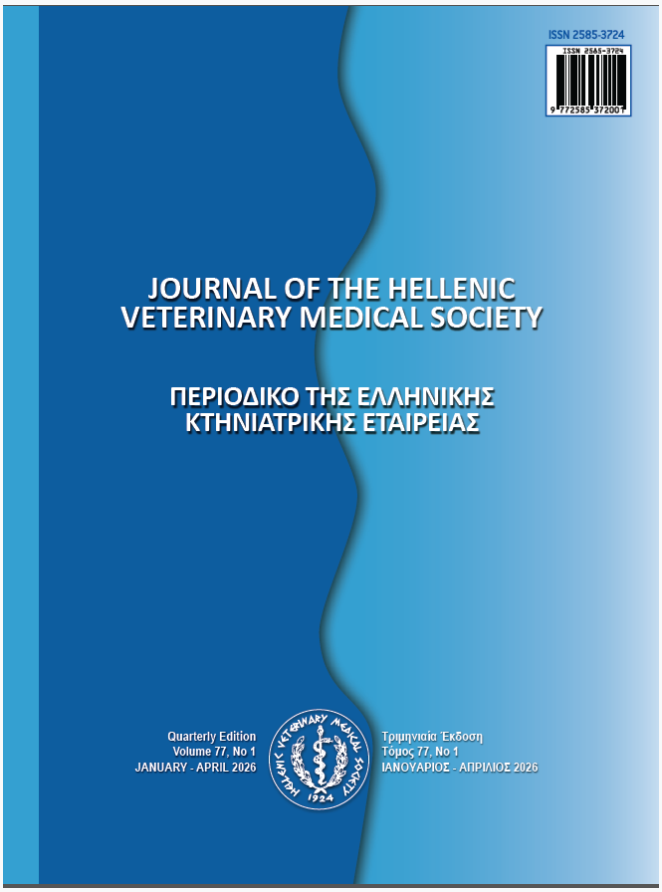
Journal of the Hellenic Veterinary Medical Society

Vol 77, No 1 (2026)



Effects of Curcumin and Nanocurcumin on Biochemical Parameters, and Performance of Broiler Chickens under Physiological Stress

M Fathi, S Saidian , Z Baghaeifar , P Mardani, Z Zandiyah, G Mansory, V Rezaee

doi: 10.12681/jhvms.41130

To cite this article:

Fathi, M., Saidian , S., Baghaeifar , Z., Mardani, P., Zandiyah, Z., Mansory, G., & Rezaee, V. (2026). Effects of Curcumin and Nanocurcumin on Biochemical Parameters, and Performance of Broiler Chickens under Physiological Stress. *Journal of the Hellenic Veterinary Medical Society*, *77*(1), 10135–10144. https://doi.org/10.12681/jhvms.41130

J HELLENIC VET MED SOC 2026, 77 (1): 10135-10144
ΠΕΚΕ 2026, 77 (1): 10135-10144

Research article
Ερευνητικό άρθρο

Effects of Curcumin and Nanocurcumin on Biochemical Parameters, and Performance of Broiler Chickens under Physiological Stress

Mokhtar Fathi,[1*] Shahriar Saidian,[2] Zahra Baghaeifar,[2] Parastoo Mardani,[2] Zahra Zandiyah,[2] Golnar Mansory[2] and Vahid Rezaee[1]

[1]*Department of Animal Science, Payame Noor University, Tehran, Iran*

[2]*Department of Biology, Payame Noor University, Tehran, Iran*

ABSTRACT: This study aimed to evaluate the effects of curcumin and nanocurcumin on growth performance, antioxidant status, inflammatory response, and hematological changes in male broiler chickens subjected to experimentally induced stress via in-feed dexamethasone (DEX). A total of 400 one-day-old male Ross 308 chicks were randomly assigned to four groups: (1) a positive control (PC) group with no treatment, (2) a negative control (NC) group receiving 1.5 mg/kg DEX, (3) a group receiving 1.5 mg/kg DEX and 200 mg/kg curcumin (Cur), and (4) a nanocurcumin (Nano-Cur) group receiving 1.5 mg/kg DEX and 200 mg/kg nanocurcumin. Each group consisted of five replicates with 20 birds per replicate. Dietary supplementation with curcumin or nano-curcumin mitigated the adverse effects of DEX on body weight, feed conversion ratio, and mortality. During the stress period, Nano-Cur supplementation enhanced serum superoxide dismutase and glutathione peroxidase activity while reducing malondialdehyde levels. Additionally, Cur/Nano-Cur supplementation lowered serum total cholesterol, triglycerides, aspartate aminotransferase (AST), and alanine transaminase (ALT) levels, while increasing IgG and IgM compared to the NC group. Dexamethasone-induced physiological stress elevated IL-10 without affecting IL-8 or TNF-α levels. However, dietary supplementation with curcumin or nanocurcumin reduced TNF-α and increased IL-8 and IL-10 levels. Furthermore, curcumin/nanocurcumin supplementation alleviated the adverse effects of DEX by decreasing heterophil counts and the heterophil-to-lymphocyte ratio, while increasing lymphocyte counts, hematocrit (HCT), and hemoglobin (HGB) levels. In conclusion, dietary curcumin and nanocurcumin supplementation can mitigate DEX-induced oxidative stress and inflammatory responses, supporting their potential role in improving stress resilience in broiler chickens

Keyword: Broiler; curcumin; nanocurcumin; oxidative stress; dexamethasone; immune response; inflammation response; stress

Correspondence author:
Mokhtar Fathi,
Department of Animal Science, Payame Noor University, Tehran, Iran
E-mail address: Mokhtarfathi@pnu.ac.ir

Date of submission: **15-4-2025**
Date of acceptance: **15-7-2025**

INTRODUCTION

Broiler chickens are routinely exposed to various stressors—including vaccination, feed withdrawal, high stocking density, thermal fluctuations, handling, and transportation—that can impair their physiological homeostasis, thereby reducing growth and productivity (Attia et al., 2016, 2018; Fathi et al., 2023). Stress is closely associated with immunosuppression, increased disease susceptibility, and oxidative imbalance (Lin et al., 2006a, b). The activation of the hypothalamic-pituitary-adrenal (HPA) axis during stress leads to glucocorticoid release, particularly corticosterone, which is a widely recognized biomarker of stress in poultry (Osho and Adeola, 2020). Excessive glucocorticoid levels cause lymphoid organ atrophy (e.g., thymus, bursa of Fabricius), lymphopenia, and elevated heterophil-to-lymphocyte ratios—established hematological markers of stress (Al-Sultan and Gameel, 2004; Barzegar Yarmohammadi et al., 2020).

Although glucocorticoids are essential for metabolic and immune modulation, chronic elevations impair protein synthesis, promote muscle degradation, and lead to oxidative stress via excessive free radical production (Furukawa et al., 2016; Wang et al., 2016). This oxidative stress contributes to lipid peroxidation, poor meat quality, and weakened immune defense (Lin et al., 2004). Experimental models often induce stress by administering corticosterone or synthetic analogs such as dexamethasone (DEX), which elicit predictable immunosuppressive and oxidative effects (Eid et al., 2003; Li et al., 2009; Fathi et al., 2023).

Nutritional strategies to mitigate these adverse effects have included dietary antioxidants such as selenium (Huang et al., 2021), black seed (Eladl et al., 2019), and lycopene (Fathi et al., 2022; Haldar et al., 2011). Among natural bioactives, curcumin—the primary polyphenol in *Curcuma longa*—has attracted interest for its broad pharmacological spectrum, including antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory properties (Sandur et al., 2007; Singh et al., 2010; Cleary, 2004). Curcumin can reduce levels of pro-inflammatory cytokines such as TNF-α and IL-1β (Huang et al., 2008; Gorabi et al., 2021), yet its poor bioavailability due to rapid metabolism and low absorption limits its clinical and nutritional applications (Anand et al., 2007).

Recent advances in nanotechnology have enabled the development of nanocurcumin formulations that significantly enhance curcumin's bioavailability and tissue distribution (Ma et al., 2007; Nabavi et al., 2014). Prior studies suggest that both curcumin and nanocurcumin improve growth, oxidative stability, and gut function in broilers under heat or cold stress (Heidary et al., 2020; Rahmani et al., 2017, 2018). However, limited data exist regarding their role under physiological stress conditions, such as those induced by glucocorticoid challenge.

Therefore, the present study aims to evaluate the effects of curcumin and nanocurcumin supplementation on growth performance, biochemical indicators, and stress-related biomarkers in broiler chickens under experimentally induced physiological stress.

MATERIALS AND METHODS

All experimental procedures used in this study were approved by the Animal Ethics Committee of the Payam Noor University, Tehran, Iran (Ethics ID: IR.PNU.REC.1402.147).

Birds, Diets and Experimental design

This study was performed on *total of 400* one-day-old *male* broiler chickens *(Ross 308)* with an average body weight of *42±05 g,* were purchased from *Behshadafarin Company in Gorgan, Iran. The* broiler chickens randomly distributed among four treatments. Each treatment consisted of -five replications, with each replicate pen housing 20 broiler chickens. The following four groups were used in this study: the positive control group (PC, without any treatment), negative control (NC, with 1.5 mg/kg DEX), a third group received 1.5 mg/kg DEX and 200 mg/kg curcumin (Cur) and the last one was (Nano-Cur) which received 1.5 mg/kg DEX and 200 mg/kg nanocurcumin. Each group has five replicates (20 birds /replicate). The optimum dietary concentration of DEX for broiler chickens was determined to be 1.5 mg/kg (Osho and Adeola, 2020; Fathi et al., 2023).

DEX (0.6 mg/kg of BW) was administered in mash diet through time from the seventeenth to the twenty-second day in order to induce physiological stress over a period of six days. Each DEX pill contained 0.5 mg of DEX (9 fluoro-11, 17, 21-trihydroxy-16 methylpregna-1, 4-diene-3, 20-diene; IranHormone, Iran). After calculating the amounts of DEX mg/kg BW, the pills were milled into powder every three days and were distilled in soybean oil, then mixed with the components of the experimental diet (Barzegar Yarmohammadi et al., 2020).

All birds were fed with the basal diet (Table 1) for

Table 1. The ingredient composition and nutrient content of the basal diets

	Starter diet	Grower diet	Finisher diet
Ingredients (%)			
Mize, 8% CP	47.53	51.63	57.56
Soybean meal, 44%CP	42.35	37.99	32.35
Soybean oil, 9000 kcal/kg	5.54	6.24	6.29
Limestone, 38% Ca	1.20	1.12	1.05
Di-calcium phosphate	1.79	1.56	1.34
Vitamin premixb	0.25	0.25	0.25
Mineral premixc	0.25	0.25	0.25
NaCl	0.40	0.40	0.40
DL-Methionine, 99%	0.37	0.32	0.28
Lysine, 78%	0.28	0.22	0.22
Threonine, 98.5%	0.05	0.02	0.00
Calculated values d			
Metabolizable energy, kCal/kg	2990	3082	3218
Crude protein, %	23	21.3	19.3
Calcium (Ca), %	0.96	0.87	0.79
Available phosphorus, %	0.456	0.409	0.361
Sodium (Na), %	0.16	0.16	0.16
Met, %	0.71	0.64	0.58
Met + Cys, %	1.07	0.89	0.89
Lys, %	1.46	1.30	1.17
Arg, %	1.56	1.45	1.30
Thr, %	0.96	0.87	0.78
Try, %	0.35	0.32	0.29

[b] Vitamin concentrations per kilogram of diet: retinol, 13.50 mg; cholecalciferol, 4.15 mg; tocopherol acetate, 32.00 mg; vitamin K3, 2 mg; thiamin, 2 mg; riboflavin, 6.00 mg; biotin, 0.1 mg; cobalamin, 0.015 mg; pyroxidine, 3 mg; niacin, 11.00 mg; d-pantothenic acid, 25.0; menadione sodium bisulphate, 1.10; folic acid, 1.02; choline chloride, 250 mg; nicotinamide, 5 mg;

[c] Mineral concentrations per kilogram of diet:calcium pantothenate, 25 mg; Fe (from ferrous sulphate), 35 mg; Cu (from copper sulphate), 3.5 mg; Mn (from manganese sulphate), 60 mg; Zn (from zinc sulphate), 35 mg; I (from calcium iodate), 0.6 mg; Se (from sodium selenite), 0.3 mg.

starter (1-10), grower (11-24) and finisher (25-42) periods according to Ross 308 nutrient recommendations. The house was maintained at a temperature based on the age of the birds. It was initially 32°C then was reduced by 3°C each week, to be 21 °C at the fifth week of age. This was controlled by an air conditioner. A continuous exposure of lighting program *was set at 23L: 1D throughout the duration of experiment.* For each cage of under experiment was used spherical pen feeders and drinkers, So the size of each one was 200 × 120 cm. Vaccinated against Newcastle disease and other infectious diseases regularly.

Curcumin and nanocurcumin

Curcumin was obtained from Sami Labs Limited, Bangalore, India, and used without any treatment. The commercially available source of curcumin is usually composed of 77% curcumin, 18% demethoxycurcumin and 5% bisdemethoxycurcumin (Basnet et al. 2010). Nanocurcumin, used in our experiment, was a nanomicelle containing curcumin and registered as curcumin product (Sina-Curcumin®) for human oral use which has been developed in the Nanotechnology Research Center of the Mashhad University of Medical Science and marketed by Exir NanoSina Company, Tehran, Iran

(IRC:1228225765). Nanocurcumin is prepared from GRAS (generally recognized as safe) pharmaceutical excipients and C3-complex form of curcumin. The encapsulation of curcumin in this nanomicelle is near 100% and the sizes are around 10 nm. Nanocurcumin has a significantly higher bioavailability after oral use compared to curcumin powder (Rahmani et al., 2018).

Data collection

Growth Performance

Body weight gain (BWG) was calculated as the difference between initial and final body weight. Feed intake was determined daily by subtracting the remaining feed from the previous day from the feed offered to each replicate within each group. Feed conversion ratio (FCR) was also computed as the proportion of total feed intake to total weight gain. Mortality percentages were recorded on a replicate basis every day and totaled for the entire experimental period.

Hematological and Biochemical Examination

On day 42, after 8-hour fasting (Wang et al., 2013), 2 broilers per group randomly selected. Two blood samples were taken by wing vein puncture, under gentle restraint without anesthesia. One of the blood samples (3 mL) was taken into a tube containing anticoagulant (disodium EDTA) and kept on ice for hematological examination (Al wakeel et al., 2017). The second blood sample (3 mL) was taken without anticoagulant to measure biochemical parameters in serum. Serum was separated by centrifugation for 10 min at 2,500 rpm and stored at -20 °C until assayed.

Hematological parameters including white blood cells (WBCs), red blood cells (RBCs), hemoglobin (HGB), hematocrit (HCT), heterophil (HET) and lymphocytes (LYM) in whole blood were analyzed using an automatic blood analyzer (ADVIA 120, Bayer, NY, USA). For, differential leukocyte counts (HET/LYM ratio), a drop of blood was smeared on a glass slide, left to dry and then stained with Giemsa stain. One hundred leucocytes were counted on each slide including heterophils and lymphocytes. The HET/LYM ratio was calculated by dividing the number of heterophils by the number of lymphocytes. Two slides were counted and the means were calculated for each bird (Al wakeel et al., 2017).

The concentration of aspartate amino transferase (AST), alanine amino transferase (ALT) in serum were measured with appropriate laboratory kits (Pars Azmoon, Tehran, Iran). The level of GSH-Px was determined with a commercially available enzyme kit (Ransel, RANDOX/RS-504 supplied by Randox Laboratories, Crumlin, UK), SOD was determined with the commercially available enzyme kit (Ransod, RANDOX/SD-125 supplied by Randox Laboratories) and autoanalyzer (Alcyon 300, USA) according to the manufacturers' protocols. The level of malondialdehyde (MDA) concentration in serum was measured with the tiobarbituric-acid reaction by the method of Fathi et al. (2022). Serum lipid profile including cholesterol, and triglyceride were measured by spectrophotometer with standard commercial kits (Pars Azmoon, Tehran, Iran) according to the manufactures instructions.

The IgG and IgM serum concentrations were determined using an ELISA kit from BethylLaboratories (Montgomery, AL, USA), as described by Gao et al. (2008). The immunoglobulin serum levels were determined using a standard curve and were expressed in nanograms per milliliter serum. The inflammatory parameters in serum such, IL-8, IL-10 and TNF-α concentrations were determined by with ELISA kits (Pars Azmoon, Tehran, Iran) according to the manufacturer's instructions.

Statistical Analysis

The collected data in the current study were analyzed using SPSS 18.0 software (SPSS Inc., IL). A t-test was performed to compare the negative control (NC) and positive control (PC) groups. For comparisons among all treatment groups, one-way ANOVA followed by Tukey's post hoc test was used to determine significant differences at $P < 0.05$. Data are presented as means ± pooled standard error of the mean (SEM). Assumptions of normality and homogeneity of variances were checked prior to analysis, and data transformations were applied if necessary.

RESULTS

Growth performance and mortality

The effects of DEX and dietary curcumin/ nanocurcumin supplementation on the growth performance and mortality of broiler chickens are shown in Table 2. DEX supplemented group (NC) has decreased average Body weight gain (BGW) and increased Feed conversion ratio (FCR) compared with control positive group (PC, without treatment) ($P<0.05$). Supplementation of diet with nanocurcumin increased birds'BWG, but curcumin/ nanocurcumin at the rate of 200 mg/kg improved the FCR and reduced the mortality of birds compared to those fed control diet ($P < 0.05$).

Table 2. Effects of experimental treatments on performance of broiler chickens at 1–42 day of age

	Groups					
Indices	**NC**	**PC**	**Cur**	**Nano-Cur**	**Pooled SEM**	**P-value**
Feed Intake [g]	4475	4488	4182	4292	190	0.12
Body weight gain [g]	2680^{a}	2400^{c}	2460^{c}	2540^{b}	95	0.001
Feed conversion ratio [g/g]	1.67^{b}	1.87^{a}	1.70^{b}	1.69^{b}	0.09	0.001
Mortality (%)	0.04^{c}	0.24^{a}	0.12^{b}	0.04^{c}	0.01	0.001

$^{a, b, c}$ Mean values in the same row with different superscript letters were significantly. (N=10)
NC: negative control (no-DEX, no-additive); PC: positive control (1.5 mg/kg DEX, no-additive), Cur (PC+ 200 mg Cur/kg diet), Nano-Cur (PC+ 200 mg Nano-Cur/kg diet).

Table 3. Effect of experimental treatments on serum antioxidant activities of broiler chickens at day 42 of age

	Groups					
Indices	**NC**	**PC**	**Cur**	**Nano-Cur**	**Pooled SEM**	**P-value**
GSH-Px (U/g Hb)	1563.26^{a}	1243.59^{b}	1287.06^{b}	1449.88^{a}	35.10	0.012
SOD (U/g Hb)	480.66^{a}	342.10^{cd}	351.09^{c}	368.56^{b}	5.50	0.001
MDA (**Nmol/L**)	18.19^{b}	20.19^{a}	19.38^{ab}	18.17^{b}	0.31	0.021

$^{a, b, c}$ Mean values in the same row with different superscript letters were significantly. (N=10)
NC: negative control (no-DEX, no-additive); PC: positive control (1.5 mg/kg DEX, no-additive), Cur (PC+ 200 mg Cur/kg diet), Nano-Cur (PC+ 200 mg Nano-Cur/kg diet). GPx, Glutathione peroxidase; SOD, *Superoxide dismutase*; MDA, Malondialdehyde

Table 4. Effect of experimental treatments on some biochemical parameters of broiler chickens at day 42 of age

	Groups					
Indices	**NC**	**PC**	**Cur**	**Nano-Cur**	**Pooled SEM**	**P-value**
TG (mg/dL)	107.58^{b}	243.12^{a}	96.74^{c}	90.62^{d}	1.59	0.021
TC (mg/dL)	111.06^{b}	147.39^{a}	106.19^{b}	105.54^{b}	2.30	0.023
ALT (U/L)	10.425^{c}	20.75^{a}	19.425^{a}	17.180^{b}	0.35	0.010
AST (U/L)	130.39^{c}	189.58^{a}	178.36^{b}	130.74^{c}	1.50	0.025
IgG (U/ml)	5.56^{b}	4.68^{c}	6.01^{b}	6.95^{a}	0.31	0.01
IgM (U/ml)	3.67^{bc}	2.20^{d}	4.12^{b}	4.91^{a}	0.25	0.01

$^{a, b, c}$ Mean values in the same row with different superscript letters were significantly. (N=10)
NC: negative control (no-DEX, no-additive); PC: positive control (1.5 mg/kg DEX, no-additive), Cur (PC+ 200 mg Cur/kg diet), Nano-Cur (PC+ 200 mg Nano-Cur/kg diet). TG, triglyceride; TC, total cholesterol. IgG, Immunoglobulin G; IgM, Immunoglobulin M.

Serum Redox status

As shown in Table 3, DEX administration, reduced levels of *GSH-Px* and SOD in serum (Table 3) ($P < 0.05$). Moreover, values for MDA in serum for PC group birds also increased in compared with the NC group birds ($P < 0.05$). Under physiological stress condition, the inclusion of nanocurcumin, improved the antioxidant status in serum ($P < 0.05$). Dietary curcumin treatment had no significant influence on serum redox status.

Biochemical parameters

As shown in Table 4, physiological-stressed by DEX administration increased the serum contents of ALT, AST, TG, and TC in NC group birds than the PC group birds ($P < 0.05$). Also, the serum levels of IgG and IgM significantly were reduced by DEX administration ($P<0.05$). Inclusion of curcumin/nanocurcumin, in diet caused a decrease in AST, ALP, TG, and TC in serum ($P<0.01$). Moreover, values for IgG and IgM in serum were increased

by curcumin/nanocurcumin supplementation in diet ($P < 0.05$).

Inflammation response

The results of treatments on *Inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-8 (IL-8), and interleukin-10 (IL-10) concentrations in serum of birds* are summarized in Table 5. Results showed that Physiological stress without affecting *TNF-α and cytokines IL-8*, causes an increase in *IL-10 in serum compared to those under* unstressed *birds (NC group). At the same time,* inclusion of curcumin/nanocurcumin, in diet caused a decrease in *TNF-α and cytokines IL-8* and increase in *IL-10 of broiler chickens subjected to* DEX administration ($P < 0.05$).

Hematological parameters

Hematological parameters showed differences among PC and NC birds (Tables 5). Generally, over the stress period the total count of White Blood Cells (WBC) and Red Blood Cells (RBC) were not affected by DEX administration. However, the DEX administration significantly reduced the HGB, HCT, and LYM and increased the HET and HET: LYM ratio in blood of PC birds compared NC ($P < 0.05$). *At the same time,* inclusion of curcumin/nanocurcumin, in diet caused an increased the HGB, HCT, and LYM and reduced the HET and HET: LYM ratio in blood of birds subjected dexamethasone administration ($P<0.05$).

DISCUSSION

Broiler chickens raised in intensive systems commonly experience immunosuppressive stressors such as oxidative stress, high stocking density, and transportation, which negatively affect their growth and health (Galha et al., 2008; Osho and Adeola, 2020). In this study, physiological stress induced by DEX **significantly reduced BWG and increased**

Table 5. Effect of experimental treatments on inflammation response in serum of broiler chickens at day 42 of age

	Groups					
Indices	**NC**	**PC**	**Cur**	**Nano-Cur**	**Pooled SEM**	**P-value**
IL-8 (ug/ml)	10.85^{b}	11.21^{b}	14.50^{a}	15.25^{a}	0.87	0.02
IL-10 (ug/ml)	11.31^{d}	13.01^{c}	14.5^{b}	16.25^{a}	0.95	0.01
TNF-α (ug/ml)	9.25^{a}	8.95^{a}	6.50^{b}	5.15^{c}	0.52	0.03

$^{a, b, c}$ Mean values in the same row with different superscript letters were significantly. (N=10)
NC: negative control (no-DEX, no-additive); PC: positive control (1.5 mg/kg DEX, no-additive), Cur (PC+ 200 mg Cur/kg diet), Nano-Cur (PC+ 200 mg Nano-Cur/kg diet).

Table 6. Effect experimental treatments on hematological parameters of broiler chickens at day 42 of age

	Groups					
Indices	**NC**	**PC**	**Cur**	**Nano-Cur**	**Pooled SEM**	**P-value**
RBCs count (× 10^{6}/ µl)	2.76	2.14	2.29	2.75	0.68	0.19
HGB (g/dl)	15.2^{a}	10.75^{c}	11.85^{c}	13.15^{b}	0.95	0.02
HCT (%)	36.15^{a}	25.8^{c}	29.9^{b}	34.45^{a}	1.01	0.03
WBCs count (10^{3} cells/mm^{3})	6.18^{a}	6.20^{a}	5.88^{ab}	5.58^{b}	0.75	0.02
HET (%)	8.02^{c}	13.25^{a}	10.72^{b}	9.50^{bc}	0.78	0.01
LYM (%)	84.10^{a}	66.21^{b}	70.01^{b}	89.20^{a}	0.042	0.01
HET / LYM Ratio	0.095^{c}	0.200^{a}	0.153^{b}	0.106^{b}	0.015	0.01

$^{a, b, c}$ Mean values in the same row with different superscript letters were significantly. (N=10)
NC: negative control (no-DEX, no-additive); PC: positive control (1.5 mg/kg DEX, no-additive), Cur (PC+ 200 mg Cur/kg diet), Nano-Cur (PC+ 200 mg Nano-Cur/kg diet). RBCs, Red blood cells; HGB, Hemoglobin; HCT, Hematocrit; WBCs, White blood cells; HET, Heterophil; LYM, Lymphocyte,

FCR (P < 0.05), confirming previous reports that glucocorticoids impair growth performance in poultry (Puvadolpirod and Thaxton, 2000a, b; Barzegar Yarmohammadi et al., 2020). Li et al. (2009) also showed that DEX injections decrease final BWG in broilers. Stress-induced reductions in nutrient digestibility have been attributed to accelerated feed passage rates and altered water intake (Puvadolpirod and Thaxton, 2000b).

Glucocorticoids regulate metabolism by suppressing anabolic and enhancing catabolic processes (Virden and Kidd, 2009), which may explain why stressed birds allocate more energy to coping mechanisms rather than growth. Importantly, **supplementation with nanocurcumin significantly improved BWG and FCR, and reduced mortality (P < 0.05)**, demonstrating superior efficacy over curcumin, likely due to improved bioavailability and intestinal absorption (Rahmani et al., 2018). Curcumin's lipophilicity limits solubility in the intestinal water layer, whereas nanocurcumin's micellar form is hydrophilic, enhancing uptake (Rahmani et al., 2018). Previous studies reported that curcumin supplementation enhances intestinal morphology and feed conversion efficiency (Attia et al., 2017), potentially through improved digestive enzyme activities (Platel and Srinivasan, 2000; Hernandez et al., 2004). Additionally, curcumin's antioxidant properties may protect thyroid gland function, supporting growth under stress (Rahmani et al., 2017).

Glucocorticoids also disrupt redox balance and immune functions in poultry (Gao et al., 2010; Osho and Adeola, 2020). Antioxidant defense systems, including enzymatic antioxidants such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), play critical roles in combating oxidative stress (Fathi et al., 2022). Consistent with these findings, curcumin/nanocurcumin supplementation reduced oxidative damage markers like thiobarbituric acid reactive substances (TBA) and enhanced antioxidant enzyme activities in broilers under thermal stress (Rahmani et al., 2018; Suvanated et al., 2003). The phenolic structure of curcumin allows it to scavenge hydroxyl radicals, superoxide ions, and nitric oxides, thereby reducing lipid peroxidation (Rahmani et al., 2018; Reddy and Lokesh, 1996).

Physiological stress also **significantly** elevated liver enzymes AST and ALT (**P < 0.05**), indicative of liver damage and oxidative stress (Fathi et al., 2023; Arab et al., 2006). Curcumin and nanocurcumin **significantly** decreased liver MDA levels (**P < 0.05**), protecting hepatic cells by neutralizing free radicals (Donatus et al., 1990; Rahmani et al., 2018). Lower AST/ALT activities in nanocurcumin-fed birds relative to curcumin suggest higher antioxidant protection, likely due to improved bioavailability of nanoparticle formulations (Ma et al., 2007).

Immune function was also compromised by stress, as evidenced by **significantly** decreased serum IgG and IgM on day 42 (**P < 0.05**), in line with earlier reports of heat stress impairing poultry immunity and reducing lymphoid organ weights (Mashaly et al., 2004; Awad et al., 2020; Ghanima et al., 2020; Ma et al., 2019). However, dietary curcumin/nanocurcumin **significantly** enhanced IgG and IgM levels (**P < 0.05**), likely due to their antioxidant-mediated immunomodulatory effects (Abd El-Hack et al., 2021).

The observed increases in plasma total TC and TG in the DEX-stressed group were statistically significant (P < 0.05), and are consistent with previous reports demonstrating similar stress-induced elevations in lipid profiles (Houshmand et al., 2012; Rahmani et al., 2018; Fathi et al., 2022, 2023). Curcumin supplementation decreased these lipids, possibly through stimulation of hepatic cholesterol-7-alpha-hydroxylase activity, which catalyzes cholesterol conversion to bile acids (Srinivasan and Sambaiah, 1991; Zhang et al., 2009). Curcumin may also disrupt lipid micellation and absorption, further lowering triglycerides (Kim and Kim, 2010), and its antioxidant effect protects LDL from oxidation, preventing atherosclerosis (Rahmani et al., 2018).

In the present study, stress-induced inflammation was associated with significant elevations (P < 0.05) in pro-inflammatory cytokines such as TNF-α and IL-8, indicating activation of innate immune responses to physiological stressors. These findings are consistent with previous reports highlighting the role of these cytokines as key markers of inflammatory responses to tissue injury and stress (Chen et al., 2018; Jang et al., 2014; Ohtsu et al., 2015).

Excess reactive oxygen species (ROS) stimulate cytokine production, exacerbating inflammation (Jang et al., 2014). Glucocorticoids inhibit inflammatory responses by downregulating transcription factors like NF-κB and AP-1, reducing pro-inflammatory cytokine expression and increasing anti-inflammatory IL-10 (Busillo et al., 2011; Dejager et al., 2014; Osho and Adeola, 2020). Similarly, curcumin/nanocurcumin supplementation lowered pro-inflam-

matory cytokines and increased IL-10 in animals, demonstrating anti-inflammatory effects through transcription factor inhibition and cytokine modulation (Huang et al., 2008; Yadav et al., 2015; Palizgir et al., 2018; Gorabi et al., 2021; Surh et al., 2000).

HET to LYM (H: L) ratio is a reliable stress biomarker in poultry (Puvadolpirod and Thaxton, 2000a). Stress increases heterophils and decreases lymphocytes, elevating this ratio (Fathi et al., 2023). Consistent with prior research, DEX reduced total white and red blood cells and hemoglobin concentration, increased HET percentages, and lowered LYM percentages (Adedapo et al., 2004; Barzegar Yarmohammadi et al., 2020). Corticosterone induces heterophilia by releasing HET from bone marrow reserves as part of the nonspecific immune response to stress (Jain, 1993). DEX also causes lymphocytopenia through lympholysis and lymphoid tissue atrophy (Jain, 1993). Dietary curcumin/nanocurcumin reversed these effects by increasing lymphocytes and reducing HET counts and H: L ratios, possibly due to their antioxidant properties preventing oxidative stress-induced HET proliferation (Rahmani et al., 2018; Surai, 2002; Galati et al., 2002). Curcumin also promotes proliferation of B and T lymphocytes and enhances antibody production (Gautam et al., 2007; Churchill et al., 2000).

Taken together, the present findings suggest that dietary supplementation with curcumin and especially nanocurcumin effectively alleviates the detrimental effects of dexamethasone-induced physiological stress in broiler chickens. These improvements were evident across multiple parameters, including growth performance, antioxidant enzyme activity, inflammatory cytokine modulation, and hematological profiles. Notably, the nanocurcumin form demonstrated superior efficacy over conventional curcumin, likely due to enhanced bioavailability and cellular uptake. This study underscores the promising potential of nanocurcumin as a novel nutritional strategy for mitigating stress-related impairments in poultry production systems.

CONCLUSIONS

The present study demonstrates that dietary supplementation with curcumin and nanocurcumin effectively mitigates the negative effects of dexamethasone-induced physiological stress in broiler chickens. Both compounds improved growth performance, enhanced antioxidant enzyme activities, reduced oxidative damage, and modulated inflammatory and hematological responses under stress conditions. Notably, nanocurcumin showed superior efficacy, likely due to its enhanced bioavailability. These findings highlight the potential of curcumin and nanocurcumin as natural dietary additives to improve stress resilience and health in poultry production.

Future research should aim to optimize the dosage and administration protocols of curcumin and nanocurcumin, investigate the detailed molecular mechanisms underlying their protective effects, and assess their long-term impacts on broiler health and productivity under commercial farming environments. Such studies will be essential to fully validate and facilitate the practical application of these compounds in poultry nutrition and stress management.

REFERENCES

Adedapo AA, Saba AB, Dina OA, Oladejo GMA. 2004. Effects of dexamethasone on the infectivity of Trypanosoma vivax and serum biochemistry change in Nigerian domestic chickens. Veterinarski arhiv Trop J Anim Sci 74(5): 371–382.

Abd El-Hack, M. R., Bothaina A, Alaidaroos, Reem M. Farsi, Diaa E. Abou-Kassem Mohamed T. El-Saadony, Ahmed M. Saad, Manal E. Shafi, Najah M. Albaqami, Ayman E. Taha and 6. Elwy A. Ashour. 2021. Impacts of Supplementing Broiler Diets with Biological Curcumin, Zinc Nanoparticles and Bacillus licheniformis on Growth, Carcass Traits, Blood Indices, Meat Quality and Cecal Microbial Load. Anim 11, 1878.

Attia YA, Abd El AE, Abedalla AA, Berika MA, Al-Harthi MA, Kucuk O, Sahin K, Abou-Shehema BM. 2016. Laying performance, digestibility and plasma hormones in laying hens exposed to chronic heat stress as affected by betaine, vitamin C, and/or vitamin E supplementation. Springerplus 5(1):1619.

Attia YA, Al-Harthi MA, Hassan SS. Turmeric (Curcuma longa Linn.) as a phytogenic growth promoter alternative for antibiotic and comparable to mannan oligosaccharides for broiler chicks. Rev Mex Cienc Pecu 2017; 8(1): 11-21.

Attia YA, Al-Harthi MA, Sh. Elnaggar A. 2018. Productive, physiological and immunological responses of two broiler strains fed different dietary regimens and exposed to heat stress. Ital J Anim Sci 17(3):686–697.

Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. 2007. Bioavailability of curcumin: problems and promises. Mol Pharm 4:807–818.

Arab HA, Jamshidi R, Rassouli A, Shams G, Hassanzadeh MH. 2006. Generation of hydroxyl radicals during ascites experimentally induced in broilers. Bri Poult Sci. 47:216–222

Al-Sultan SI, Gameel AA. 2004. Histopathological changes in the livers of broiler chicken supplemented with turmeric (Curcuma longa). Int J Poult Sci 3:333–336.

Awad EA, Najaa M, Abidin Z, Zulkifli I, Soleimani AF. 2020. Effects of heat stress on growth performance, selected physiological and immunological parameters, caecal microflora, and meat quality in two broiler strains. *Asian-Australas J Anim Sci* 33(5): 778–787.

Al wakeel A. Al wakeel, Mustafa Shukry, Ahmed Abdel Azeez, Shawky Mahmoud & Michel Fahmy Saad. 2017. Alleviation by gamma amino butyric acid supplementation of chronic heat stress-induced degenerative changes in jejunum in commercial broiler chickens. Stress 20 (6)562–572 https://doi.org/10.1080/10253890.2017.1377177.

Barzegar Yarmohammadi A., Sharifi, S.D., Mohammadi-Sangcheshmeh, A. 2020. Efficacy of dietary supplementation of nanoparticles-chromium, chromiummethionine and zinc-proteinate, on performance of Japanese quail under physiological stress. Ital jou of anim sci 19 (1), 1123–1134. DOI: https://doi.org/10.1080/1828051X.2020.1822763.

Cleary K. 2004. Effects of oxygen and turmeric on the formulation of oxidative aldehyde in freshpack dill pickles [A Thesis submitted to the Graduate Faculty of North Carolina].

Dejager L, Vandevyver S, Petta I, Libert C. 2014. Dominance of the strongest: inflammatory cytokines versus glucocorticoids. *Cytokine Growth Factor Rev* 25: 21–33.

Donatus IA, Sardjoko IA, Vermeulen NPE. 1990. Cytotoxic and cytoprotective activities of curcumin. Effects on paracetamol-induced cytotoxicity, lipid peroxidation and glutathione depletion in rat hepatocytes. *Biochem Pharmacol* 39: 1869–1875.

Eid Y, Ohtsuka A, Hayashi K. 2003. Tea polyphenols reduce glucocorticoid-induced growth inhibition and oxidative stress in broiler chickens. *Br Poult Sci* 44(1): 127–132.

Eladl AH, Arafat N, El-Shafei RA, Farag VM, Saleh RM, Awadin WF. 2019. Comparative immune response and pathogenicity of the H9N2 avian influenza virus after administration of Immulant®, based on *Echinacea* and *Nigella sativa*, in stressed chickens. *Comparative Immunology, Microbiology and Infectious Diseases* 65: 165–175.

Fathi M, Tanha T, Saeedyan S. 2022. Influence of dietary lycopene on growth performance, antioxidant status, blood parameters and mortality in broiler chicken with cold-induced ascites. *Arch Anim Nutr* 8: 1–11. doi: 10.1080/1745039X.2022.2046451.

Fathi M, Saeedyan S, Kaoosi M. 2023. Gamma-amino butyric acid (GABA) supplementation alleviates dexamethasone treatment-induced oxidative stress and inflammation response in broiler chickens. *Stress* 26(1): 2185861. DOI: 10.1080/10253890.2023.2185861.

Furukawa K, Kikusato M, Kamizono T, Toyomizu M. 2016. Time-course changes in muscle protein degradation in heat-stressed chickens: Possible involvement of corticosterone and mitochondrial reactive oxygen species generation in induction of the ubiquitin–proteasome system. *Gen Comp Endocrinol* 228: 105–110.

Galha V, Bondan EF, Lallo MA. 2008. Relationship between immunosuppression and clinical coccidiosis in commercially raised broilers. *Rev Inst Cienc Health* 26: 432–437.

Gao J, Lin H, Song ZG, Jiao HC. 2008. Corticosterone alters meat quality by changing pre- and post-slaughter muscle metabolism. *Poult Sci* 87: 1609–1617.

Gao J, Lin H, Wang XJ, Song ZG, Jiao HC. 2010. Vitamin E supplementation alleviates the oxidative stress induced by dexamethasone treatment and improves meat quality in broiler chickens. *Poult Sci* 89: 318–327.

Gorabi AM, Razi B, Aslani S, Abbasifard M, Imani D, Sathyapalan T, Sahebkar A. 2021. Effect of curcumin on proinflammatory cytokines: A meta-analysis of randomized controlled trials. *Cytokine* 143: 155541. DOI: 10.1016/j.cyto.2021.155541.

Galati G, Sabzevari O, Wilson JX, O'Brien PJ. 2002. Prooxidant activity and cellular effects of the phenoxyl radicals of dietary flavonoids and other polyphenolics. *Toxicol* 177: 91–104.

Gautam SC, Gao X, Dulchavsky S. 2007. Immunomodulation by curcumin. *Adv Exp Med Biol* 595: 321–341.

Churchill M, Chadburn A, Bilinski RT, Bertagnolli MM. 2000. Inhibition of intestinal tumors by curcumin is associated with changes in the intestinal immune cell profile. *J Surg Res* 89: 169–175.

Ghanima MMA, Abd El-Hack ME, Othman SI, Taha AE, Allam AA, Abdel-Moneim AME. 2020. Impact of different rearing systems on growth, carcass traits, oxidative stress biomarkers, and humoral immunity of broilers exposed to heat stress. *Poult Sci* 99(6): 3070–3078.

Haldar S, Ghosh T, Bedford M. 2011. Effects of yeast (*Saccharomyces cerevisiae*) and yeast protein concentrate on production performance of broiler chickens exposed to heat stress and challenged with *Salmonella enteritidis*. *Anim Feed Sci Technol* 168: 61–71.

Hernandez F, Madrid J, Garcia V, Orengo J, Megias MD. 2004. Influence of two plant extracts on broilers performance, digestibility, and digestive organ size. *Poult Sci* 83: 169–174.

Houshmand M, Azhar K, Zulkifli I, Bejo MH, Kamyab A. 2012. Effects of prebiotic, protein level, and stocking density on performance, immunity, and stress indicators of broilers. *Poult Sci* 91: 393–401.

Heidary M, Hassanabadi A, Mohebalian H. 2020. Effects of in ovo injection of nanocurcumin and vitamin E on antioxidant status, immune responses, intestinal morphology and growth performance of broiler chickens exposed to heat stress. *J Liv Sci Techno* 8(1): 17–27. DOI: 10.22103/jlst.2020.15352.1310.

Huang WT, Niu KC, Chang CK, Lin MT, Chang CP. 2008. Curcumin inhibits the increase of glutamate, hydroxyl radicals and PGE2 in the hypothalamus and reduces fever during LPS-induced systemic inflammation in rabbits. *Eur J Pharmacol* 593: 105–111. DOI: 10.1016/j.ejphar.2008.07.017.

Huang H, Chen J, Sun Q, Teng X. 2021. NLRP3 inflammasome is involved in the mechanism of mitigative effect of selenium on lead-induced inflammatory damage in chicken kidneys. *Environ Sci Pollut Res* 28(9): 1–11.

Jang IS, Ko YH, Moon YS, Sohn SH. 2014. Effects of vitamin C or E on the pro-inflammatory cytokines, heat shock protein 70 and antioxidant status in broiler chicks under summer conditions. *Asian-Australas J Anim Sci* 27(5): 749–760.

Lin H, Buyse J, Decuypere E. 2006a. Strategies for prevention of heat stress in poultry. *Worlds Poult Sci J* 62: 71–85.

Lin H, Decuypere E, Buyse J. 2006b. Acute heat stress induces oxidative stress in broiler chickens. *Comp Biochem Physiol A Mol Integr Physiol* 144: 11–17.

Lin H, Decuypere E, Buyse J. 2004. Oxidative stress induced by cor-

ticosterone administration in broiler chickens (Gallus gallus domesticus) chronic exposure. *Comp Biochem Physiol* 139: 737–744.
Li Y, Cai HY, Liu GH, Dong XL, Chang WH, Zhang S, Zheng AJ, Chen GL. 2009. Effects of stress simulated by dexamethasone on jejunal glucose transport in broilers. *Poult Sci* 88(2): 330–337.
Lv ZP, Peng YZ, Zhang BB, Fan H, Liu D, Guo YM. 2018. Glucose and lipid metabolism disorders in the chickens with dexamethasone-induced oxidative stress. *J Anim Phys Anim Nutr* 102(2): e706.
Luo JW, Zhou ZL, Zhang H, Ma RS, Hou JF. 2013. Bone response of broiler chickens (Gallus gallus domesticus) induced by corticosterone. *Comp Biochem Physiol Part A* 164(2): 410–416.
Ma D, Liu Q, Zhang M, Feng J, Li X, Zhou Y, Wang X. 2019. iTRAQ-based quantitative proteomics analysis of the spleen reveals innate immunity and cell death pathways associated with heat stress in broilers (Gallus gallus). *J Proteom* 196: 11–21.
Mohamed AS, Abd El Latif MA, Hussein EA, Toson EM, Saleh M, Kokoszynski D, Elnesr SS, Mohany M, Al-Rejaie SS, Elwan H. 2023. Efficacy of dietary supplementation with zinc-chromium mixture, organic selenium, or their combinations on growth performance, carcass traits, and blood profiles of broilers under heat stress conditions. *Anim* 13(15): 2539.
Jain NC. 1993. *Essentials of veterinary hematology*. Philadelphia (PA): Lea and Febiger. p. 222–257.
Kim M, Kim Y. 2010. Hypocholesterolemic effects of curcumin via up-regulation of cholesterol 7a-hydroxylase in rats fed a high fat diet. *Nutr Res Pract* 4:191–195.
Kijparkorn S, Angkanaporn K. 2003. Effect of turmeric (Curcuma longa Linn.) as an antioxidant on immune status and growth performances of stressed broilers. [M.Sc. thesis]. The Chulalongkorn University, Faculty of Veterinary Science.
Ma Z, Shayeganpour A, Brocks DR, Lavasanifar A, Samuel J. 2007. High-performance liquid chromatography analysis of curcumin in rat plasma: application to pharmacokinetics of polymeric micellar formulation of curcumin. *Biomed Chromatogr* 21:546–552.
Mashaly MM, Hendricks GL, Kalama MA, Gehad AE, Abbas AO, Patterson PH. 2001. Effect of heat stress on production parameters and immune responses of commercial laying hens. *Poult Sci* 83:889–894. https://doi.org/10.1093/ps/83.6.889
Nabavi SF, Daglia M, Moghaddam AH, Habtemariam S, Nabavi SM. 2014. Curcumin and liver disease: from chemistry to medicine. *Compr Rev Food Sci Food Saf* 13:62–77.
Nazar FN, Magnoli AP, Dalcero AM, Marin RH. 2012. Effect of feed contamination with aflatoxin B1 and administration of exogenous corticosterone on Japanese quail biochemical and immunological parameters. *Poult Sci* 91(1):47–54.
Ohtsu H, Yamazaki M, Abe H, Murakami H, Toyomizu M. 2015. Heat stress modulates cytokine gene expression in the spleen of broiler chickens. *J Poult Sci* 52(4):282–287.
Osho SO, Adeola O. 2020. Chitosan oligosaccharide supplementation alleviates stress stimulated by in-feed dexamethasone in broiler chickens. *Poult Sci* 99(4):2061–2067.
Platel K, Srinivasan K. 2000. Influence of dietary spices and their active principles on pancreatic digestive enzymes in albino rats. *Nahrung* 44:42–46.
Priyadarsini KI. 1997. Free radical reactions of curcumin in membrane models. *Free Radic Biol Med* 23:838–843.
Yadav R, Jee B, Awasthi SK. 2015. Curcumin suppresses the production of pro-inflammatory cytokine interleukin-18 in lipopolysaccharide stimulated murine macrophage-like cells. *Indian J Clin Biochem* 30(1):109–112. https://doi.org/10.1007/s12291-014-0452-2
Palizgir MT, Akhtaria M, Mahmoudia M, Mostafaeia S, Rezaiemaneshc A, Shahram F. 2018. Curcumin reduces the expression of interleukin 1b and the production of interleukin 6 and tumor necrosis factor alpha by M1 macrophages from patients with Behcet's disease. *Immunopharmacol Immunotoxicol*. https://doi.org/10.1080/08923973.2018.1474921
Puvadolpirod S, Thaxton JP. 2000a. Model of physiological stress in chickens: response parameters. *Poult Sci* 79:363–369.
Puvadolpirod S, Thaxton JP. 2000b. Model of physiological stress in chickens: 2. Dosimetry of adrenocorticotropin. *Poult Sci* 79:370–376.
Rahmani M, Golian A, Kermanshahi H, Bassami MR. 2018. Effects of curcumin or nanocurcumin on blood biochemical parameters, intestinal morphology and microbial population of broiler chickens reared under normal and cold stress conditions. *J Appl Poult Sci* 46(1):200–209. https://doi.org/10.1080/09712119.2017.1284077
Rahmani M, Golian A, Kermanshahi H, Bassami MR. 2017. Effects of curcumin and nanocurcumin on growth performance, blood gas indices and ascites mortalities of broiler chickens reared under normal and cold stress conditions. *Ital J Anim Sci* 16(3):438–446. https://doi.org/10.1080/1828051X.2017.1290510
Reddy AC, Lokesh BR. 1996. Effect of curcumin and eugenol on iron-induced hepatic toxicity in rats. *Toxicol* 107:39–45.
Surai PF. 2002. *Natural antioxidants in avian nutrition and reproduction*. Nottingham: Nottingham University Press.
Surh YJ, Han SS, Keum YS, Seo HJ, Lee SS. 2000. Inhibitory effects of curcumin and capsaicin on phorbol ester-induced activation of eukaryotic transcription factors, NF-kappaB and AP-1. *Biofactors* 12:107–112.
Suvanated C, Kijparkorn S, Angkanaporn K. 2003. Effect of turmeric (Curcuma longa linn.) as an antioxidant on immune status and growth performances of stressed broilers. [M.Sc. thesis]. The Chulalongkorn University, Faculty of Veterinary Science, Thailand.
Sandur SK, Pandey MK, Sung B, Ahn KS, Murakami A, Sethi G, Limtrakul P, Badmaev V, Aggarwal BB. 2007. Curcumin, demethoxycurcumin, bisdemethoxycurcumin, tetrahydrocurcumin and turmerones differentially regulate anti-inflammatory and anti-proliferative responses through a ROS-independent mechanism. Carcino28:1765–1773.
Srinivasan K, Sambaiah K. 1991. The effect of spices on cholesterol 7 alphahydroxylase activity and on serum and hepatic cholesterol levels in the rat. Int J VitamNutr Res 61:364–369
Virden WS, Kidd MT. 2009. Physiological stress in broilers: ramifications on nutrient digestibility and responses. *J Appl Poult Res* 18:338–347.
Wang R, Jiao H, Zhao J, Wang X, Lin H. 2016. Glucocorticoids enhance muscle proteolysis through a myostatin-dependent pathway at the early stage. *PLoS One* 11(5): e0156225.
Xu YQ, Xing YY, Wang ZQ, Yan SM, Shi BL. 2018. Pre-protective effects of dietary chitosan supplementation against oxidative stress induced by diquat in weaned piglets. *Cell Stress Chaperones* 23(4):703–710.
Zhang J, Hou X, Ahmad H, Zhang H, Zhang L, Wang T. 2014. Assessment of free radicals scavenging activity of seven natural pigments and protective effects in AAPH-challenged chicken erythrocytes. *Food Chem* 145:57–65.
Zhang Z, Wang H, Jiao R, Peng C, Wong YM, Yeung VS, Huang Y, Chen ZY. 2009. Choosing hamsters but not rats as a model for studying plasma cholesterol-lowering activity of functional foods. *Mol Nutr Food Res* 53:921–930.