift by physiological and pathological factors (Scanes, 2022). Leukocyte count in the control group (T0= 138.03 x 10^3/mm^3), as shown in Table 2, was higher than in other studies in Japanese quail aged between 6 to 20 weeks (10.56 – 25.50 10^3/mm^3) (Agina *et al.*, 2017; Scanes, 2022). The difference could be due to the older age of the quails in our study (32 weeks). Factors affecting the leukocyte number in animals include age, sex, environmental conditions (such as stress and antigen challenge), management, and nutrition, whose roles significantly affect leukocyte formation and immune response (Abdul-Majeed & Abdul-Rahman, 2021; Ayoola *et al.*, 2015; Koutsos & Klasing, 2014). This study demonstrates that combining *C. aeruginosa* with standardized *C. xanthorizza* extract (equal to 200 ppm curcumin) (T2) or with *A. cordifolia* (T3) significantly increased leukocyte number ($p<0.05$). Increased leukocyte number is a normal response to the stimulation of the immune system by antigens from pathogens or stress (Scanes, 2022). However, leucocytes comprised several subsets: lymphocytes, neutrophil/heterophil, and eosinophil.

Lymphocytes in birds (B and T cells) are the subsets of leukocytes that play roles in humoral and cell-mediated immunity, responding to and eliminating foreign antigens (Scanes, 2022). In this study, the absence of endoparasites means there was no antigen stimulation to the quail's lymphocytes (Johnson *et al.*, 2022). Therefore, the increased number in T2 and T3 could indicate that the combined *C. aeruginosa* with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) or *A. cordifolia* might stimulate lymphocyte formation. Lymphocyte number may be reduced following severe viral infection due to the interference of lymphocyte formation (lymphopoiesis) (Guo *et al.*, 2021). It is also sensitive to severe nutrient deficiency (Koutsos and Klasing, 2014). In this study, there was no endoparasite, viral infection, or nutrient deficiency; therefore, increased lymphocyte number (normal range) was most likely due to improved lymphocyte formation (lymphopoiesis). The mechanism of enhanced lymphocyte formation may follow the same path as red blood cell formation mediated by bioactive components, as explained earlier. Laying birds' production period is long; therefore, improved lymphocyte numbers within the upper normal range could benefit the birds.

The bird's neutrophils, known as heterophils, are the primary components of the innate immune system and the most common granulocytes in the inflammatory response to bacterial infections (Genovese *et al.*, 2013). They actively contribute to the inflammation of pathogens by migrating to the inflammation site and producing inflammatory cytokines (Juul-Madsen *et al.*, 2014). Their actions against pathogens are mediated by phagocytosis, antimicrobial peptide release, killing by oxidative burst, attracting lymphocytes, and exerting acute inflammatory response (Scanes, 2022). Their numbers increased because of stressors such as corticosterone, hypoxia, heat stress, transportation, and bacterial challenges (Scanes, 2022). Meanwhile, eosinophils eliminate parasites and respond to allergic substances (Yasuda & Koruda, 2019). Eosinophils also play a role in the wound-healing process. When the number of eosinophils increases, it indicates a faster healing process, while a reduced number indicates slower wound healing and repair (Coden & Berdnikovs, 2020). Table 2 shows that neutrophil and eosinophil numbers were not affected by phytogenic supplementation, suggesting that the active compounds of combining *C. aeruginosa* with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) or with *A. cordifolia* leaves did not cause an inflammatory nor allergic response to the quails.

Endoparasite

The absence of endoparasites in all groups, including the control birds, was unexpected, as egg-producing birds commonly harbor endoparasites (Murwani *et al.*, 2022). The absence of endoparasites could be related to sanitation management, which is done twice daily. Furthermore, drinking water analyses revealed zero *E. coli*. The absence of endoparasite infection benefited the egg-producing birds. A complete blood cell model was created to evaluate the relationship between parasite status, one of which was eosinophils. Activated eosinophils release helminthotoxic reactive oxygen species and granular proteins that can cause direct damage to the parasite and host tissue, modulating the immune response by releasing cytokines and chemokines (Kubas *et al.*, 2022).

Serum Biochemistry Profile

Combined *C. aeruginosa* Roxb with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) or with *A. cordifolia* had no significant effect ($p>0.05$) on serum lipid profile (triglycerides, HDL_{chol}, LDL_{chol}, and total cholesterol), bilirubin, and ALT. However, the serum glucose, uric acid, creatinine, and AST increased significantly ($p<0.05$).

The serum glucose level in other Japanese quail studies (Abdul-Majeed & Abdul-Rahman, 2021; Abbas *et al.*, 2017; Bhattacherjee *et al.*, 2021; García *et al.*, 2022; Jumadin *et al.*, 2022; Kabir, 2013; Kamil *et al.*, 2021; Krupakaran, 2013; Mutlu *et al.*, 2021) ranges between 193–450 mg/dL. Therefore, increased glucose level in T2 (327 mg/dL in T2) was still within the normal range. In this study, elevated serum glucose by phytogenic additives may be due to enhanced glucose absorption from the digestive tract into the bloodstream. Following this, it would be utilized to generate energy (in the form of

ATP) to fuel the metabolism of phytogenic additives (Bešlo *et al.*, 2023; Murwani, 2021; Stromsnes *et al.*, 2021).

Uric acid is a waste product of metabolism that acts as an antioxidant in preventing lipid peroxidation (Lima *et al.*, 2015). The flavonoid of the phytogenic additive can inhibit the action of free radicals and prevent cell damage. The uric acid metabolism converts allantoin by the urate oxidase enzyme into allantoic, urea, ureidoglycolic, glyoxylic, and urea (El Ridi &Tallima, 2017). Serum uric acid is excreted in the urine as long as renal function is not compromised, while feeds low in sodium (Na) cause reabsorption (Xu *et al.*, 2017). The reabsorption of uric acid in the proximal tubule increases the concentration of uric acid, which can cause several diseases, such as chronic kidney disease and hyperlipidemia (Xu *et al.*, 2017). Failure of the kidney system to secrete uric acid can cause the accumulation of white crystals in the tissue. Increased uric acid can also cause deposition in the blood, urine, and tissues (Dissanayake *et al.*, 2020). The uric acid levels in T0, T1, T2, and T3 range between 4.14–6.66 mg/dL, while the values in other Japanese quail studies were 4.34–4.65 mg/dL (Mokhtarzadeh *et al.*, 2022; Asl *et al.*, 2023; Mutlu *et al.*, 2021). Increased uric acid in T2 and T3 (combined phytogenic) likely indicated an increased metabolic process to excrete bioactive components into uric acid.

Serum creatinine is an indicator that determines the glomerular filtration rate and kidney damage; increased serum creatinine and urea could indicate kidney damage (Dally *et al.*, 2020), depending on their values. Although combined 1% *C. aeruginosa* Roxb with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) or with 1% *A. cordifolia* significantly increased ($p<0.05$, 0.35–0.37 mg/dL) serum creatinine, the values in other Japanese quail studies were 0.09–4.23 mg/dL (Agina *et al.*, 2017; Al-Shammari *et al.*, 2024; Hamidipoor *et al.*, 2015; Mutlu *et al.*, 2021). Therefore, increased creatinine and uric acid levels with the phytogenic addition remained within the normal range. It also indicated increased kidney activity to metabolize the active phytogenic components (flavonoid, saponin, and tannin). It is known that secondary metabolites such as polyphenols from phytogenic substances are processed by the liver and kidney. Subsequently, the polyphenolic substance is converted into a more hydrophilic form to enable their excretion via bile or urine (Bešlo *et al.*, 2023; Stromsnes *et al.*, 2021).

Serum ALT and AST are indicators of liver cell damage or hepatocyte integrity (Murwani *et al.*, 2022). These enzymes catalyze processes essential for synthesizing urea and gluconeogenesis (Kallas *et al.*, 2021). They are found in the kidney, liver, and skeletal muscles, and to a lesser degree in the spleen, small intestine, and brain, despite the liver having the highest concentration (Moriles & Azer, 2022). These enzymes can leak and become apparent with even the slightest disturbance in the permeability of the hepatocyte membrane, which could be a sign of cell death (Guicciardi *et al.*, 2013).

Serum ALT and AST in other Japanese quail studies ranges from 18.3–146 U/L and 31.25–285.60 U/L, respectively (Abbas *et al.*, 2017; Arif *et al.*, 2022; Asl *et al.*, 2023; Devarasetti *et al.*, 2016; El-Heck *et al.*, 2023; Karimi *et al.*, 2020; Majrashi, 2022; Mokhtarzadeh *et al.*, 2022; Prakash *et al.*, 2017; Sakamoto *et al.*, 2018). Combining *C. aeruginosa* Roxb rhizome with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) or 1% *A. cordifolia* had no significant effect on ALT levels. On the other hand, the phytogenic addition significantly increased the serum AST. Aspartate aminotransferase (AST) is a transaminase enzyme found in the liver, kidneys, skeletal muscles, and lungs (Ndrepepa, 2021), while alanine transferase (ALT) is an enzyme used in protein metabolism in the liver (Yang *et al.*, 2009). ALT and AST measurements are used to determine the presence of abnormalities in the liver cells (Yang *et al.*, 2014). An increase in AST levels, without an increase in ALT, indicated an extrahepatic source (Center, 2023). However, in particular, in animals, AST could be a more sensitive indicator of liver injury (Center, 2023). This study could indicate elevated metabolic activities related to phytogenic bioactive substances in the liver and kidney. These metabolic activities aligned with the increased uric acids in T2 and T3 and creatinine concentrations in T1, T2, and T3, indicating higher metabolic activity in the kidney due to phytogenic metabolism.

Intestinal and Liver Histopathology

Phytogenic addition in the quail's diet did not affect intestinal villi height and crypt depth. However, it significantly reduced inflammation ($p<0.05$). Intestinal inflammation in T1 (single phytogenic 1% *C. aeruginosa* Roxb rhizome powder) and T2 (combined with 200 ppm *C. xanthorizza* extract) was lower than in the control group, while T3 was comparable to the control group. In the control group, intestinal inflammation could be related to the intestine's role in digestion. The intestinal epithelium experiences constant aggression from the harsh lumen environment and mechanical abrasion that causes high levels of cell death, so all epithelial cells are lost daily in the intestine (Creff *et al.*, 2021). Following injury, the gut employs several responses to help reinstate intestinal epithelial integrity. Restitution is the initial rapid period of re-epithelialization and is a crucial component of intestinal epithelial wound healing that occurs in minutes to hours following damage. Subsequent restitution is the regenerative response, which occurs in the hours to days following injury and is linked to increased proliferation and restitution. The mRNA of cytokine TGF-β1 is increased within 2 hours following wounding, in line with the increased crypt stem cells and improved epithelial barrier function (Fink & Wrana, 2023). Compared to control, low intestinal inflammation with phytogenic additives could indicate better maintenance of the epithelial barrier due to a harsh intestinal environment. So overall, it benefits the quail's small intestinal condition.

The liver is a central organ for metabolizing carbohydrates, fats, proteins, vitamins, and minerals and detoxification (Simon *et al.*, 2020; Zaefarian *et al.*, 2019). Combined *C. aeruginosa* Roxb with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) (T2)

significantly increased liver scoring ($p<0.05$). Increased liver scoring in T2 could be due to the elevation of the liver's metabolic process to convert combined phytogenic bioactive (alkaloid, saponin, flavonoid, polyphenol, and curcumin) into more polar compounds so that it can be excreted. However, liver scoring in T3 is equal to control T0 and T1 (single phytogenic), suggesting that *A. cordifolia* leaf powder could prevent damage to liver cells. Polyphenols in *A. cordifolia* could have significant hepatoprotection by inhibiting inflammation and oxidative stress, downregulating the expression of NF-κB and CYP2E1 (Li *et al.,* 2018).

CONCLUSION

Overall, combining phytogenic *C. aeruginosa* Roxb with *C. xanthorizza* extract (equal to 200 ppm standardized curcumin) or 1% *A. cordifolia* leaf powder given to laying quails with an excellent standard diet, quality drinking water, and good sanitation could improve erythrocytes, hemoglobin, hematocrit, leukocytes, lymphocytes and reduce normal intestinal inflammation, benefiting the producing birds. The combined *C. aeruginosa* Roxb with the *A. cordifolia* increased egg production at the end of four-week experiments. Increased serum glucose, uric acid, creatinine, and AST indicated an elevated metabolic activity of phytogenic bioactive substances in the liver and kidney. This phytogenic still needs further research to be used as a commercial feed additive.

CONFLICT OF INTEREST

We declare no conflict of interest with any financial, personal, or other relationships with other people or organizations related to the material discussed in the manuscript.

ACKNOWLEDGEMENT

This study was supported by LPPM (Institute of Research and Community Services Universitas Diponegoro, Semarang, Indonesia [RPI competitive grant No. 569-84/UN7.D2/PP/VII/2022]. Thank you to Berliana Putri Aulia Dewi for formatting the manuscript.

REFERENCES

Abbas, R. J., K. Ch. K. Al-Salhie, & S. K. M. Al-Hammod. 2017. The effect of using different levels of pomegranate (*Punica granatum*) peel powder on productive and physiological performance of Japanese quail (*Coturnix coturnix japonica*). Livest. Res. Rural. Dev. 29:1-7. http://www.lrrd.org/lrrd29/12/rj.a29231.html

Abdul-Majeed, A. F. & S. Y. Abdul-Rahman. 2021. Impact of breed, sex and age on hematological and biochemical parameters of local quail. Iraqi J. Vet. Sci. 35:459-464. https://doi.org/10.33899/ijvs.2020.126960.1432

Al-Khayri, J. M., G. R. Sahana, P. Nagella, B. V. Joseph, F. M. Alessa, & M. Q. Al-Mssallem. 2022. Flavonoids as potential anti-inflammatory molecules: A review. Molecules. 27:2901. https://doi.org/10.3390/molecules27092901

Arif, M., A. Ur Rehman, K. Naseer, S. H. A. Hafez, F. M. Almiderej, M. T. El-Saadony, M. E. A. El-Heck, A. E. Taha, S. S. Elnesr, H. M. Salem, & Alagawany. 2022. Effect of Aloe vera and clove powder supplementation on growth performance, carcass and blood chemistry of Japanese quails. Poult. Sci. 101:101702. https://doi.org/10.1016/j.psj.2022.101702

Agina, O. A., W.S. Ezema, & E. M. Iwouha. 2017. The haematology and serum biochemistry profile of adult Japanese quail (*Coturnix coturnix japonica*). Not. Sci. Biol. 9:67–72. https://doi.org/10.15835/nsb919928

Alagawany, M., M. Nasr, A. Al-Abdullatif, R. A. Alhotan, M. M. Azzam, & F. M. Reda. 2020. Impact of dietary cold-pressed chia oil on growth, blood chemistry, haematology, immunity and antioxidant status of growing Japanese quail. Ital. J. Anim. Sci. 19:896-904. https://doi.org/10.1080/1828051X.2020.1807420

Alba, T. M., C. M. G. de Pelegrin, & A. M. Sobottka. 2020. Ethnobotany, ecology, pharmacology, and chemistry of *Anredera cordifolia* (Basellaceae): A review. Rodriguesia. 71: e01042019. https://doi.org/10.1590/2175-7860202071060

Al-Shammari, K. I. A., S. J. Zamil, & J. Batkowska. 2024. The antioxidative influence of dietary creatine monohydrate and L-carnitine on laying performance, egg quality, ileal microbiota, blood biochemistry, and redox status of stressed laying quails. Poult. Sci. 103:103166. https://doi.org/10.1016%2Fj.psj.2023.103166

Akarchariya, N., S. Sirilun, J. Julsrigival, & S. Chansakaowa. 2017. Chemical profiling and antimicrobial activity of essential oil from *Curcuma aeruginosa* Roxb., *Curcuma glans* K. Larsen & J. Mood and *Curcuma* cf. *xanthorrhiza* Roxb. collected in Thailand. Asian. Pac. J. Trop. Biomed. 7:881-885. https://doi.org/10.1016/j.apjtb.2017.09.009

Anggraeni, N., A. Farajallah, & Astuti, D. A. 2016. Blood profile of quails (*Coturnix coturnix japonica*) fed ration containing silkworm pupae (*Bombyx mori*) powder extract. Med. Pet. 39:1–8. https://doi.org/10.5398/medpet.2016.39.1.1

Ashour, E. A., M. S. El-Kholy, M. Alagawany, M. E. Abd El-Hack, L. A. Mohamed, A. E. Taha, A. I. El Sheikh, & V. Laudadio. 2020. Effect of dietary supplementation with *Moringa oleifera* leaves and/or seeds powder on production, egg characteristics, hatchability and blood chemistry of laying Japanese quails. Sustainability 12:2463. https://doi.org/10.3390/su12062463

Asl, R. M., A. Nobakht, V. Palangi, A. Maggiolino, & G. Centoducati. 2023. The effect of using bovine colostrum and probiotics on performance, egg traits, blood biochemical and antioxidant status of laying Japanese quails. Animals. 13:1-13. https://doi.org/10.3390/ani13132166

Ayoola, A. A., L. T. Egbeyale, O. M. Sogunle, D. A. Ekunseitan, & A. A. Adeyemi. 2015. Effects of age and sex on haematological and serum biochemistry in Japanese quails. Bull. Anim. Health. Prod. Afr. 63:43-21. https://bit.ly/3UvBOZe

Aziz, J. A., N. B. Saidi, R. Ridzuan, A. K. S. Mohammed, M. A. Aziz, A. Kadir, M., N. A. P. Abdulah, S. Hussein, & H. Yusoff. 2021. Chemical profiling of *Curcuma aeruginosa* Roxb. essential oil and their antimicrobial activity against pathogenic microbes. J. Essent. Oil. Bear. Pl. 24:1059-1071. http://dx.doi.org/10.1080/0972060X.2021.1971570

Bhattacherjee, A., P. K. Mohanty, & B. K. Mallik. 2021. Hematological and cytometrical parameters of Japanese quails *Coturnix coturnix japonica*, Temminck & Schlegel, 1848 as per sex and different stages of growth. Research Square. https://doi.org/10.21203/rs.3.rs-722063/v1

Bešlo, D., N. Golubić, V. Rastija, D. Agić., M. Karnaš, D. Šubarić, & B. Lučić. 2023. Antioxidant activity, metabolism, and bioavailability of polyphenols in the diet of animals. Antioxidants 12:1141. https://doi.org/10.3390/antiox12061141

Burapan, S., M. Kim, Y. Paisooksantivatana, B. E. Eser, & J. Han. 2020. Thai *Curcuma* species: Antioxidant

and bioactive compounds. Foods 9:1219. https://doi.org/10.3390/foods9091219

Center, S. A. 2023. Enzyme activity in hepatic disease in small animals. MSD Manual Veterinary manual. https://msdmnls.co/49pcick. [December 13, 2023]

Coden, M. E. & S. Berdnikovs. 2020. Eosinophils in wound healing and epithelial remodeling: Is coagulation a missing link? J. Leukoc. Biol. 108: 93-103. https://doi.org/10.1002/jlb.3mr0120-390r

Creff, J., L. Malaquin, & A. Besson. 2021. In vitro models of intestinal epithelium: Toward bioengineered systems. J. Tissue Eng. 1:1-16. https://doi.org/10.1177/2041731420985202.

Dally, M., J. Butler-Dawson, R. J. Johnson, L. Krisher, D. Jaramillo, K. L. Newman, & L. S. Newman. 2020. Creatinine fluctuations forecast cross-harvest kidney function decline among sugarcane workers in Guatemala. Kidney. Int. 5: 1558-1566. https://doi.org/10.1016/j.ekir.2020.06.032

Devaraj, S., S. Ismail, S. Ramanathan, & M. F. Yam. 2014. Investigation of antioxidant and hepatoprotective activity of standardized *curcuma xanthorrhiza* rhizome in carbon tetrachloride-induced hepatic damaged rats. Sci. World. J. 1:1–9. https://doi.org/10.1155/2014/353128

Devarasetti, A. K., E. S. A. Kumar, & K. V. Ramana. 2016. Supplementation of dietary yeast on body performance in Japanese quails. Int. J. Vet. Sci. Anim. Husb. 1:27-29.

Dissanayake, L. V., D. R. Spires, O. Palygin, & A. Staruschenko. 2020. Effects of uric acid dysregulation on the kidney. Am. J. Physiol. Renal. Physiol. 318: F1252-F1257. https://doi.org/10.1152/ajprenal.00066.2020

El-Heck, M. E. A., M. F. A. Elmaati, W. F. Abusudah, O. F. Awlya, N. H. Almohmadi, W. Fouad, H. S. Mohamed, I. M. Youssef, N. A. Al-Gabri, S. I. Othman, A. A. Allam, A. E. Taha, G. T. Isaias, & A. M. Mansour. 2023. Consequences of dietary cinnamon and ginger oils supplementation on blood biochemical parameters, oxidative status, and tissue histomorphology of growing Japanese quails. Poult. Sci. 103:103314. https://doi.org/10.1016/j.psj.2023.103314

El Ridi, R. & H. Tallima. 2017. Physiological functions and pathogenic potential of uric acid: A review. J. Adv. Res. 8:487-493. https://doi.org/10.1016%2Fj.jare.2017.03.003

Farzaei, M. H., M. Zobeiri, F. Parvizi, F. F. El-Senduny, I. Marmouzi, E. Coy-Barrera, & M. Abdollahi. 2018. Curcumin in liver diseases: a systematic review of the cellular mechanisms of oxidative stress and clinical perspective. Nutrients 10:855. https://doi.org/10.3390/nu10070855

Fink, M. & J. L. Wrana. 2023. Regulation of homeostasis and regeneration in the adult intestinal epithelium by the TGF-β superfamily. Dev. Dyn. 252:445-462. https://doi.org/10.1002/dvdy.500

Fitria, R., D. S. H. Seno, B. P. Priosoeryanto, & W. Nurcholis. 2019. Volatile compound profiles and cytotoxicity in essential oils from rhizome of *Curcuma aeruginosa* and *Curcuma zanthorrhiza*. Biodiversitas 20:2943–2948. https://doi.org/10.13057/biodiv/d201024

García, A. S., B. Sevim, O. Olgun, & A. S. Gökmen. 2022. Effects of different inorganic selenium levels in laying quails (*Coturnix coturnix japonica*) diets on performance, egg quality, and serum biochemical parameters. Veterinaria México OA 9: e1046. https://doi.org/10.22201/fmvz.24486760e.2022.1046

Genovese, K. J., H. He, C. L. Swaggerty, & M. H. Kogut. 2013. The avian heterophil. Dev. Comp. Immunol. 41:334-340. https://doi.org/10.1016/j.dci.2013.03.021

Guicciardi, M. E., H. Malhi, J. L. Mott, & G. J. Gores. 2013. Apoptosis and necrosis in the liver. Compr. Physiol. 3: 977–1010. https://doi.org/10.1002/cphy.c120020

Guo, Z., Z. Zhang, M. Prajapati, & Y. Li. 2021. Lymphopenia Caused by Virus Infections and the Mechanisms Beyond Viruses 13:1876. https://doi.org/10.3390%2Fv13091876

Hamidipoor, F., H. R. Pourkhabbaz, M. Banaee, & S. Javanmardi. 2015. Sub-lethal toxic effects of deltamethrin on blood biochemical parameters of Japanese quail, *Coturnix japonica*. Toxicol. Environ. Chem. 97:1217–1225. http://dx.doi.org/10.1080/02772248.2015.1093131

Herve, T., K. J. Raphaël, N. Ferdinand, N. V. Herman, N. M. W. Marvel, T. C. D. Alex, & F. T. L. Vitrice. 2019. Effects of ginger (*Zingiber officinale, Roscoe*) essential oil on growth and laying performances, serum metabolites, and egg yolk antioxidant and cholesterol status in laying Japanese quail. Vet. Med. J. 13:7857504. https://doi.org/10.1155/2019/7857504

Hestianah, E. P., I. Kusumawati, L. T. Suwanti, & S. Subekti. 2014. Toxic compounds of *Curcuma aeruginosa* causes necrosis of mice hepatocytes. Universa Medicina 33:118–126. https://doi.org/10.18051/UnivMed.2014.v33.118-125

Indarto, I., W. Narulita, B. S. Anggoro, & A. Novitasari. 2019. Antibacterial activity of binahong leaf extract against propionibacterium acnes. Biosphere: Tadris. J. Biol. 10: 67–78. http://dx.doi.org/10.24042/biosfer.v10i1.4102

Johnson, T. E., C. E. Gonzalez, Rollins, Dale, J. G. Cross, & R. S. Luna. 2022. Histopathological Analysis of Quails in the Trans-Pecos Ecoregion of Texas. National Quail Symposium Proceedings 9:185–191. https://doi.org/10.7290/nqsp09qIw1

Jose, S. & T. D. Thomas. 2014. Comparative phytochemical and antibacterial studies of two indigenous medicial plants *Curcuma caesia* Roxb. and *Curcuma aeruginosa* Roxb. Int. J. Green. Pharm. 8:65–71. http://dx.doi.org/10.4103/0973-8258.126828

Jumadin, L., H. Maheshwari, N. Ulupi, & A. S. Satyaningtijas. 2022. Physiological and productivity performances of Japanese Quails supplemented with Cassava Leaf Paste. Trop. Anim. Sci. J. 45: 460-466. https://doi.org/10.5398/tasj.2022.45.4.460

Juul-Madsen, H. R., B. Viertlboeck, S. Hartle, A. L. Smith, & T. W. Gobel. 2014. Chapter 7 - Innate Immune Responses. In: Schat, K. A., B. Kaspers, & P. Kaiser. 2nd ed. Avian Immunology. Acad Press. Cambridge, USA. p. 121–147.

Kabir, A. 2013. Blood chemistry analyses of Japanese quail (*Coturnix coturnix Japonica*). J. Agri. Sci. 3:132-136. https://bit.ly/3HOatKm

Kalas, M. A., L. Chavez, M. Leon, P. T. Tawessedt, & S. Surani. 2021. Abnormal liver enzymes: A review for clinicians. World. J. Hepatol. 13:1688-1698. https://doi.org/10.4254/wjh.v13.i11.1688

Kamil, Y. M., Th. Katab, & A. B. M. Mohammed. 2021. Effect of supplementing laying Japanese quail (*Coturnix coturnix japonica*) diets with amla and green tea extracts on the product performance and biochemical parameters. IOP Conf. Ser.: Earth Environ. Sci. 761:012109. http://doi.org/10.1088/1755-1315/761/1/012109

Karimi, O., R. M. Mofidi, & M. S. Saeidabadi. 2020. Impact of turmeric *Curcuma longa* on the body weight and liver function of Japanese quails exposed to dietary aflatoxins. Iranian. J. Toxicol. 14:115-122. http://dx.doi.org/10.32598/ijt.14.2.412

Koutsos, E. A. & K. C. Klasing. 2014. Factors modulating the Avian Immune system. In: Schat K. A., B. Kaspers, & P. Kaiser (Eds.). 2nd ed. Avian Immunology. Acad. Press, Amsterdam. Pp.299-313.

Krupakaran, R. P. 2013. Serum biochemical profile of Japanese quails (*Coturnix coturnix japonica*). Indian. J. Fundam. Appl. Life. Sci. 3:182-183. https://bit.ly/42ARjRQ

Kubas, E. A., J. R. Fischer, & E. N. Hales. 2022. Endoparasitism of Golden Retrievers: prevalence, risk factors, and associated clinicopathologic changes. PLoS ONE 17:e0263517. https://doi.org/10.1371/journal.pone.0263517

Kusumanti, E. & R. Murwani. 2018. Reduction of fecal parasites by *Arecha catechu L.* seed and *Anredera cordifolia (Ten) Steenis* leaves powder in laying hens. IOP Conf. Ser.: Earth Environ. Sci. 116:012102. http://dx.doi.org/10.1088/1755-1315/116/1/012102

Leliqia, N. P., E. Y. Sukandar, & I. Firdrianny. 2017. Overview of efficacy, savety and phytochemical study of *Anredera cordifilia (Ten) Steenis*. PharmacologyOnLine. 1:124-131. https://bit.ly/49svExf

Lenz, C., A. Rebel, K. F. Waschke, R. C. Koehler, & T. Frietsch. 2007. Blood viscosity modulates tissue perfusion – sometimes and somewhere. Transfus. Altern. Transfus. Med. 9:265–272. https://doi.org/10.1111%2Fj.1778-428X.2007.00080.x

Lima, W. G., M. E. S. M. Santos, & V. E. Chaves. 2015. Uric acid as a modulator of glucose and lipid metabolism. Biochimie. 116:17-23. https://doi.org/10.1016/j.biochi.2015.06.025

Li, S., H. Y. Tan, N. Wang, F. Cheung, M. Hong, & Y. Feng. 2018. The potential and action mechanism of polyphenols in the treatment of liver diseases. Oxid. Med. Cell. Longev. ID 394818

Livestock & Animal Health. 2020. Statistik Peternakan dan Kesehatan Hewan. Kementerian Pertanian I, Jakarta, Indonesia.

Majrashi, K. A. 2022. Effects of supplementing quails' (*Coturnix japonica*) diets with a blend of clove (*Syzygium aromaticum*) and black cumin (*Nigella sativa*) oils on growth performance and health aspects. Life. 12:1-10. https://doi.org/10.3390/life12111915

Maksudi, M., F. Manin, S. Wigati, & A. Insulsyawati. 2018. Effects of phytobiotic of *Curcuma aeruginosa*, *Curcuma longa* and *Zingiber officinale* on the performance and carcass quality in broiler. J. Ilmiah Ilmu – Ilmu Peternakan. 21:78–85. https://dx.doi.org/10.22437/jiiip.v21i2.6772

Marlani, H. P. E. K., E. Kusumanti, & R. Murwani. 2017. *Arechaatechu* L. seed and *Anredera cordifolia (Ten) Steenis* leaf powder supplementation reduced serum transaminase in laying hens. Livest. Res. Rural. Dev. 29:1–5. https://doi.org/10.1080%2F23144599.2022.2090732

Maryana, D., R. Malaka, & F. Maruddin. 2019. Antibacterial activity of pasturized milk supplemented with binahong leaf extract (*Anredera cordifilia (Ten) Steenis*) and sucrose toward *Escherichia coli* and *Staphylococcus aereus*. IOP Conf. Ser.: Earth Environ. Sci. 247:012065. https://doi.org/10.1088/1755-1315/247/1/012065

Mat, K., N. A. S. Mohamad, N. D. Rusli, M. M. Rahman, C. H. Hasnita, S. M. Al-Amsyar, & M. Mahmud. 2021. Preliminary study on the effect of feeding Black Soldier Fly Larvae (BSFL) on growth and laying performance of Japanese Quail (*Cortunix japonica*). Int. J. Agric. Technol. 17:977-986. http://hdl.handle.net/123456789/2036

Matos, R. D. & J. K. Morrisey. 2022. Case 26.6 - Marek's Disease. In: Orsini, J. A., N. S. Grenager and A. de Lahunta. (Ed). Comparative veterinary anatomy a clinical approach. Acad Press, Elsevier, USA. https://doi.org/10.1016/B978-0-323-91015-6.00126-6

Mokhtarzadeh, S., A. Nobakht, Y. Mehmannavaz, V. Palangi, H. Eseceli, & M. Lackner. 2022. Impacts of continuous and intermittent use of bovine colostrum on laying Japanese quails: edd performance and traits, blood biochemical and antioxidant status. Animals 12:1-9. https://doi.org/10.3390/ani12202811

Moriles K. E. & S. A. Azer. 2022. Alanine Amino Transferase. In: StatPearls, Treasure Island (FL). PMID: 32644704. https://www.ncbi.nlm.nih.gov/books/NBK559278/. Access 13th December 2023.

Murtini, S., R. Murwani R, F. Satrija, & E. Handayani. 2010. Anti Marek's virus activity of *Scurrula oortiana* (Tea Mistletoe) stem extract in embryonated chicken egg. Int. J. Poult. Sci. 9:879–885. https://doi.org/10.3923/ijps.2010.879.885

Murwani, R. & A. Bayuardhi. 2007. Broilers serum cholesterol and glutamic oxaloacetic transaminase and their relation to antibiotic in feed and medication programs in four broiler producers in Semarang Region-Central Java, Indonesia. J. Int. Poult. Sci. 6:266–270. http://dx.doi.org/10.3923/ijps.2007.266.270

Murwani, R. 2008a. Aditif Pakan, Aditif Alami Pengganti Antibiotika (Feed Additives, Natural Additives to Replace Antibiotics). Unnes Press, Semarang.

Murwani, R. 2008b. Effect of corn or sorghum in combination with soybean meal or mungbean as feed ingredients on the serum antibody titers to NDV vaccine in broiler chickens. Int. J. Poult. Sci. 7:497–501. http://dx.doi.org/10.3923/ijps.2008.497.501

Murwani, R. 2021. Buku Ajar Biokimia (Biochemistry Text Book). BP UNDIP, Semarang.

Murwani, R., E. Kusumanti, & E. N. Naumova. 2022. *Areca catechu L.* and *Anredera cordifolia (Ten) Steenis* supplementation reduces faecal parasites and improves caecal histopathology in laying hens. Int. J. Vet. Sci. Med. 10:52–63. https://doi.org/10.1080/23144599.2022.2090732

Mustariani, B. A. A., A. Izuddin, D. M. Hasyim, & I. Batubara. 2017. Uji toksisitas dan aktivitas antimakan ekstrak rimpang temu hitam (*Curcuma aeruginosa* Roxb). J. Farmasetis 6:1–8. http://dx.doi.org/10.32583/farmasetis.v6i1.262

Mutlu, S. I., Y. Baykalir, M. A. Zman, & U. G. Simsek. 2021. The effects of dietary supplementation of olive leaf extract and eggshell with membrane on performance, egg quality, blood biochemical, and bone parameters in laying Japanese quail. Ankara. Univ. Vet. Fak. Derg. 68:251-258. http://dx.doi.org/10.33988/auvfd.717013

Ndrepepa, G. 2021. Aspartate aminotransferase and cardiovascular disease—a narrative review. J. Lab. Precis. Med. 6(6). https://doi.org/10.21037/jlpm-20-93

Nurcholis, W., N. Khumaida, M. Syukur, & M. Bintang. 2017. Evaluation of free radical scavenging activity in ethanolic extract from promising accessions of *Curcuma aeruginosa* Roxb. Molekul. 2:25–29. http://dx.doi.org/10.20884/1.jm.2017.12.2.350

Olgun, O., A. Yıldız, & Şentürk, E. T. 2020. The effect of supplementation of organic copper to commercial quail diets on performance, egg quality and haematological parameters. Turkish J. Agric. Food Sci. Technol. 8: 1517-1521. https://doi.org/10.24925/turjaf.v8i7.1517-1521.3390

Özbilgin, A. & K. Kara. 2023. Effect of adding lavender oil to laying quail diets on performance, egg quality, oxidative status, and fatty acid profile. Trop. Anim. Health. Prod. 55:1-10. https://doi.org/10.1007/s11250-023-03596-2

Prakash, S., J. Palod, R. K. Sharma, & S. K. Singh. 2017. Effect of graded levels of nucleotide supplementation on certain serum biochemical parameters in Japanese quails. Indian J. Anim. Res. 51:93–96. http://dx.doi.org/10.18805/ijar.8411

Pramono, S., F. H. Arifah, F. H. Pribadi, & A. E. Nugroho. 2018. Hepatoprottective activity of *Curcuma xanthorrhiza* Roxb. Paracetamol induced liver damage in rats and correlation with their chemical compounds. Thai. J. Pharm. Sci. 42: 138–142. https://digital.car.chula.ac.th/tjps/vol42/iss4/3/

Rahmat, E., J. Lee, & Y. Kang. 2021. Javanese Turmeric (*Curcuma xanthorrhiza* Roxb.): ethnobotany, phytochemistry, biotechnology, and pharmacological activities. Evid. Based Complementary Altern. Med. 13:1-15. https://doi.org/10.1155/2021/9960813

Sari, A. P. & U. Supratman. 2022. Mini-Review: Phytochemistry and biological activities of *Curcuma aeruginosa* (Roxb.). Indones. J. Chem. 2022 :576–598. http://dx.doi.org/10.22146/ijc.70101

Sari, M. K., B. S. Tumangger, B. J. Sorbakti, F. Helmalia, & Fadhliani. 2020. Effectiveness of the binahong leaf extract

(*Anredera cordifolia*) in devoting bacterial growth Vibrio cholerae in vitro. IOP Conf Ser.: Mater. Sci. Eng. 725:012073. http://dx.doi.org/10.1088/1757-899X/725/1/012073

Sakamoto, M. I., A.E. Murakami, A.M. Fernandes, I.C. Ospina-Rojas, K.C. Nunes, & A.K. Hirata. 2018. Performance and serum biochemical profile of Japanese quail supplemented with silymarin and contaminated with aflatoxin B1. Poult. Sci. 97:159-166. https://doi.org/10.3382/ps/pex277

Scanes, C. G. 2022. Blood. In: Scanes, C. G. & S. Dridi. (Ed.). 7th ed Sturkie's Avian Physiology. Acad Press, Elsevier, USA.

Septaningsih, D. A., L. K. Darusman, F. M. Afendi, & R. Heryanto. 2018. Liquid chromatography-mass spectrometry (LC-MS) fingerprint combined with chemometrics for identification of metabolites content and biological activities of C*urcuma aeruginosa*. Indonesia. J. Chem. 18:43–52. https://doi.org/10.22146/ijc.25456

Setyati, W., S. Subagiyo, R. Pramesti, & D. Pringgenies. 2019. Effectiveness of herbal extract (*Piper retrofractum, Curcuma aeruginosa,* and *Curcuma xanthorrhiza*) as immunomodulator in non-specific immunity system of tiger grouper (*Epinephelus fuscoguttatus*) against infection from *Vibrio alginolyticus* and *Vibrio parah*. Sci. Technol. Indonesia. 4:94-100. https://doi.org/10.26554/sti.2019.4.4.94-100

Simoh, S., S. Y. Shin, F. A. Rahim, & M. Aizuddin. 2018. Comparative analysis of metabolites and antioxidant potentials from different plant parts of *Curcuma aeruginosa* Roxb. Sains Malaysiana 47:3031–3041. http://dx.doi.org/10.17576/jsm-2018-4712-13

Simon, J., M. C. Andrés, N. G. Usandizaga, M. S. Maciá, & M. L. M. Chantar. 2020. Nutraceutical Properties of Polyphenols against Liver Diseases. Nutrients. 12:3517. http://dx.doi.org/10.3390/nu12113517.

Stromsnes, K., R. Lagzdina, G. Olaso-Gonzalez, L. Gimeno-Mallenc, & J. Gambini. 2021. Pharmacological properties of polyphenols: bioavailability, mechanisms of action, and biological effects in in vitro studies, animal models, and humans. Biomed. 9:1074. https://doi.org/10.3390/biomedicines9081074

Sukandar, E. Y., D. Safitri, & N. N. Aini. 2016. The study of ethanolic extract of binahong leaves (*Anredera cordifilia (Ten) Steenis*) and mulberry leaves (*Morus Nigra L.)* in combination on hyperlipidemic-induced rats. Asian J. Pharm. Clin. Res. 9:288-292. http://dx.doi.org/10.22159/ajpcr.2016.v9i6.14412

Sukowati Y. K., A. Johan, & R. Murwani. 2019. Ethanol extracts of *Ficus carica* fruit and leaf normalize high serum lipid profile, TNF-α, and MDA due to high fat diet in Sprague Dawley rat. Curr. Res. Nutr. Food Sci. 7:772–782. http://dx.doi.org/10.12944/CRNFSJ.7.3.16

Sumardi., R. Murwani, S. Kismiati, & P. Bintoro. 2021. Improved broiler growth, carcass and meat yields by phyto-additive Chromanone Deamine (ChD) from *Aegle marmelos* (L) *Correa fruits*. Livest Res. Rural Dev. 33: 1–6. https://www.cabidigitallibrary.org/doi/full/10.5555/20210101223

Syaefudin, A. A., R. Murwani, & I. Isroli. 2017. Tepung temu hitam (*Curcuma aeruginosa* Roxb) dalam ransum memperbaiki produktifitas dan High Density Lipoprotein (HDL) serum itik pedaging Peking. J. Ilmu-Ilmu Peternakan 26:1–5. https://doi.org/10.21776/ub.jiip.2016.026.03.01

Tanod, W. N. L., R. Murwani, S. Susanti, & E. Kusumanti. 2015. Addition of cashew (*Annarcadium occidentale*) apple powder into diet can increase body weight and intestinal relative weight in broiler. Pak. J. Nutr. 14: 629–631. https://doi.org/10.3923/pjn.2015.629.631

Vanda, H., R. Parindra, M. Hambal, & F. Athailah. 2020. Anthelmintic activity of *Curcuma aeruginosa* Roxb extract on *Fasciola gigantica in vitro*. Proc of E3S Web of Conf. Aceh (Indonesia): 1st ed Int. Conf. Vet. Anim. Environ. Sci. (ICVAES) Universitas Syiah Kuala. p. 1–3. https://doi.org/10.1051/e3sconf/202015101046

Vargas, F., P. Romecín, A. I. García-Guillén, R. Wangesteen, P. Vargas-Tendero, M. D. Paredes, N. M. Atucha, & J. García-Estañ. 2018. Flavonoids in kidney health and disease. Front. Physiol. 9:394. https://doi.org/10.3389/fphys.2018.00394

Wang, X., Y. Cao, S. Chen, J. Lin, J. Bian, & D. Huang. 2021. Anti-inflammation activity of flavones and their structure–activity relationship. J. Agric. Food Chem. 69:7285-7302. https://doi.org/10.1021/acs.jafc.1c02015

Wardiny, T. M., Y. Retnani, & Taryati. 2012. Pengaruh ekstrak daun mengkudu terhadap profil darah puyuh starter. J. Ilmu dan Teknologi Peternakan. 2:110–120. https://doi.org/10.20956/jitp.v2i2.709

Xu, L., Y. Shi, S. Zhuang, & N. Liu. 2017. Recent advances on uric acid transporters. Oncotarget 8:100852-100862. https://doi.org/10.18632/oncotarget.20135

Yang, R. Z., S. Park, W. J. Reagan, R. Goldstein, S. Zhong, M. Lawton, F. Rajamohan, K. Qian, L. Liu, & D. W. Gong. 2009. Alanine aminotransferase isoenzymes: molecular cloning and quantitative analysis of tissue expression in rats and serum elevation in liver toxicity. Hepatology 49:598-607. https://doi.org/10.1002/hep.22657

Yang, X., L. K. Schnackenberg, Q. Shi, & W. F. Salminen. 2014. Hepatic toxicity biomarkers. In: Gupta, R. C. (Ed.). Biomarkers in Toxicology. Academic Press. Kentucky, United States. http://dx.doi.org/10.1016/B978-0-12-404630-6.00013-0

Yasuda, K. & Kuroda E. 2019. Role of eosinophils in protective immunity against secondary nematode infections. Immunol. Med. 42:148-155. https://doi.org/10.1080/25785826.2019.1697135

Yuniarti, W. M. & B. S. Lukiswanto. 2017. Effects of herbal ointment containing the leaf extracts of Madeira vine (*Anredera cordifolia (Ten) Steenis)* for burn wound healing process on albino rats. Vet. World. 10:808-813. https://doi.org/10.1080/25785826.2019.1697135

Zaefarian, F., M. R. Abdollahi, A. Cowieson, & V. Ravindran. 2019. Avian liver: the forgotten organ. Animals 9:63. http://dx.doi.org/10.3390/ani9020063

Zhang, J., H. Han, M. Shen, L. Zhang, & T. Wang. 2019. Comparative studies on the antioxidant profiles of curcumin and bisdemethoxycurcumin in erythrocytes and broiler chickens. Animals 9:953. https://doi.org/10.3390/ani9110953

Zhang, L., A. G. W. Gong, K. Riaz, J. Y. Deng, C. M. Ho, H. Q. Lin, T. T. Dong, Y. K. Lee, & K. W. Tsim. 2017. A novel combination of four flavonoids derived from Astragali Radix relieves the symptoms of cyclophosphamide-induced anemic rats. FEBS Open Bio. 7:318-323. https://doi.org/10.1002%2F2211-5463.12146

Zheng, K. Y., R. C. Choi, A. W. Cheung, A. J. Guo, C. W. Bi, K. Y. Zhu, Q. Fu., Y. Du, W. L. Zhang, J. Y. Zhan, R. Duan, D. T. Lau, T. T. Dong, & K. W. Tsim. 2011. Flavonoids from Radix Astragali induce the expression of erythropoietin in cultured cells: a signaling mediated via the accumulation of hypoxia-inducible factor-1α. J. Agric. Food Chem. 59:1697-1704. https://doi.org/10.1021/jf104018u

Zulfiah, Z., M. Megawati, H. Herman, H. A. S. Lau, Hasyim, M. F. Murniati, F. Roosevelt, A. Kadang, & G. Patandung. 2020. Uji toksisitas ekstrak rimpang temu hitam (*Curcuma aeruginosa* Roxb.) terhadap larva udang (*Artemia salina Leach*) dengan metode brine shrimp lethality test (BSLT). J. Farmasi Sandi Karsa. 6*:* 44–49. https://dx.doi.org/10.36060/jfs.v6i1.67