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Effects of Coenzyme Q_{10} Supplementation on Growth Performance, some Hematological Parameters, Plasma Enzymes Activities in Broilers with Pulmonary Hypertension Syndrome (PHS)

Research Article

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ABSTRACT

This study investigated the effects of coenzyme Q_{10} (CoQ_{10}) supplementation on hematological, enzymes activities and biochemical parameters in broilers with pulmonary hypertension syndrome (PHS). Two hundred and forty 1-d-old Ross 308 male broiler chicks were randomly allocated into 3 groups with 4 replicates. From d 14, the diets were supplemented with CoQ_{10} at levels of 0, 20 and 40 mg/kg, respectively, while exposing them to low ambient temperature (10 to 15 ˚C) to induce PHS until d 42. Mortality was inspected to determine cause of death and diagnose of PHS. Hematological, biochemical and pathological tests were used to determine the incidence of PHS: total red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), plasma protein and glucose, activity of alanine transaminase (ALT), aspartate transaminase (AST) and lactate dehydrogenase (LDH). Blood samples were taken at d 21 and 42. At the end of the experiment (wk 6), 2 chicks from each replicate were randomly selected and slaughtered. The heart was removed; the right ventricle was dissected away from the left ventricle and septum and the ratio of right ventricle weight to total ventricle weight (RV/TV) was calculated. Average BW gain and average feed intake were measured weekly from d 15 and average feed conversion ratio was calculated and reported weekly. The results showed that 40 mg/kg CoQ_{10} supplementation improved feed conversion ratio (FCR) ($P<0.05$). Moreover, RBC count and plasma protein and glucose level were significantly decreased by 40 mg/kg CoQ_{10} compared to the other groups, but no significant changes were observed in HGB and HCT. The LDH activity decreased by CoQ_{10} supplementation ($P<0.05$). Measurement of malondialdehyde (MDA) content in plasma, RV / TV and mortality due to PHS decreased by 40 mg/kg CoQ_{10} supplementation ($P<0.05$). In conclusion, CoQ_{10} exerted preventive roles in PHS, possible through delivering antioxidant effect of cardiac myocytes and erythrocytes.

KEY WORDS blood parameters, broiler chicks, coenzyme Q_{10}, PHS, plasma enzymes activity.

INTRODUCTION

Pulmonary hypertension syndrome (PHS) is a metabolic disorder that mostly occurs in fast-growing broiler chickens (Arab *et al*. 2006). The PHS is a common problem that causes considerable mortality (Julian, 1993). Pulmonary hypertension and cardiac dysfunction are the most important features of PHS. Pathological findings indicate that the creation of a cavity on the exterior surface of the right ventricular wall is the first sign of damage in pulmonary hypertension. As the injury progresses, it leads to dilation and hypertrophy of the right ventricle resulting in increased blood viscosity, reduced oxygen supply, congestive heart failure (CHF) and accumulation of fluids in the abdominal cavity (Julian, 1993). Oxidative stress is also involved in the pathophysiological progression leading to PHS. Recent

investigations on the etiology of PHS in chickens focused on 3 aspects: (1) pulmonary hypertension, (2) miscellaneous cardiac pathologies and (3) cellular damage caused by reactive oxygen species and peroxidative damage (Geng *et al*. 2004).

Ubiquinol, the reduced form of CoQ_{10}, can serve as an important antioxidant to protect biological membranes against peroxidative damage in tissues and subcellular fractions (Forsmark-Andre´e *et al*. 1997).

Coenzyme Q (2, 3-dimethoxy, 5-methyl, 6-polyisoprene parabenzoquinone, ubiquinone) is present in all membranes of cells (Kale´n *et al*. 1987). Because of its ubiquitous distribution in nature CoQ is also known as ubiquinone. CoQ_{10} has a fundamental role in cellular bioenergetics as a cofactor in the mitochondrial electron transport chain (respiratory chain) and is therefore essential for the production of ATP (Hemmin *et al*. 2006). The redox functions of CoQ_{10} extend beyond its role in the mitochondria. Furthermore, CoQ_{10} in its reduced form as the hydroquinone (called ubiquinol) is a potent lipophilic antioxidant and is capable of recycling and regenerating other antioxidants such as tocopherol and ascorbate (Hemmin *et al*. 2006). Its antioxidant properties contribute to prevention of lipid peroxidation. It has been found to be efficient in preventing LDL oxidation which is an important step in evolution of atherosclerosis (Yokoyama *et al*. 1996).

It may be advantageous to supplement CoQ_{10} in the diet when tissue CoQ_{10} content is decreased in ischemia-reperfusion syndrome, inflammation, and other pathologic processes (Tribble *et al*. 1994; Upston *et al*. 1997; Haramaki *et al*. 1998). Beneficial effects of CoQ_{10} supplementation have been demonstrated in patients with cardiovascular disease (Mortensen, 1993), hypertension (Montaldo *et al*. 1991) and chronic obstructive pulmonary disease (Fujimoto *et al*. 1993).

Nakamura *et al*. (1996) fed broilers with diets supplemented with 40 mg/kg CoQ_9 (which has a hydrophobic side chain with 9 isoprenoid units) and showed that dietary CoQ_9 supplementation was beneficial in reducing the PHS incidence in broilers. These authors suggested that there was a possibility of preventing PHS in broiler chickens by supplementing diets with ubiquinone. Geng *et al*. (2004) showed that preventive effect of dietary CoQ_{10} on PHS induced in young broilers. It is possible that CoQ_{10} protects the cell membrane and cell structure against peroxidation and thus enables cardiac myocytes and erythrocytes to be healthier and more tolerant to the metabolic stress. Determine the effects of dietary CoQ_{10} supplementation on growth performance, PHS incidence and mortality in cold induced PHS broilers was the first aim of this study and activity of lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) enzymes and plasma protein and glucose were investigated as a second aim.

MATERIALS AND METHODS

Birds and diets

Two hundred and forty one-d-old male broiler chicks (Ross 308) were used in this experiment. Chicks were allocated randomly into 3 treatments groups with 4 replicates each and 20 chicks per replicate (cage). All the chicks were fed a basal corn-soybean meal diet in mash form, including 22.04% crude protein (CP) and 3200 kcal/kg metabolizable energy (ME) during starter period (1 to 21 days of age) and 20.26% CP and 3200 kcal ME during grower period (22 to 42 days of age) (Table 1).

Table 1 Composition of experimental diets

Item	Starter (0 to 21 d)	Grower (21 to 42 d)
Ingredients (%)		
Corn	54.47	59.25
Soybean meal (44% protein)	22.5	20.75
Corn gluten meal	7	8
Fish meal	6.16	3
Soybean oil	6	5.7
Dicalcium phosphate	1.72	1.22
Limestone	1.2	1.3
Vitamin and mineral premix[1]	0.5	0.5
Common salt	0.25	0.25
DL-methionine	0.2	0
L-lysine HCl	0	0.03
Total	100	100
Calculated analysis		
ME (kcal/kg)	3200	3200
CP (%)	22.04	20.66
Calcium (%)	0.9	0.9
Available phosphorus (%)	0.4	0.35
Arginine (%)	1.3	1.3
Lysine (%)	1.14	1
Methionine (%)	0.53	0.4
Methionine + cystine (%)	0.9	0.75

[1] Supplied per kilogram of diet: vitamin A: 11000 IU; vitamin D_3: 5000 IU; vitamin E: 40 IU; vitamin K: 4 mg; vitamin B_6: 4 mg; vitamin B_{12}: 0.011 mg; Riboflavin: 5 mg; Niacin: 50 mg; Biotin: 0.01 mg; Thiamine: 3 mg; Zinc: 80 mg; Manganese: 100 mg; Selenium: 10 mg and Iron: 80 mg.
ME: metabolizable energy and CP: crude protein.

At day 15 of age, these three treatment groups were supplemented with 0, 20 or 40 mg CoQ_{10}/kg (Antiaging Institute of California Beverly Hills, CA90210, USA). Feed and water provided *ad libitum* during the experiment.

Management

For inducing PHS, all the birds were raised under 32 ˚C and 30 ˚C during the first and second week of age (respectively and then the house temperature was decreased to 15 ˚C during week 3 and maintained between 10 and 15 ˚C for the rest of the study (Fathi *et al*. 2011; Fathi *et al*. 2012). Mor-

tality was recorded daily and all of the dead birds inspected for diagnosis of PHS. Diagnosis of PHS generally depends on observation of the following symptoms: 1) right ventricle hypertrophy, cardiac muscle laxation; 2) swollen and stiff liver and 3) clear, yellowish, colloidal fluid in the abdominal activity (Geng *et al*. 2004). Average BW gain (ABWG) and average feed intake (AFI) were measured weekly from d 15 and average feed conversion ratio (AFCR) was calculated and reported weekly.

Sampling

At day 21 and 42 of age, two chicks from each replicate were randomly selected. Then blood samples were taken from the wing vein after a 3-h starvation period. At the end of experiment, one bird per replicate was killed and its abdomen opened for signs of heart failure and ascites. About 5 grams of liver tissue were removed, homogenated and used for MDA determination. The heart was dissected and removed from the body to determine the ratio of right ventricular (RV) weight to total ventricular (TV) weight ratio. Birds having RV / TV values more than 0.299% were considered to have ventricular hypertrophy (Julian, 1987). Blood samples were collected in tubes with EDTA anticoagulant tubes.

Portions of each blood sample were immediately used for determining total red blood cell (RBC) count, hematocrit (HCT) and hemoglobin (HGB). The remaining was centrifuged and their plasma was collected and stored at -80 ˚C for further enzymatic and chemical analyses.

Malondialdehyde (MDA) assay

The blood was centrifuged at 1500 × g for 5 min; plasma was collected in labeled tubes and stored at -80 ˚C until analysis. After thawing, 500 µL of plasma was placed in a labeled glass tube and mixed with the reagents of a commercial kit for the measurement of thiobarbituric acid reactive substances (TBARS). Each tube was covered with a glass marble and incubated at 95 ˚C for 45 min. The tubes were removed from incubation and allowed to cool in an ice bath for 10 min. Once cooled, the tubes were centrifuged at 3000 × g for 10 min and the supernatant carefully removed from the tubes for analysis. The absorbance of the supernatants was measured at 532 nm using a UV/VIS spectrophotometer (Gildford Instrument Laboratories, Inc., Oberlin, OH) and the results were compared against a standard curve made with 100, 50, 25, 12.5 and 0 nmol/mL of malondialdehyde dimethyl acetyl.

LDH, AST and ALT activity and biochemical parameters assay

Plasma LDH, AST and ALT enzymes activities and glucose and protein in plasma were determined using an autoanalyzer (Autolab, K4500, Autoanalyzaer Medical System, Germany).

Statistical analysis

The data were analyzed based on a completely randomized design using the GLM procedure of SAS (2002). Contrasts between treatments means were evaluated by Tukey's test at a $P < 0.05$.

RESULTS AND DISCUSSION

Growth performance

Average feed intake (AFI), average body weights gain (ABWG) and average feed conversion ratio (AFCR) of control and CoQ_{10} treated birds are shown in Table 2. There were no significant difference for AFI and ABWG between 3 treatments at all weeks, while AFCR was greater ($P<0.05$) just at whole period of study (3-6 week) in control treated birds.

Mortality due to PHS and RV / TV ratio

Mortality due to ascites and RV/TV is shown in Table 3. Data presented in table 3 shows that 40 mg/kg CoQ_{10} reduced mortality due to PHS and RV / TV ratio.

Plasma and liver MDA content

The MDA content of plasma and liver of birds are shown in Table 4. At d 21, MDA content in plasma and liver was not affected by treatments. But at d 42, supplementation of 40 mg/kg CoQ_{10} reduced MDA in plasma ($P<0.05$).

Biochemical parameters

The plasma glucose and protein were the biochemical parameters that were significantly ($P<0.05$) influenced by treatments. As showed in Table 5, supplementation of 40 mg/kg CoQ_{10} reduced these two parameters in broilers under ascites induced.

Hematology

The results in Table 5 showed that supplementation 40 mg/kg CoQ_{10} significantly decreased RBC of broilers at d 42. Blood hematocrite (HCT) and hemoglobin (HGB) contents of birds were not affected by treatments ($P<0.05$).

Enzymes

The activities of plasma ALT, AST and LDH are shown in Table 6; there was no significant difference between treatment groups for ALT and AST enzymes ($P<0.05$), but supplementation 40 mg/kg CoQ_{10} significantly decreased plasma LDH activity ($P<0.05$). The measurements from the lipid peroxidation (malondialdehyde (MDA) equivalents) in the present study showed that, CoQ_{10} supplementation significantly reduced MDA in plasma (Table 4).

Table 2 Growth performance of broilers treatments

	Week				
Treatments (CoQ_{10} mg/kg)	3	4	5	6	3-6
Average feed intake (g)					
0	295±40	441±54	702±51	882±107	2311±151
20	350±37	450±48	690±42	800±89	2309±140
40	374±41	482±51	651±49	812±95	2320±135
Average BW gain (g)					
0	141±21	295±27	363±31	420±41	1200±51
20	156±18	310±25	415±35	431±35	1350±47
40	174±22	364±29	477±27	462±40	1477±45
Average feed conversion ratio					
0	2.25±0.22	1.47±010	1.92±0.11	2.19±0.21	1.95±0.10^{a}
20	2.24±0.20	1.45±016	1.66±0.17	1.85±0.17	1.71±0.10^{ab}
40	2.22±0.15	1.29±021	1.40±0.19	1.79±0.19	1.67±0.12^{b}

The means within the same columns with at least one common letter, do not have significant difference (P>0.05).

Table 3 RV / TV ration and mortality percentage of broilers in different treatments

Treatment (CoQ_{10} mg/kg)	RV / TV ratio	Total mortality percentage due to ascites (%)
0	0.31±0.01^{a}	38±4^{a}
20	0.29±0.01^{a}	34±4^{a}
40	0.25±0.02^{b}	21±1^{b}

The means within the same columns with at least one common letter, do not have significant difference (P>0.05).

Table 4 MDA equivalents levels in plasma and liver tissue of broilers in different treatments

Day	Treatment (CoQ_{10} mg/kg)	MDA in plasma (nm/mL)	MDA in liver (nm/mL)
21	0	2.5±0.19	1.32±0.23
	20	2.2±0.17	1.33±0.24
	40	2.2±0.21	1.30±0.12
42	0	6.27±0.43^{a}	2.6±0.25
	20	5.55±0.23^{a}	2.7±0.29
	40	2.15±0.18^{b}	2.4±0.39

The means within the same columns with at least one common letter, do not have significant difference (P>0.05).
MDA: malondialdehyde.

Table 5 Hematological and biochemical parameters of broilers in different treatments

Day	Treatment (CoQ_{10} mg/kg)	RBC (106/µL)	HGB (g/dL)	HCT (%)	Glucose (mg/dL)	Protein (mg/dL)
21	0	2.42±0.16	8.57±0.49	34.27±2.04	277.5±34	3.60±0.23
	20	2.38±0.17	8.53±0.45	32.34±0.95	288.4±43	3.95±0.24
	40	2.28±0.07	8.40±0.33	28.70±0.73	292.5±17	4.45±0.14
42	0	2.80±0.17^{a}	11.2±0.35	39.30±2.27	321.2±6^{a}	3.50±0.05^{a}
	20	2.55±0.28^{a}	10.6±0.67	38.55±1.54	311.3±5^{a}	3.10±0.12^{a}
	40	2.08±0.08^{b}	9.60±0.43	37.62±1.21	274.5±5^{b}	2.95±0.06^{b}

The means within the same columns with at least one common letter, do not have significant difference (P>0.05).
RBC: red blood cell; HGB: hemoglobin and HCT: hematocrit.

Table 6 ALT, AST and LDH levels in plasma of broilers in different treatments

Day	Treatment (CoQ_{10} mg/kg)	ALT (U/L)	AST (U/L)	LDH (U/L)
21	0	4.00±0.41	223.5±11	3100±250^{a}
	20	3.35±0.33	235.0±15	2920±550^{a}
	40	3.32±0.65	283.2±24	2107±530^{b}
42	0	7.37±0.25	240.5±17	4920±674^{a}
	20	6.60±0.71	255.2±23	4750±520^{ab}
	40	5.00±0.41	269.2±17	4550±595^{b}

The means within the same columns with at least one common letter, do not have significant difference (P>0.05).
ALT: alanine transaminase; AST: aspartate transaminase and LDH: lactate dehydrogenase.

It had hypothesis that CoQ_{10}'s antioxidant properties result in quenching of free radicals that cause inactivation of endothelium derived relaxing factor and / or fibrosis of arteriolar smooth muscle (Ignarro *et al*. 1989).

Its antioxidant properties contribute to prevention of lipid peroxidation. It has been found to be efficient in preventing LDL oxidation which is an important step in evolution of atherosclerosis (Yokoyama *et al*. 1996).

CoQ_{10} has a direct anti-atherogenic effect, which has been demonstrated in apolipoprotein E-deficient mice fed with a high-fat diet. In this model, supplementation with CoQ_{10} at pharmacological doses was capable of decreasing the absolute concentration of lipid hydroperoxides in atherosclerotic lesions and of minimizing the size of atherosclerotic lesions in the whole aorta. Whether these protective effects are only due to the antioxidant properties of CoQ or due to some other mechanisms remains to be established (Littarru and Tiano, 2007).

In our study, decrees in the number of erythrocytes (Table 5), which also contributed to a significant lowering RV / TV by CoQ_{10}, was found to be involved the positive effects of CoQ_{10} on erythrocyte membrane and cell geometry. Geng *et al*. (2004) had reported that, CoQ_{10} can serves as an antioxidant in erythrocyte membrane and had a protective effect on structure and extensibility of erythrocyte membrane and cell geometry.

Another antioxidant mechanism of CoQ might have practical implications in the ischemia-reperfusion damage. It is known that interaction of myoglobin with hydrogen peroxide leads to the formation of ferrylmyoglobin and / or its radical form: these transformation products of myoglobin are regarded as powerful oxidizing agents capable of attacking important cellular constituents. Formation of ferrylmyoglobin is an event that might have considerable practical importance, since skeletal muscle and the myocardium are rich in myoglobin and the formation of hydrogen peroxide arising from ischemia reperfusion might trigger myoglobin oxidation to ferrylmyoglobin, with further damage.

PHS heart index (RV/TV), that is, the ratio of right ventricle weight to total ventricle weight, was suggested to be a sensitive indicator of prior exposure of the heart to increased pulmonary arterial pressures (Burton *et al*. 1968). Broilers with an AHI < 0.27 without fluid in the abdomen were regarded as normal, whereas those with an AHI ≥ 0.30 with fluid accumulation were regarded as having pulmonary hypertension (Cawthon *et al*. 2001).

The present study showed that CoQ_{10} supplementation significantly decreased RV / TV ratio compared with the control ($P \leq 0.05$), with 40 mg/kg CoQ_{10} appearing more effective in decreasing RV / TV ratio than 20 mg/kg (Table 3). This further supported the idea that CoQ_{10} might offer some protection to chicks' cardiac myocytes by improving the availability of slow action potentials as described by Azuma *et al*. (1985).

Moreover, it has been suggested that the membrane-stabilizing property of CoQ_{10} has been postulated to involve the phospholipid-protein interaction that increases prostaglandin (especially prostacyclin) metabolism.

It is thought that CoQ_{10} stabilizes myocardial calcium-dependent ion channels and prevents the depletion of metabolites essential for ATP synthesis. CoQ_{10} also decreases blood viscosity and improves blood flow to cardiac muscle in patients with ischemic heart disease (Kato and Yoneda, 1990).

It is also, suggested that Heart failure is often characterized by an energy depletion status that has been associated with low endogenous CoQ_{10} levels. Since CoQ_{10} participates in the transport of electrons from organic substrates to oxygen in the respiratory chain of mitochondria with the production of energy, it has a role in providing energy for the functioning of the failing and energy depleted heart (Kumar *et al*. 2007).

In our study, CoQ_{10} supplementation reduced plasma protein (Table5). It has reported that Lipid peroxidation can alter the membrane properties of cellular and subcellular organelles (mitochondria and sarco-endoplasmic reticulum) crucial for maintenance of normal cardiomyocyte function. Broilers with congestive heart failure (CHF) show evidence of calcium overload in these subcellular components (Maxwell *et al*. 1993; Li *et al*. 2006) and evidence of breakdown and release of the protein of contractile apparatus, such as myosin and troponin T, into the circulation (Maxwell *et al*. 1994).

Based on our finding, CoQ_{10} (40 mg/kg) supplementation decreased plasma glucose and LDH activity (Table 6). High protein and glucose in plasma and high LDH activity in other treatments were observed. Arab *et al*. (2006) reported that high LDH activity in birds under PHS induced. Theses researchers suggested that resulting in tissue oxidative injury in organs, including lung and heart and liver.

Reduced plasma glucose and protein by CoQ_{10} (40 mg/kg) supplementation were simultaneous with reduced LDH activity. It might be concluded that the main portion of increased plasma glucose is generated from plasma proteins by gluconeogenesis and possibly a slight portion of this glucose might come from triglyceride sources. Diaz-Cruz *et al*. (1996) detected a greater concentration of glucose in the liver of broilers with altitude-induced PHS. They attributed it to gluconeogenesis, because this pathway uses substrates other than carbohydrates such as lactate and amino acids to produce glucose. They also observed a greater ammonium and as a result greater protein catabolism of liver in the prepared hepatocytes of broilers with PHS in comparison with healthy birds. They suggested that deaminated amino acids might contribute to the high rate of gluconeogenesis found in hepatocytes of broiler with PHS. Despite chemical reactions like gluconeogenesis, these changes may be related to exudation of serum protein from extra cellular fluids.

Tankson *et al*. (2002) reported that reduction in both serum protein and cholesterol may well be adaptive physiological responses to the impending loss of extra cellular fluids via PHS.

CONCLUSION

Dietary CoQ_{10} enhanced high growth rate and alleviated heart failure and PHS. It is possible that CoQ_{10} protects the cell membrane and cell structure against peroxidation and thus enables cardiac myocytes and erythrocytes to be healthier and more tolerant to the metabolic stress.

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REFERENCES

Arab H.A., Jamshidi R., Rassouli A., Shams G. and Hassanzadeh M.H. (2006). Generation of hydroxyl radicals during ascites experimentally indued in broilers. *Br. Poult. Sci*. **47(2),** 216-222.

Azuma J., Harada H., Sawamura A., Ohta H., Awata N., Yamauchi K., Kishimoto S. and Sperelakis N. (1985). Beneficial effect of coenzyme Q on myocardial slow action potentials in hearts subjected to decreased perfusion pressure-hypoxia- substrate-free perfusion. *Basic Res. Cardiol*. **80,** 147-155.

Burton R.R., Besch E.L. and Smith A.H. (1968). Effect of chronic hypoxia on the pulmonary arterial blood pressure of the chicken. *Am. J. Physiol*. **214,** 1438-1442.

Cawthon D., Beers K. and Bottje W.G. (2001). Electron transport chain defect and inefficient respiration may underlie pulmonary hypertension syndrome (ascites)-associated mitochondrial dysfunction in broilers. *Poult. Sci*. **80,** 474-484.

Diaz-Cruz A., Nava C., Villanueva R., Serret M., Guinzberg R. and Pina E. (1996). Hepatic and cardiac oxidative stress and other metabolic changes in broilers with the ascites syndrome. *Poult. Sci*. **75,** 900-903.

Fathi M., Nazer Adl K., Ebrahimnezhad Y., Aghdam Shahryar H., daneshyar M. and Tanha T. (2011). The role of oxidative stress in development of congestive heart failure (CHF) in broilers with pulmonary hypertension syndrome (PHS). *J. Anim. Vet. Adv*. **10(20),** 2724-2729.

Fathi M., Nazer Adl K., Ebrahimnezhad Y., Aghdam Shahryar H., Daneshyar M. and Tanha T. (2012). Plasma enzymes activities and antioxidant status characterization in pulmonary hypertension syndrome (PHS) in broilers. *African J. Agric. Res*. **7(5),** 1414-1419.

Forsmark-Andre´e P., Lee C.P., Dallner G. and Ernster L. (1997). Lipid peroxidation and changes in the ubiquinone content and the respiratory chain enzymes of submitochondrial particles. *Free Radic. Biol. Med*. **22,** 391-400.

Fujimoto S., Kurihara N., Hirata K. and Takeda T. (1993). Effects of CoQ_{10} administration on pulmonary function and exercise performance in patients with chronic lung diseases. *Clin. Invest*. **71,** 162-166.

Geng A.L., Guo Y.M. and Yang Y. (2004). Reduction of ascites mortality in broilers by CoQ_{10}. *Poult. Sci*. **83,** 1587-1593.

Haramaki N., Stewart D.B., Aggarwal S., Ikeda H., Reznick A.Z. and Packer L. (1998). Networking antioxidants in the isolated rat heart are selectively depleted by ischemiareperfusion. *Free Radic. Biol. Med*. **25,** 329-339.

Hemmin B. and Rajak C. (2006). CoQ_{10}: absorption, tissue uptake, metabolism and pharmacokinetics. *Free Radic. Res*. **40(5),** 445-453.

Ignarro L.J. (1989). Biological actions and properties of endothelium-derived nitric oxide formed and released from artery and vein. *Circ. Res*. **65,** 1-21.

Julian R.J. (1993). Ascites in poultry. *Avian Pathol*. **22,** 419-454.

Julian R.J., Friars G.W., French H. and Quinton M. (1987). The relationship of right ventricular hypertrophy, right ventricular failure, and ascites to weight gain in broiler and roaster chickens. *Avian Dis*. **31,** 130-135.

Kale´n A., Norling B., Appelkvist E.L. and Dallner G. (1987). Ubiquinone biosynthesis by the microsomal fraction from rat liver. *Biochim. Biophys. Acta*. **926,** 70-78.

Kato T. and Yoneda S. (1990). Reduction in blood viscosity by treatmentwith CoQ_{10} in patients with ischemic heart disease. *Int. J. Clin. Pharmacol. Ther. Toxicol*. **28(3),** 123-126.

Kumar A., Kaur H., Devi P. and Mohan V. (2007). Role of coenzyme Q_{10} (CoQ_{10}) in cardiac disease, hypertension and Meniere-like syndrome. *Pharmacol. Therapeut*. **124,** 259-268.

Li K., Qiao J., Zhao L., Dong S., Ou D., Wang J., Wang H. and Xu T. (2006). Increased calcium deposits and decreased Ca2 + -ATPase in right ventricular myocardium of ascitic broiler chickens. *J. Vet. Med*. **53,** 458-463.

Littarru G.P. and Tiano L. (2007). Bioenergetic and antioxidant properties of CoQ_{10}: recent developments. *Mol. Biotechnol*. **37,** 31-37.

Maxwell M.H., Robertson G.W. and Moseley D. (1994). Potential role of serum troponin T in cardiomyocyte injury in the broiler ascites syndrome. *Br. Poult. Sci*. **35,** 663-667.

Maxwell M.H., Robertson G.W. and Mitchell M.A. (1993). Ultrastructural demonstration of mitochondrial calcium overload in myocardial cells from broiler chickens with ascites and induced hypoxia. *Res. Vet. Sci*. **54,** 267-277.

Mortensen S.A. (1993). Perspectives on therapy of cardiovascular diseases with CoQ_{10} (ubiquinone). *Clin. Invest*. **71,** 116-123.

Montaldo P.L., Fadda G., Salis S., Satta G., Tronci M., Cesare R.D., Reina R. and Concu A. (1991). Effects of the prolonged administration of CoQ_{10} in borderline hypertensive patients: a hemodynamic study. Pp. 417-424 in Biomedical and Clinical Aspects of Coenzyme Q. K. Folkers, G.P. Littarru and T. Yamagami, Eds. Elsevier Science, Amsterdam.

Nakamura K., Noguchi K., Aoyama T., Nakajlma T. and Tanimura N. (1996). Protective effect of ubiquinone (CoQ_9) on ascites in broiler chickens. *Br. Poult. Sci*. **37,** 189-195.

SAS Institute. (2002). SAS®/STAT Software, Release 9.1. SAS Institute, Inc., Cary, NC. USA.

Tankson J.D., Thaxton J.P. and Vizzier-Thaxton Y. (2002). Biochemical and immunological changes in chickens experienc-

ing pulmonary hypertension syndrome caused by *Enterococcus faecalis*. *Poult. Sci*. **81,** 1826-1831.

Tribble D.L., Van Den Berg J.J., Motchnik P.A., Ames B.N., Lewis D.M., Chalt A. and Krauss R.M. (1994). Oxidative susceptibility of low density lipoprotein subfractions is related to their Q_{10} and alpha-tocopherol content. *Proc. Natl. Acad. Sci. USA*. **91,** 1183-1187.

Upston J.M., Neuzil J., Witting P.K., Alleva R. and Stocker R. (1997). Oxidation of free fatty acids in low density lipoprotein by 15-lipoxygenase stimulates nonenzymic, α-tocopherol-mediated peroxidation of cholesterylesters. *J. Biol. Chem*. **272,** 30067-30074.

Yokoyama H., Lingle D.M., Crestanello J.A., Kamelgard J., Kott B.R., Momeni R., Millili J., Mortensen S.A. and Whitman G.J. (1996). CoQ_{10} protects coronary endothelial function from ischemia reperfusion injury via an antioxidant effect. *Surgery*. **120(2),** 189-196.