ISSN 1682-8356
ansinet.org/ijps

INTERNATIONAL JOURNAL OF

POULTRY SCIENCE

ANSInet
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan
Mob: +92 300 3008585, Fax: +92 41 8815544
E-mail: editorijps@gmail.com

International Journal of Poultry Science 11 (11): 718-729, 2012
ISSN 1682-8356

Role of Dietary L-Arginine in Poultry Production

A.M. Fouad[1,2], H.K. El-Senousey[1,2], X.J. Yang[1] and J.H. Yao[1]
[1]College of Animal Science and Technology, Northwest A&F University,
Yangling, Shaanxi, 712100, China
[2]Department of Animal Production, Faculty of Agriculture, Cairo University, Giza 12613, Egypt

Abstract: As a result of impressive progress that made in economic traits such as body weight gain, feed efficiency and breast yield to meet the demands of consumers, nowadays, poultry became more susceptible to obesity, stressors and less ability to resist the common diseases in commercial farms. L-Arginine (L-Arg) supplementation in poultry diets improves egg production, egg weight, modulates lipid metabolism toward reducing total body fat accumulation to improve meat quality and increases antioxidant defense under normal conditions. Also under stress conditions L-Arg has the ability to alleviate this stress and to normalize the growth performance. Dietary L-Arg supplementation reduces ascites mortality under low ambient temperatures, attenuates the adverse effects of heat stress and high stock density, activates the immune system and enhances its responses to different common diseases in poultry farms. Therefore, L-Arg plays a pivotal role in poultry production.

Key words: L-Arginine, poultry, carcass yield, stress, immune

INTRODUCTION

In the last few decades, chickens have genetically been selected to improve body weight gain, feed efficiency, growth rate and breast muscle weight (Burt, 2002). As a consequence of this selection for economically important production traits, firstly, this has led to increase the ability of chickens to synthesis fatty acids (Cui *et al*., 2012) which led to excessive accumulation of fat in the body that negatively affects production efficiency, consumer perception and marketability of chickens (Zhou *et al*., 2006). Secondly, negatively affects the immune system efficiency and its ability to resist the diseases. So the susceptibility of modern commercial chickens to diseases increased (Swaggerty *et al*., 2009). Thirdly, this make chickens more susceptible to different stressors such as heat stress compared with unimproved chickens (Lin *et al*., 2006). Improving the immune system efficiency and its resistance to pathogens and enhancing meat quality by reducing total body fat deposition and alleviating stressors such as heat stress through nutrients, are considered practical and efficient solution in enhancing productive performance of modern broiler chickens (Kidd, 2004; Shahin and ABD-EL-Azeem, 2006; Mujahid, 2011).

L-arginine (L-Arg), a basic amino acid, is an important amino acid for chickens because they, like other birds, are unable to obtain Arg from endogenous sources since they lack almost all the enzymes that are involved in the urea cycle (Tamir and Ratner, 1963). L-Arg is a substrate for biosynthesis of many molecules, including protein, nitric oxide, creatine, ornithine, glutamate, polyamines, proline, glutamine, agmatine and dimethylargininesa, thereby it serves a number of important biological and physiological functions in poultry (Khajali and Wideman, 2010).

Allen (1999), Deng *et al*. (2005) and D'Amato and Humphrey (2010) observed that inclusion of L-Arg in broilers diet activated the immune system and improved its efficiency under normal and infection conditions. Al-Daraji *et al*. (2011), Corzo *et al*. (2003) and Wu *et al*. (2011) demonstrated that increasing L-Arg level in broilers, quails and ducks diet reduced total body fat deposition. Addition of L-Arg in poultry diets is required to avoid the harmful influences of excessive free radicals that produced during normal metabolism (Atakisi *et al*., 2009) and to relieve the adverse effects of heat stress (Attia *et al*., 2011). Tan *et al*. (2007) reported that supplementation of L-Arg at the level of 1% reduced incidence of ascites in broilers exposed to low ambient temperature. Srinongkote *et al*. (2004) reported that supplementing 1.36% L-Arg with increasing L-lysine level to maintain the same ratio between L-Arg and L-lysine reduced the negative effects of chronic stress of high stock density in broiler chickens. Furthermore, Manwar *et al*. (2006) reported that increasing dietary L-Arg level led to a significant improve in egg production. Therefore, L-Arg plays a pivotal role in poultry nutrition under different conditions. So this review discusses the effects of L-Arg supplementation and how L-Arg-induces its effects under different conditions.

Corresponding Author: J.H. Yao, College of Animal Science and Technology, Northwest A&F University, Yangling, Shaanxi, 712100, China

L-arginine and egg production: Nitric oxide, a highly reactive and short-lived radical, is implicated in regulating the reproductive functions in poultry (Kumar and Chaturvedi, 2008; Sundaresan *et al*., 2007). Manwar *et al*. (2003) noticed that level of nitric oxide in serum is linked to high egg production in quails. Therefore, Manwar *et al*. (2006) conducted two experiments in quails to investigate the relationship between nitric oxide production and egg production in the first experiment and to evaluate the influence of L-Arg and L-NAME on egg production in the second experiment. They observed that nitric oxide synthesis in Japanese quails was significantly higher in good layer than poor layer in the first experiment. And also they reported that feeding quails diet supplemented with 5% L-Arg significantly increased egg production compared with the control in the second experiment. Furthermore, they found that inhibiting the production of nitric oxide in quails by supplementing L-NAME led to a significant reduction in the concentration of nitric oxide in serum and a significant reduction in yolk weight. Atakisi *et al*. (2009) documented that dietary 5 mg/kg L-Arg supplementation in laying quails significantly increased egg weight and nitric oxide synthesis. So, Basiouni (2009) conducted his experiment to explore why dietary L-Arg supplementation improved egg production and egg weight. Basiouni (2009) demonstrated that inclusion of L-Arg in laying hens diet significantly elevated luteinizing hormone concentration compared with the control. Luteinizing hormone and follicle stimulating hormone govern follicular development, ovulation and egg laying through ovarian steroids (Hartree and Cunningham, 1969). Although experimental evidence showed that dietary L-Arg supplementation can improve egg quality but till now no experiment has designed to investigate the impact of L-Arg on egg quality.

L-arginine and carcass traits: Early study showed that feeding chicken diets deficient in Arg resulted in a significant reduction not only in breast and leg yield but also in muscle creatine (Kratzer and Earl, 1975). Creatine, an endogenous metabolite of Arg, is a unique organic compound that is involved in protein metabolism and is participated in the muscle energy buffering system (Khajali and Wideman, 2010; Chen *et al*., 2011). More recently, Jiao *et al*. (2010) demonstrated that feeding broiler chickens from 1 to 42 days of old 80% of their Arg requirement led to a significant reduction in breast muscle and leg muscle weight and percentages. Khajali *et al*. (2011) confirmed that carcass yield and breast meat yield significantly reduced in broilers fed diets deficient in Arg. Corzo *et al*. (2003) observed that increasing dietary Arg level not only significantly improved carcass yield but also significantly reduced abdominal fat content in heavy broiler chickens from 42 to 56 days of age. Fernandes *et al*. (2009) noted significant enhancements in breast weight, breast fillet weight and thickens and in myofiber diameter of broiler chickens when they fed diets supplemented with L-Arg at the level of 0.1, 0.2 or 0.3% from 1 to 21 days of age compared with the control diets. Carcass yield, breast and thigh muscle percentages of broilers significantly increased by inclusion of L-Arg in the diets at the level of 0.04% (Al-Daraji and Salih, 2012). Similar results were obtained by Wu *et al*. (2011) and Al-Daraji *et al*. (2011) in White Pekin ducks and Japanese quails. Wu *et al*. (2011) reported that providing 1% additional L-Arg above NRC (1994) recommendations for ducks from 21 to 42 days of age not only reduced skin with fat and abdominal fat (undesirable fat) weight relative to body weight but also increased the breast muscle percentage and intramuscular fat content (desirable fat) in breast muscle. Al-Daraji *et al*. (2011) noticed a significant reduction in abdominal fat percentages and a significant enhancement in carcass yield, breast muscle and leg muscles percentage in Japanese quails at 42 days of age when they hatched from eggs injected with 2% L-Arg at 0 day of incubation. It is well documented that increase fat deposition (undesirable fat such as skin fat abdominal fat) leads economic losses as a result of poor feed efficiency and poor meat yield in avian species (Gaya *et al*., 2006; Xiong *et al*., 2010). On the other hand, increase deposition of fat between muscles (intramuscular fat %) is considered desirable trait in avian species and other farm animals because it linked to other important meat quality traits that consumers prefer it such as flavor, juiciness, water holding capacity, tenderness drip loss and cooking loss (Hocquette *et al*., 2010). Therefore, dietary L-Arg supplementation plays a key role in enhancing meat quality.

In avian species, supplementation of L-Arg improves carcass yield, breast and thigh muscles percentage may be due to L-Arg is a substrate for biosynthesis of several molecular including protein, creatine, proline, ornithine, polyamines, glutamate and glutamine (Khajali and Wideman, 2010) which are essential for growth (Chen *et al*., 2011; Graber and Baker, 1973; Emmerson *et al*., 1997; Young and Ajami, 2000; Bartell and Batal, 2007) as shown in Fig. 1. Emadi *et al*. (2011) confirmed that L-Arg is essential for productive performance in broilers where inclusion of L-Arg at the level of 2.5% resulted in a significant increase in total protein concentration in serum. Moreover, inclusion of L-Arg in broiler chicken diets at the level of 250% of their requirement from 1 to 49 days of age significantly reduced the concentration of triglyceride in serum at 49 days of age (Emadi *et al*., 2011). Serum triglyceride level and abdominal fat content significantly declined in Japanese quails at 42 days of age when they injected by 2% L-Arg at 0 day of incubation (Al-Daraji *et al*., 2011). Santoso *et al*. (1995) found that triglyceride level in blood is directly associated with fatty acid synthesis in broiler chickens. One of the

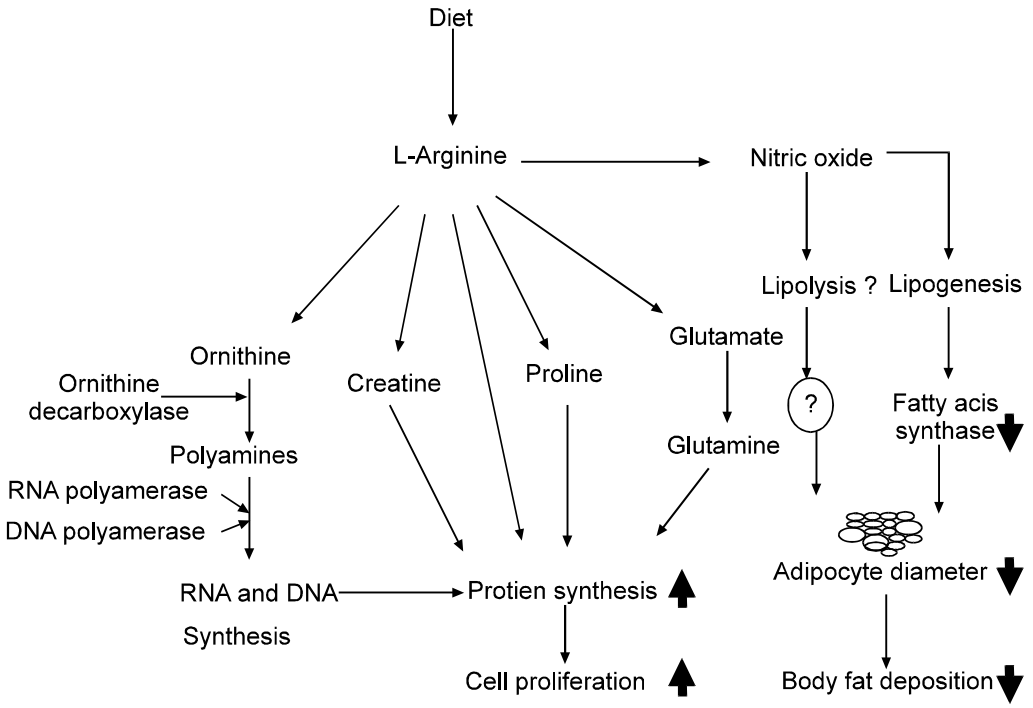

Fig. 1: Effect of L-Arginine on deposition of protein and fat.
▲ = Decrease; ▼ = Increase.

main functions of abdominal fat cells is stored triglyceride that synthesis in the liver (Cartwright, 1991). Abdominal fat has high ability to grow compared with other fat depots (Cartwright, 1991). Abdominal fat ratio to live body weight in avian species can use to monitor total body fat deposition (Becker *et al*., 1979). Because abdominal fat ratio to live body weight in avian species is highly correlated with fat accretion in fat depots (Becker *et al*., 1979). Therefore, dietary L-Arg supplementation can reduce abdominal fat content by reducing fatty acid synthesis. However, Wu *et al*. (2011) found that feeding White Pekin ducks diets supplemented with 1% L-Arg from 21 to 42 d of age led to a significant depressed in the hepatic activity of lipogenic enzymes at 42 d of age. So inclusion of L-Arg at the level of 1% in duck diets significantly reduced total body fat deposition. Now, the important question is why dietary L-Arg supplementation reduces the undesirable fat in poultry. It is well known that nitric oxide is the most putative metabolite of L-Arg and it is implicated in regulating fat metabolism (Jobgen *et al*., 2006). Therefore, dietary L-Arg supplementation can modulate total body fat deposition through nitric oxide (Fig. 1).

L-arginine and metabolic disorder: Rearing broiler chickens under cold ambient temperatures or at high altitudes create an oxygen deficit, so the oxygen requirement and cardiac output increases (Witzel *et al*., 1990; Beker *et al*., 2003; van As *et al*., 2010). Under cold ambient temperatures, broiler chickens consume more feed to increase their heat production to maintain their body temperature, so the oxygen requirement and cardiac output increase (Decuypere *et al*., 2000). Increasing oxygen requirement promotes the heart to raise its cardiac output (Decuypere *et al*., 2000). Above mentioned conditions raise hematocrit, hemoglobin and activate the formation of red blood cells in the bone marrow, thereby the viscosity of blood will elevate (Ipek and Sahan, 2006; Li *et al*., 2011). Additionally, the right ventricle to total ventricle weight ratio increases (Xiang *et al*., 2002; Li *et al*., 2011). All theses changes indicate that broiler chickens suffer from ascites (Ipek and Sahan, 2006; Nain *et al*., 2008). Beside these common changes, ascites syndrome in broiler chickens is accompanied by decreasing the intracellular antioxidants (nonenzymatic antioxidants) including glutathione, vitamin C and vitamin E and the antioxidant indices including total antioxidant capacity and superoxide dismutase activity (Iqbal *et al*., 2002; Han *et al*., 2005; Tan *et al*., 2008). Fathi *et al*. (2011) observed that ascites syndrome in broiler chickens is associated with a significant increase in the activity of glutathione peroxidase in the plasma and in the liver and companied by a significant increase in the lipid peroxidation in the plasma and in the liver of chickens (Table 1). Increased the activity of glutathione peroxidase with elevating lipid peroxidation in the plasma and in the liver of the chickens indicate that antioxidant system of

Table 1: Effect of ascites on antioxidant defense in broiler chickens

Item					
Age (day)	Treatment	MDA in plasma	MDA in liver	GPX in plasma	GPX in liver
21	Control	1.30±0.31[b]	0.85±0.03[b]	33.00±1.92	0.23±0.01
21	PHS	2.50±0.33[a]	1.32±0.23[a]	39.32±2.80	0.25±0.02
42	Control	1.60±0.20[b]	1.10±0.04[b]	22.25±1.10[b]	0.19±0.01[b]
42	PHS	6.27±0.43[a]	2.60±0.25[a]	30.72±0.82[a]	0.25±0.02[a]

Fathi *et al.* (2011).
MDA: Mononaldehyde (nm m/L); GPX: Glutathione peroxidase (unit/ml); PHS: Pulmonary hypertension syndrome (Ascites).
Means in a column without a common superscript letter were different at $p<0.05$.

an organism is unable to remove the excess free radical. So broiler chickens that suffered from ascites exhibit a significant increase in the activity of glutathione peroxidase and in the lipid peroxidation in the plasma and in the live. Moreover, concentrations of Arg, ornithine and nitric oxide declined in ascitic chickens (Ruiz-Feria *et al*., 2001; Han *et al*., 2005; Hassanpour *et al*., 2009). Ascites is not only a metabolic disorder which results in an increase in the amount of lymph naturally found in the peritoneal spaces and heart failure (Broz and Ward, 2007) but also leads a significant reduction in carcass yield, breast (% of cold carcass), thigh weight, drum weight and in meat shelf-life in poultry (Rajani *et al*., 2011; Veldkamp *et al*., 2000). Therefore, mortality due to ascites syndrome and low meat quality in ascitic poultry has become one of the major problems in the poultry industry. Swire (1980) and Julian *et al*. (1986) documented that 5% of broilers and 20% of roaster birds die due to ascites around the world. Maxwell and Robertson (1997) found that about $1 billion annually is the economic losses all over the world due to ascites. L-Arg is not only a substrate for biosynthesis of several molecular e.g., ornithine and nitric oxide (Khajali and Wideman, 2010) that are insufficient and also required in ascitic chickens (Ruiz-Feria *et al*., 2001; Han *et al*., 2005; Hassanpour *et al*., 2009) but also is a powerful antioxidant where Atakisi *et al*. (2009) found that dietary 5 mg/kg L-Arg supplementation significantly improved total antioxidant capacity and production of nitric oxide and significantly declined lipid peroxidation in Japanese quails. Inclusion of L-Arg at the level of 0.06% in broiler diets under thermoneutral conditions had a positive effect on blood traits including hematocrit, hemoglobin and red blood cell number (Al-Daraji and Salih, 2012). Also results of Al-Daraji and Salih (2012) indicated that L-Arg may attenuate the adverse effects of rearing chickens under cold ambient temperatures or at high altitudes. Furthermore, feeding broiler chickens diet deficient in Arg under cold stress at high altitudes depressed nitric oxide synthesis, decreased feed intake, reduced body weight gain, increased right ventricle to total ventricle weight ratio and mortality rate as well as ascites mortality (Izadinia *et al*., 2010). Khajali *et al*. (2011) observed a significant reduction in feed intake, body weight gain and in concentration of nitric oxide with a concomitant increase in right ventricle to total ventricle weight ratio and in ascites mortality in cold-stressed chickens at high altitudes that fed diet deficient in Arg. In a study conducted in broiler chickens from 21 to 42 d of age at high attitudes to investigate the influence of L-Arg on growth performance and ascites mortality, Basoo *et al*. (2012) reported that chickens fed diets contained 80% Arg of NRC (1994) showed a significant decline in growth performance and a significant increase in right ventricle to total ventricle weight ratio and in ascites mortality compared with the control diets that formulated to meet NRC (1994) recommendations for all nutrients including Arg. Moreover, Basoo *et al*. (2012) demonstrated that inclusion of L-Arg at the level of 0.1% in broiler diets under oxygen-deficit conditions improved body weight gain, feed conversion ratio and elevated nitric oxide concentration in plasma with a concomitant reduction in right ventricle to total ventricle weight ratio and in mortality percent due to ascites compared with 0 (control), 0.2 or 0.3% L-Arg. Additionally, Fathi *et al*. (2011) reported that chickens exposed to low ambient temperature, fed the same basal diet but consumed water supplemented with L-Arg at the level of 0.3% not only had lower hemoglobin, hematocrit and red blood cells number but also had higher glutathione peroxidase activity and lower level of lipid peroxidation than control. They also observed that the reduction in right ventricle to total ventricle weight ratio and in ascites mortality was associated with higher glutathione peroxidase activity and lower level of lipid peroxidation in the chickens that consumed water supplemented with L-Arg at the level of 0.3%. Results of Bautista-Ortega and Ruiz-Feria (2010) indicated that induce conditions mimicking rearing broiler chickens at altitude of 3000 m above the sea level with inclusion of 0.8% L-Arg in the diets can lead to improvements in the heart functions. Han *et al*. (2005) found that increasing Arg level from 100 to 200% of NRC (1994) in diets of cold stressed-chickens significantly enhanced nitric oxide synthase, nitric oxide production and superoxide dismutase activity and significantly depressed membrane damage and ascites mortality. In three studies conducted to explain why dietary L-Arg supplementation (1%L-Arg) reduces ascites mortality in broilers that exposed to low ambient temperatures, Tan *et al*. (2005, 2006, 2007) suggested that supplemental

L-Arg suppressed pulmonary vascular remodeling that occurred secondary to increased pulmonary pressure and also depressed pulmonary arterioles protein kinase cá expression that is implicated in inducing of ascites by inhibiting the decline in nitric oxide synthase in the pulmonary endothelium and increasing nitric oxide production. Also in an earlier study, Wideman *et al.* (1995) noted that exposing chickens to cool environmental temperatures with adding 1% L-Arg in the diets achieved the lowest right ventricle to total ventricle weight ratio and ascites mortality compared with 0 (control), 0.25 or 0.75% L-Arg.

L-arginine and stress: Undoubtedly, birds are exposed to multiple stressors during their rearing period including photoperiod time (Guo *et al*., 2010), noise level (Campo *et al*., 2005), stocking density (Beloor *et al*., 2010), heat (Yang *et al*., 2010) and cold stress (Fathi *et al*., 2011) and at market age including feed withdrawal (Milinkovic-Tur *et al*., 2007), catching (Nijdam *et al*., 2005) and transport stress (Zhang *et al*.,2010), and at slaughter house (Xu *et al*., 2011). It is well known that the oxidative damage is associated with different stress in poultry production. In practice, under commercial conditions of broiler production, broiler chickens expose to continuous (24-h or 23-h) lighting during their fatting period (Olanrewaju *et al*., 2006). Guo *et al*. (2010) found that following 12-h light as a light regime in broiler chickens caused a reduction in lipid peroxidation compared with 23, 20 or 16-h light. Campo *et al*. (2005) reported that exposure laying hens to 90 dB elevated heterophil: lymphocyte ratio that is considered a reliable indictor of stress in poultry. Voslarova *et al*. (2011) observed that exposure broiler chickens to 80 dB was sufficient to impair the productive performance. Stocking density is an important factor in poultry production. Because high density induces stress in poultry that resulting in a reduction in the productive performance and an increase in mortality (Beloor *et al*., 2010). Results of Beloor *et al*. (2010) in broiler chickens and Sohn *et al*. (2012) in laying hens showed that increasing number of birds/m^2 increased heat shock protein 70 and 3-hydroxyl-3-methyl-glutaryl coenzyme A reductase mRNA expression in the blood lymphocyte and in the liver of the chickens. Heat shock protein 70 is a reliable index of stress in chickens (Hasheimi *et al*., 2012) and 3-hydroxyl-3-methyl-glutaryl coenzyme A reductase is an essential enzyme in cholesterol biosynthesis (Cui *et al*., 2010) which has been performed as an indictor of stress in avian species (Sohn *et al*., 2012). Cholesterol is the main substrate that required to synthesis corticosterone and cortisol, the most putative markers of stress in poultry (Lechner *et al*., 2001). Thus, 3-hydroxyl-3-methyl-glutaryl coenzyme A reductase is an important biomarker to monitor stress in avian species (Beloor *et al*., 2010; Sohn *et al*., 2012). As a result of climate changes, heat stress has become one of the most important challenges in poultry production, especially in tropical and subtropical area. Heat stressed-chickens exhibit higher production of reactive oxygen species and higher level of lipid peroxidation than chickens subjected to normal conditions (25°C) as reported by Yang *et al*. (2010). Heat stress induces oxidative stress though increasing the level of lipid peroxidation and declined the activities of superoxide dismutase, catalase and glutathione peroxidase in liver of chickens (Sahin *et al*., 2011). Heat stress led to oxidative damage in chicken muscles (Mujahid *et al*., 2007) which adversely affected meat quality in poultry (Sporer *et al*., 2012; Zhang *et al*., 2012). The adverse impact of cold stress seems like the adverse impact of heat stress, cold-stressed chickens also suffer from oxidative stress as documented by Han *et al*. (2005), Tan *et al*. (2008) and Fathi *et al*. (2011). In chickens, Han *et al*. (2005), Tan *et al*. (2008) and Fathi *et al*. (2011) found a significant decline in the activities of superoxide dismutase and a significant elevation in the lipid peroxidation. Poultry not only suffer from stress during fatting period in meat-type poultry and during egg production period in egg-type poultry but also suffer from stress at market age e.g., feed withdrawal before slaughter, transport time and killing way may lead to oxidative damage. Milinkovic-Tur *et al*. (2007) observed that feed withdrawal resulted in a significant decrease in the activity of glutathione peroxidase and a significant increase in cholesterol synthesis in avian species. Zhang *et al*. (2010) noted that in broilers, 3-h transport stress with 3-h recovery before slaughter was not sufficient to relieve the transport stress that caused a significant increase in the level of reactive oxygen species and in the level of lipid peroxidation in thigh muscle of chickens. Xu *et al*. (2011) demonstrated that killing chickens by electrical stunning (50 V) significantly increased cholesterol synthesis and elevated the oxidative damage in breast muscle of chickens compared with traditional way. Thereby, under the conditions of commercial poultry production, all avian species are exposed to stress. As we discussed above, different types of stress lead oxidative stress and oxidative damage which is not only negatively affects productive performance (Azad *et al*., 2010) but also negatively affects meat quality and shelf-life of meat (Yesilbag *et al*., 2011). However, Atakisi *et al*. (2009) reported that dietary L-Arg supplementation significantly enhanced total antioxidant capacity and production of nitric oxide and significantly declined the level of lipid peroxidation in Japanese quails. And also Al-Daraji and Salih (2012) noticed that increasing L-Arg level from 0.0 (control as recommended by NRC) to 0.06% significantly reduced heterophil: lymphocyte ratio that is considered a reliable marker of stress in poultry. Emadi *et al*. (2011) found that providing 2.5% additional L-Arg above NRC (1994) recommendations for broilers significantly

declined cholesterol synthesis at 27 d of age (Cholesterol is the main substrate that required to synthesis corticosterone and cortisol, the most putative markers of stress in poultry). Feeding broiler chickens diet supplemented with 2.07, 1.68 and 1.56% L-Arg for starter, grower and finisher phase respectively, caused a significant reduction in cholesterol biosynthesis at 49 d of age (Emadi *et al*. 2010a). Kurauchi *et al*. (2009) recorded that the concentrations of L-Arg, L-ornithine and L-proline in plasma of stressed-chickens declined significantly compared with unstressed-chickens. Zhao *et al*. (2009) reported that injected corticosterone to induce-stress in broiler reduced the concentration of nitric oxide in plasma and declined the activity of nitric oxide synthase. Previous studies showed that chickens required more L-Arg than NRC (1994) recommendations under stress conditions (Brake *et al*., 1998; Balnave *et al*., 1999; Chamruspollert *et al*., 2004ab). As reported by Khajali and Wideman (2010), L-Arg is a substrate for biosynthesis of several molecular e.g., ornithine and nitric oxide. Results of previous studies indicated that L-Arg and its metabolites (L-ornithine and L-proline) is effective in alleviating the stress in birds (Suenaga *et al*., 2008; Hamasu *et al*., 2009; Kurauchi *et al*., 2010). Attia *et al*. (2011) suggested that inclusion of L-Arg in the diets to alleviate heat stress in chickens. Srinongkote *et al*. (2004) reported that broiler chickens reared under high stock density and fed diet supplemented with 1.36% L-Arg with increasing L-lysine level to maintain the same ratio between L-Arg and L-lysine as the control, achieved the same productive performance like control group (chickens reared under standard stock density). Above results have shown that poultry expose to numerous stresses and L-Arg directly or indirectly by its metabolites can play a crucial role in attenuating the stress in poultry.

L-arginine and immune response: In 1960, meat of broiler chickens contributed by 10% of the total meat consumption and this contribution is elevated by 5% per year. In 2000, the price of beef and pork meat increased compared with poultry meat. Therefore, the total consumption of poultry meats including broilers increased to be 46.2% of total meat consumption (Ishibashi *et al*., 2002). In 1953, producers of chickens were needed more than 70 days to produce chickens have almost 1.5 kg as final body weight (Havenstein *et al*., 2003). Above mentioned factors led to promote the producers and scientists to find a way to increase chickens meat production to meet consumers' requirements. They found that the extensive selection of broiler chickens is a powerful tool to improve growth rate, feed conversion ratio and carcass yield (Nadaf *et al*., 2009). Extensive selection of broiler chickens is succeeded in improving growth rate, feed conversion ratio and carcass yield but the immune system efficiency and its ability to resist the diseases has been neglected, thereby susceptibility of modern commercial chickens to diseases increased (Swaggerty *et al*., 2009). Improving the immune system efficiency and its resistance to pathogens through nutrients, are considered practical and efficient solution in enhancing productive performance of modern broiler chickens (Kidd, 2004). However, Kwak *et al*. (1999) demonstrated that feeding chickens diet deficient in Arg resulted in a significant decline in relative weight of lymphoid organs (% of body weight) including thymus, spleen and bursa. Deng *et al*. (2005) observed that increasing L-Arg level from 100% of NRC (1994) to 130% of NRC (1994) caused a significant improvement in primary antibody levels against sheep red blood cells in chickens. Abdukalykova and Ruiz-Feria (2006) reported that providing 0.3% additional L-Arg above the NRC requirements for broiler chickens significantly enhanced the antibody titers to sheep red blood cells. Al-Daraji and Salih (2012) reported that chickens fed 0.06% L-Arg achieved a significant increase in white blood cell number. Therefore, L-Arg directly or indirectly by its metabolites can improve the immune response of poultry reared under conventional conditions or reared under unconventional conditions (challenged with infectious diseases).

It is estimated that poultry industry loses more than $3 billion annually due to avian coccidiosis (Williams, 1999). Therefore, Coccidia infections in chickens is classified as one of the most common and important diseases in poultry production (Laurent *et al*., 2001). There are seven species of *Eimeria* have been identified as pathogenic in broiler chickens: *Eimeria acervulina*, *Eimeria tenella*, *Eimeria mitis*, *Eimeria praecox*, *Eimeria maxima*, *Eimeria necatrix* and *Eimeria brunette* (McDougald, 2003). Coccidia infections in chickens leads to a reduction in body weight gain and in egg production as a result of destroying the epithelial cells and trauma to the intestinal mucosa and submucosa which negatively affects absorption of nutrients and positively affects blood losses and elevates the rate of mortality and the susceptibility to other diseases (Ruff and Allen, 1990).

Nitric oxide is a free radical molecule that is produced as a result of L-Arg metabolism (Khajali and Wideman, 2010). Nitric oxide synthesis elevated significantly in infected chickens with different species of *Eimeria* such as *Eimeria tenella*, *Eimeria maxima* and *Eimeria acervulina* as well documented by Allen (1997ab) and Allen and Fetterer (2000). Also plasma L-Arg significantly declined in infected chickens with *Eimeria acervulina* (Allen and Fetterer, 2000). All theses evidences indicate that L-Arg can play a vital role in poultry during coccidia infections. So, Allen (1999) carried out two experiments to investigate the effect of daily oral administration of L-Arg on the growth performance and nitric oxide

synthesis in the chicks that infected with *Eimeria acervulina*, *Eimeria maxima*, or *Eimeria tenella*. Allen (1999) reported that once or twice daily oral administration of L-Arg (500 mg/kg) can be used to alleviate the negative impact of *Eimeria tenella* in chickens by declining its oocytes shedding. Perez-Carbajal *et al*. (2010) found that inclusion L-Arg at the level of 0.3 or 0.6% with vitamin E led to a significant enhancements in antibodies production including IgG and IgM and in the oxidative burst activity of heterophils and monocytes in the chickens that infected with cocktail of *Eimeria* (*E. acervulina*, *E.maxima* and *E. tenella*). Although avian coccidiosis causes oxidative stress as documented by Allen (1997) and Bun *et al*. (2011), and dietary L-Arg supplementation significantly enhanced total antioxidant capacity and production of nitric oxide and significantly declined the level of lipid peroxidation in Japanese quails (Atakisi *et al*., 2009), but till now information available about the impact of L-Arg supplementation on the antioxidant status and immune responses of broilers challenged with *Eimeria*.

Infectious Bursal Disease (IBD) is a viral disease attacking mainly an important lymphoid organ in chickens and results in destroying of immature B-lymphocytes in the bursa of Fabricius, thymus and spleen (Maroufyan *et al*., 2012). There by, IBD is considered an important threat to the commercial poultry industry as a result of its heavy economic losses to the poultry industry due to high mortality rate and poor growth performance (McIlroy *et al*., 1989). Tayade *et al*. (2006) found that inclusion L-Arg at the level of 2% significantly improved the antibody responses to infectious bursal disease virus and the proliferation of intestinal intraepithelial lymphocytes and its toxicity against infectious bursal disease virus in the chickens that vaccinated and challenged with live intermediate plus strain of infectious bursal disease compared with the chickens that vaccinated and challenged with live intermediate plus strain of infectious bursal disease virus but without supplemented 2% L-Arg. Ruiz-Feria and Abdukalykova (2009) demonstrated that broilers fed diet providing with 1% L-Arg and 80 mg vitamin E/kg and challenged at 20 d with vaccine strain of infectious bursal disease virus achieved higher thymus weight (% of body weight), antibody responses to infectious bursal disease virus and sheep red blood cells than control group. Abdukalykova *et al*. (2008) observed that chickens challenged at 20 d with vaccine strain of infectious bursal disease virus are required diet containing Arg and vitamin E higher than NRC (1994) recommendation to improve their immune responses. They documented that providing 1% additional L-Arg and 80 mg vitamin E/kg diet above NRC requirements for chicken significantly enhanced B cells and T lymphocytes as a result of increasing $CD4^+$ and $CD8^+$ lymphocytes. Emadi *et al*. (2010b) reported that feeding broiler chickens starter, grower and finisher diet supplemented with 2, 77, 2.25 and 2.08% L-Arg respectively and then challenged with vaccine strain of infectious bursal disease virus at 28 d led to a significant increase in IgG, interferon-alpha and interferon-gamma synthesis with a significant decline in the bursa and spleen lesion scores compared with the chickens that fed diet containing Arg as recommended by NRC (1994) and challenged with vaccine strain of infectious bursal disease virus at 28 d. Emadi *et al*. (2011) reported that feeding chickens diet provided with 2.5% additional L-Arg above NRC (1994) recommendations and immunized them with vaccine strain of infectious bursal disease virus at 28 d resulted in a significant enhancements in body weight gain, feed intake and feed conversion ratio and in the production of antibody (IgG), interferon-α and interferon-γ and a significant reduction in the bursa and spleen lesion scores compared with the control.

Munir *et al*. (2009) documented that providing 2% additional L-Arg above NRC requirements for broilers reduced the immunosuppressive effects of Hydropericardium Syndrome Virus (HPSV), increased body weight, enhanced thymus and spleen weight and improved HPSV-specific humoral response against HPSV. Therefore, we can conclude that dietary L-Arg supplementation improves the immune system efficiency and its resistance to common diseases in poultry farms.

Conclusion: L-Arg plays multiply functions in poultry production. Dietary L-Arg supplementation enhances carcass yield by reducing abdominal fat content (undesirable fat), alleviates the adverse effects of different types of stress and declines the immunosuppressive of vaccine, enhances the immune system efficiency and its resistance to common diseases in poultry farms.

ACKNOWLEDGMENTS

The work was supported by the Science and Technological Project of Shaanxi Province, China (2010ZDGC-02, 2011KTCQ02-02 and 2011KTDZ02-01-01).

REFERENCES

Abdukalykova, S.T. and C.A. Ruiz-Feria, 2006. Arginine and vitamin E improve the cellular and humoral immune response of broiler chickens. Int. J. Poult. Sci., 5: 121-127.

Abdukalykova, S.T., X. Zhao and C.A. Ruiz-Feria, 2008. Arginine and vitamin E modulate the subpopulations of T lymphocytes in broiler chickens. Poult. Sci., 87: 50-55.

Al-Daraji, H.J. and A.M. Salih, 2012. The influence of dietary arginine supplementation on blood traits of broiler chickens. Pak. J. Nutr., 11: 258-264.

Al-Daraji, H.J. and A.M. Salih, 2012. Effect of dietary L-arginine on carcass traits of broilers. Res. Opin. Anim. Vet. Sci., 2: 40-44.

Al-Daraji, H.J., A.A. Al-Mashadani, W.K. Al-Hayani, A.S. Al-Hassani and H.A. Mirza, 2011. Influence of in ovo injection of L-arginine on productive and physiological performance of quails. Res. Opin. Anim. Vet. Sci., 7: 463-467.

Allen, P.C. and R.H. Fetterer, 2000. Effect of *Eimeria acervulina* infections on plasma L-arginine. Poult. Sci., 79: 1414-1417.

Allen, P.C., 1999. Effects of daily oral doses of L-arginine on coccidiosis infections in chickens. Poult. Sci., 78: 1506-1509.

Allen, P.C., 1997b. Production of free radical species during *Eimeria maxima* infections in chickens. Poult. Sci., 76: 814-821.

Allen, P.C., 1997a. Nitric oxide production during *Eimeria tenella* infections in chickens. Poult. Sci., 76: 810-813.

Atakisi, O., E. Atakisi and A. Kart, 2009. Effects of dietary zinc and L-arginine supplementation on total antioxidants capacity, lipid peroxidation, nitric oxide, egg weight and blood biochemical values in Japanese quails. Biol. Trace. Elem. Res., 132: 136-143.

Attia, Y.A., R.A. Hassan, A.E. Tag El-Din and B.M. Abou-Shehema, 2011. Effect of ascorbic acid or increasing metabolizable energy level with or without supplementation of some essential amino acids on productive and physiological traits of slow-growing chicks exposed to chronic heat stress. J. Anim. Physiol. J. Anim. Nutr., 95: 744-755.

Azad, K.M., M. Kikusato, A.M. Hoque and M. Toyomizu, 2010. Effect of chronic heat stress on performance and oxidative damage in different strains of chickens. J. Poult. Sci., 47: 333-337.

Balnave, D., J. Hayat and J. Brake, 1999. Dietary arginine:lysine ratio and methionine activity at elevated environmental temperatures. J. Appl. Poult. Res., 8: 1-9.

Bartell, S.M. and A.B. Batal, 2007. The effect of supplemental glutamine on growth performance, development of the gastrointestinal tract and humoral immune response of broilers. Poult. Sci., 86: 1940-1947.

Basiouni, G.F., 2009. The Effect of feeding an extra amounts of arginine to local saudi hens on luteinizing hormone secretion. J. Biolog. Sci., 9: 617-620.

Basoo, H., F. Khajali, E. Asadi Khoshoui, M. Faraji and R.F. Wideman, 2012. Estimation of arginine requirements for broilers grown at high altitude during the 3- to 6-week period. J. Poult. Sci., 49: 3023-307.

Bautista-Ortega, J. and C.A. Ruiz-Feria, 2010. L-Arginine and antioxidant vitamins E and C improve the cardiovascular performance of broiler chickens grown under chronic hypobaric hypoxia. Poult. Sci., 89: 2141-2146.

Becker, W.A., J.V. Spencer, L.W. Mirosh and J.A. Verstrate, 1979. Prediction of fat and fat free live weight in broiler chickens using back-skin fat, abdominal fat and live weight. Poult. Sci., 58: 835-842.

Beker, A., S.L.Vanhooser, J.H. Swartzlander and R.G. Teeter, 2003. Graded atmospheric oxygen level effects on performance and ascites incidence in broilers. Poult. Sci., 82: 1550-1553.

Beloor, J., H.K. Kang, Y.J. Kim, V.K. Subramani, I.S. Jang and S.H. Sohn, 2010. The effect of stocking density on stress related genes and telomeric length in broiler chickens. Asian-australas. J. Anim. Sci., 23: 437-443.

Brake, J., D. Balnave and J.J. Dibner, 1998. Optimum dietary arginine: Lysine ratio for broiler chickens is altered during heat stress in association with changes in intestinal uptake and dietary sodium chloride. Br. Poult. Sci., 39: 639-647.

Broz, J. and N.E. Ward, 2007. The role of vitamins and feed enzymes in combating metabolic challenges and disorders. J. Appl. Poult. Res., 16: 150-159.

Bun, S.D., Y.M. Guo, F.C. Guo, F.J. Ji and H. Cao, 2011. Influence of organic zinc supplementation on the antioxidant status and immune responses of broilers challenged with Eimeria tenella. Poult. Sci., 90: 1220-1226.

Burt, D.W., 2002. Applications of biotechnology in the poultry industry. World's Poult. Sci. J., 58: 5-13.

Campo, J.L., M.G. Gil and S.G. Da´vila, 2005. Effects of specific noise and music stimuli on stress and fear levels of laying hens of several breeds. Appl. Anim. Behav. Sci., 91: 75-84.

Cartwright, A.L., 1991. Adipose cellularity in Gallus domesticus: Investigations to control body composition in growing chickens. J. Nutr., 121: 1486-1497.

Chamruspollert, M., G.M. Pesti and R.I. Bakalli, 2004a. Chick responses to dietary Arg and met levels at different environmental temperatures. Br. Poult. Sci., 45: 93-100.

Chamruspollert, G., M. Pesti and R.I. Bakalli, 2004b. Influence of temperature on the arginine and methionine requirements of young broiler chicks. J. Appl. Poult. Res., 13: 628-638.

Chen, J., M. Wang, Y. Kong, H. Ma and S. Zou, 2011. Comparison of the novel compounds creatine and pyruvate on lipid and protein metabolism in broiler chickens. Anim., 5: 1082-1089.

Corzo, A., E.T. Jr. Moran and D. Hoehler, 2003. Arginine need of heavy broiler males: Applying the ideal protein concept. Poult. Sci., 82: 402-407.

Cui, H.X., M.Q. Zheng, R.R. Liu, G.P. Zhao, J.L. Chen and J. Wen, 2012. Liver dominant expression of Fatty Acid Synthase (FAS) gene in two chicken breeds during intramuscular-fat development. Mol. Biol. Rep., 39: 3479-3484.

Cui, H.X., S.Y. Yang, H.Y. Wang, J.P. Zhao, R.R. Jiang, G.P. Zhao, J.L. Chen, M.Q. Zheng, X.H. Li and J. Wen, 2010. The effect of a mutation in the 3-UTR region of the HMGCR gene on cholesterol in Beijing-you chickens. Anim. Biotechnol., 21: 241-251.

D'Amato, J.L. and B.D. Humphrey, 2010. Dietary arginine levels alter markers of arginine utilization in peripheral blood mononuclear cells and thymocytes in young broiler chicks. Poult. Sci., 89: 938-947.

Decuypere, E., J. Buyse and N. Buys, 2000. Ascites in broiler chickens: Exogenous and endogenous structural and functional causal factors. World's Poult. Sci. J., 56: 367-377.

Deng, K., C.W. Wong and J.V. Nolan, 2005. Long-term effects of early life L-arginine supplementation on growth performance, lymphoid organs and immune responses in Leghorn type chickens. Br. Poult. Sci., 46: 318-324.

Emadi, M., F. Jahanshiri, K. Kaveh, M. Hair-Bejo, A. Ideris and A.R. Alimon, 2011. Nutrition and immunity: The effects of the combination of arginine and tryptophan on growth performance, serum parameters and immune response in broiler chickens challenged with infectious bursal disease vaccine. Avian. Pathol., 40: 63-72.

Emadi, M., K. Kaveh, M.H.Bejo, A. Ideris, F.Jahanshiri, M. Ivan and R.A. Alimon, 2010a. Growth performance and blood parameters as influenced by different levels of dietary arginine in broiler chickens. J. Anim. Vet. Adv., 9: 70-74.

Emadi, M., F. Jahanshiri, F. Azizi Jalalian, K. Kaveh, M.H. Bejo and A. Ideris, 2010b. Immunostimulatory effects of arginine in broiler chickens challenged with vaccine strain of infectious bursal disease virus. J. Anim. Vet. Adv., 9: 594-600.

Emmerson, D.A., K.A. Turner, D.N. Foster, N.B. Anthony and K.E. Nestor, 1997. Ornithine decarboxylase activity in muscle, liver and intestinal tissue of turkeys during a short-term feed withdrawal and following refeeding. Poult. Sci., 76: 1563-1568.

Fathi, M., K. Nazeradl, Y.E. Nezhad, H.A. Shahryar, M. Daneshyar and T. Tanha, 2011. Antioxidant enzyme activities characterization in Pulmonary Hypertension Syndrome (PHS) in broilers. Res. J. Biolog. Sci., 6: 118-123.

Fernandes, J.I., A.E. Murakami, E.N. Martins, M.I. Sakamoto and E.R. Garcia, 2009. Effect of arginine on the development of the pectoralis muscle and the diameter and the protein: Deoxyribonucleic acid rate of its skeletal myofibers in broilers. Poult. Sci., 88: 1399-1406.

Gaya, L.G., J.B. Ferraz, F.M. Rezende, G.B. Mourão, E.C. Mattos, J.P. Eler and T. Michelan Filho, 2006. Heritability and genetic correlation estimates for performance and carcass and body composition traits in a male broiler line. Poult. Sci., 85: 837-843.

Graber, G. and D.H. Baker, 1973. The essential nature of glycine and proline for growing chickens. Poult. Sci., 52: 892-896.

Guo, Y.L., W.B. Li and J.L. Chen, 2010. Influence of nutrient density and lighting regime in broiler chickens: Effect on antioxidant status and immune function. Br. Poult. Sci., 51: 222-228.

Hamasu, K., T. Haraguchi and Y. Kabuki, 2009. L-Proline is a sedative regulator of acute stress in the brain of neonatal chicks. Amino Acids, 37: 377-382.

Han, B., S.S. Yoon, H.R. Han, W.J. Qu and F. Nigussie, 2005. Effect of low ambient temperature on the concentration of free radicals related to ascites in broiler chickens. Asian-Aust. J. Anim. Sci., 18: 1182-1187.

Hartree, S.A. and F.J. Cunningham, 1969. Purification of chickien pituitary follicle-stimulating hormone and luteinizing hormone. J. Endocrinol., 43: 609-616.

Hasheimi, S.R., I. Zulkifli, M.N.Somchit, Z. Zunita, T.C. Loh, A.F. Soleimani and S.C. Tang, 2012. Dietary supplementation of *Zingiber officinale* and *Zingiber zerumbet* to heat-stressed broiler chickens and its effect on heat shock protein 70 expression, blood parameters and body temperature. J. Anim.Phys. Anim. Nutr., doi: 10.1111/j.1439-0396.2012.01302.x

Hassanpour, H., A.K. Moghaddam and H. Zarei, 2009. Effect of citric acid on electrocardiographic parameters of broiler chickens with pulmonary hypertension. Acta Vet. Hung., 57: 229-238.

Havenstein, G.B., P.R. Ferket and M.A. Qureshi, 2003. Growth, livability and feed conversion of 1957 versus 2001 broilers when fed representative 1957 and 2001 broiler diets. Poult. Sci., 92: 1500-1508.

Hocquette, J.F., F. Gondret, E. Baéza, F. Médale, C. Jurie and D. W.Pethick, 2010. Intramuscular fat content in meat-producing animals: Development genetic and nutritional control and identification of putative markers. Animal, 4: 303-319.

Ipek, A. and U. Saha, 2006. Effect of cold stress on broiler performance and ascites susceptibility. Asian-Aust. J. Anim. Sci., 19: 734-738.

Ishibashi, T. and C. Yonemochi, 2002. Possibility of amino acid nutrition in broiler. Anim. Sci. J., 73: 155-165.

Iqbal, M., D. Cawthon, K. Beers, R.F. Jr. Wideman and W.G. Bottje, 2002. Antioxidant enzyme activities and mitochondrial fatty acids in pulmonary hypertension syndrome (PHS) in broilers. Poult. Sci., 81: 252-260.

Izadinia, M., M. Nobakht, F. Khajali, M. Faraji, F. Zamani, D. Qujeq and I. Karimi, 2010. Pulmonary hypertension and ascites as affected by dietary protein source in broiler chickens reared at high altitudes. Anim. Feed. Sci. Technol., 155: 194-200.

Jiao, P., Y. Guo, X. Yang and F. Long, 2010. Effects of dietary arginine and methionine levels on broiler carcass traits and meat quality. J. Anim. Vet. Adv., 11: 1546-1551.

Jobgen, W.S., S.K. Fried, W.J. Fu, C.J. Meininger and G. Wu, 2006. Regulatory role for the arginine-nitric oxide pathway in metabolism of energy substrates. J. Nutr. Biochem., 17: 571-588.

Julian, R.J., J. Summers and J.B. Wilson, 1986. Right ventricular failure and ascites in broiler chickens caused by phosphorus deficient diets. Avian Dis., 30: 453-459.

Khajali, F. and R.F. Wideman, 2010. Dietary arginine: Metabolic, environmental, immunological and physiological interrelationships. World's Poult. Sci. J., 66: 751-766.

Khajali, F., M. Tahmasebi, H. Hassanpour, M.R. Akbari, D. Qujeq and R.F. Wideman, 2011. Effects of supplementation of canola meal-based diets with arginine on performance, plasma nitric oxide and carcass characteristics of broiler chickens grown at high altitude. Poult. Sci., 90: 2287-2294.

Kidd, M.T., 2004. Nutritional modulation of immune function in broilers. Poult. Sci., 83: 650-657.

Kratzer, F.H. and L. Earl, 1975. Effect o f arginine deficiency on normal and dystrophic chickens. Proc. Sot. Exp. Biol. Med., 148: 656-659.

Kumar, P. and C.M. Chaturvedi, 2008. Correlation of gonadal function and nitric oxide activity in Japanese quail, *Coturnix coturnix japonica*, following temporal phase relation of serotonergic and dopaminergic oscillations. Anim. Reprod. Sci., 106: 48-64.

Kurauchi, I., K. Shigemi and Y. Kabuki, 2010Central L-ornithine but not polyamines, induces a hypnotic effect in neonatal chicks under acute stress. Nutr. Neurosci., 13: 17-20.

Kurauchi, I., K. Hamasu, D.M. Denbow and M. Furuse, 2009. Plasma amino acid concentration in neonatal chicks modified by acute stress. J. Anim. Vet. Adv., 8: 1838-1841.

Kwak, H., R.E. Austic and R.R. Dietert, 1999. Influence of dietary arginine concentration on lymphoid organ growth in chickens. Poult. Sci., 78: 1536-1541.

Laurent, F., R. Mancassola, S. Lacroix, R. Menezes and M. Naciri, 2001. Analysis of chicken mucosal immune response to *Eimeria tenella* and *Eimeria maxima* infection by quantitative reverse transcription-PCR. Infect. Immun., 69: 2527-2534.

Lechner, O., H. Dietrich, G.J. Wiegers, M. Vacchio and G. Wick, 2001. Glucocorticoid production in the chicken bursa and thymus. Int. Immunol., 13: 769-776.

Li, K., Z. Lihong, G. Guangrui, M. Liqin, D. Shishan, X. Tong, W. Jianlin, W. Huiyu, T. Yong and Q. Jian, 2011. Increased calcium deposits and decreased Ca^{2+}-ATPase inerythrocytes of ascitic broilerchickens Res. Vet. Sci., 90: 468-473.

Lin, H., H.C. Jiao, J. Buyse and E. Decuypere, 2006. Strategies for preventing heat stress in poultry. World's Poult. Sci. J., 62: 71-85.

Manwar, S.J., R.P. Moudgal, K.V.H. Sastry, J. Mohan, J.B. Tyagi and R. Raina, 2006. Role of nitric oxide in ovarian follicular development and egg production in Japanese quail (*Coturnix coturnix japonica*). Theriogenology, 65: 1392-1400.

Manwar, S.J., R.P. Moudgal, K.V.H. Sastry, J.S. Tyagi and V.K. Saxena, 2003. Nitric oxide regulating immune functions in egg type Japanese quail. Ind. J. Poult. Sci., 38: 133-136.

Maroufyan, E., A. Kasim, M.Ebrahimi, T.C. Loh, M. Hair-Bejo and A.F. Soleimani, 2012. Dietary methionine and n-6/n-3 polyunsaturated fatty acid ratio reduce adverse effects of infectious bursal disease in broilers. Poult. Sci., 91: 2173-2182.

Maxwell, M.H. and G.W. Robertson, 1997. World broiler ascites survey 1996. Poult. Int., 36: 16-30.

McDougald, L.R., 2003. Protozoal infections. In: Diseases of Poultry. Saif, J.R.G.Y.M., A.M. Fadly, L.R. McDougald and D.E. Swayne (Eds.), Iowa State Press, Ames, pp: 974-990.

McIlroy, S.G., E.A. Goodall and R.M. Mccracken, 1989. Economic effects of sub-clinical infectious bursal disease on broiler production. Avian Pathol., 18: 465-480.

Milinkovic-Tur, S., Z. Stojevic, J. Pirsljin, M. Zdelar-Tuk, N. Poljicak-Milas, B.B. Ljubic and B. Gradinski-Vrbanac, 2007. Effect of fasting and refeeding on the antioxidant system in cockerels and pullets. Acta Vet. Hung., 55: 181-189.

Mujahid, A., 2011. Nutritional strategies to maintain efficiency and production of chickens under high environmental temperature: A review. J. Poult. Sci., 48: 145-154.

Mujahid, A., N. Pumford, W. Bottje, Y. Akiba and M. Toyomizu, 2007. Mitochondrial oxidative damage in chicken skeletal muscle induced by acute heat stress. J. Poult. Sci., 44: 439-445.

Munir, K., M.A. Muneer, E. Masaoud, A. Tiwari, A. Mahmud and R.M. Chaudhry, 2009. Dietary arginine stimulates humoral and cell-mediated immunity in chickens vaccinated and challenged against hydropericardium syndrome virus. Poult. Sci., 88: 1629-1638.

Nadaf, J., F. Pitel and H. Gilbert, 2009. QTL for several metabolic traits map to loci controlling growth and body composition in an F2 intercross between high- and low-growth chicken lines. Physiol. Genomics, 38: 241-249.

Nain, S., B. Ling, J. Alcorn, C.M. Wojnarowicz, B. Laarveld and A.A. Olkowski, 2008. Biochemical factors limiting myocardial energy in a chicken genotype selected for rapid growth. Comp. Biochem. Physiol. A Mol. Integr. Physiol., 149: 36-43.

Nijdam, E., E. Delezie, E. Lambooij, M.J.A. Nabuurs, E. Decuypere and J.A. Stegeman, 2005. Feed withdrawal of broilers before transport changes plasma hormone and metabolite concentrations. Poult. Sci., 84: 1146-1152.

NRC, National Research Council, 1994. Nutrient requirements for poultry. 9th End. (Washington DC.National Academy Press).

Olanrewaju, H.A., J.P. Thaxton, W.A. Dozier, J. Purswell, W.B. Roush and S.L. Branton, 2006. A review of lighting programs for broiler production. Int. J. Poult. Sci., 5: 301-308.

Perez-Carbajal, C., D.M. Caldwell, K. Farnell, S. Stringfellow, G. Pohl, A. Casco, Pro-Martinez and C.A. Ruiz-Feria, 2010. Immune response of broiler chickens fed different levels of arginine and vitamin E to a coccidiosis vaccine and *Eimeria* challenge. Poult. Sci., 89: 1870-1877.

Rajani, J., M.A. Karimi Torshizi and S. Rahimi, 2011. Control of ascites mortality and improved performance and meat shelf-life in broilers using feed adjuncts with presumed antioxidant activity. Anim. Feed. Sci. Technol., 170: 239-245.

Ruff, M.D. and P.C. Allen, 1990. Pathophysiology. In: Coccidiosis of Man and Domestic Animals. Long, P.L. (Ed.), CRC Press, Boca Raton, FL, pp: 263-280.

Ruiz-Feria, C.A. and S.T. Abdukalykova, 2009. Arginine and vitamin E improve the antibody response to Infectious Bursal Disease Virus (IBDV) and sheep red blood cells in broiler chickens. Br. Poult. Sci., 50: 291-297.

Ruiz-Feria, C.A., M.T. Kidd and R.F. Wideman, 2001. Plasma levels of arginine, ornithine and urea and growth performance of broilers fed supplemental l-arginine during cool temperature exposure. Poult. Sci., 80: 358-369.

Sahin, K., C. Orhan, F. Akdemir, M. Tuzcu, S. Ali and N. Sahin, 2011. Tomato powder supplementation activates Nrf-2 via ERK/Akt signaling pathway and attenuates heat stress-related responses in quails. Anim. Feed. Sci. Tech., 165: 230-237.

Santoso, U., K. Tanaka and S. Ohtani, 1995. Effect of dried Bacillus subtilis culture on growth, body composition and hepatic lipogenic enzyme activity in female broiler chicks. Br. J. Nutri., 74: 523-529.

Shahin, K.A. and F.A. ABd-EL-Azeem, 2006. Effect of breed, sex and diet and their interactions on fat deposition and partitioning among depots of broiler chickens. Arch. Tierz., Dummerstorf., 49: 181-193.

Sohn, S.H., V.K. Subramani, Y.S. Moon and I.S. Jang, 2012. Telomeric DNA quantity, DNA damage and heat shock protein gene expression as physiological stress markers in chickens. Poult. Sci., 91: 829-836.

Sporer, K.R.B., H.R. Zhou, J.E. Linz, A.M. Booren and G.M. Strasburg, 2012. Differential expression of calcium-regulating genes in heat-stressed turkey breast muscle is associated with meat quality. Poult. Sci., 91: 1418-1424.

Srinongkote, S., M. Smrige and Y. Toride, 2004. Diet supplied with L-lysine and L-arginine during chronic stress of high stock density normalizes growth of broilers. Anim. Sci. J., 75: 339-343.

Suenaga, R., S. Tomonaga, H. Yamane, I. Kurauchi, Y. Tsuneyoshi, H. Sato, D.M. Denbow and M. Furuse, 2008. Intracerebroventricular injection of L-arginine induces sedative and hypnotic effects under an acute stress in neonatal chicks. Amino Acids., 35: 139-146.

Sundaresan, N.R., V.K. Saxena, K.V. Sastry, D. Anish, M. Saxena, K. Nagarajan and K.A. Ahmed, 2007. Nitric oxide: A possible mediator of ovulation and postovulatory follicle regression in chicken. Anim. Reprod. Sci., 101: 351-357.

Swaggerty, C.L., I.Y. Pevzner, H. He, K.J. Genovese, D.J. Nisbet, P. Kaiser and M.H. Kogut, 2009. Selection of broilers with improved innate immune responsiveness to reduce on-farm infection by food borne pathogens. Foodborne Pathog. Dis., 6: 777-783.

Swire, P.W., 1980. Ascites in broilers. Vet. Rec., 107:541.

Tamir, H. and S. Ratner, 1963. Enzymes of arginine metabolism in chicks. Arch. Biochem. Biophys., 102: 249-258.

Tan, X., J.Q. Pan, J.C. Li, Y.J. Liu, W.D. Sun and X.L. Wang, 2005. L-Arginine inhibiting pulmonary vascular remodelling is associated with promotion of apoptosis in pulmonary arterioles smooth muscle cells in broilers. Res. Vet. Sci., 79: 203-209.

Tan, X., S.H. Hu and X.L. Wang, 2008. The effect of dietary L-carnitine supplementation on pulmonary hypertension syndrome mortality in broilers exposed to low temperatures. J. Anim. Physiol. Anim. Nutr., 92: 203-210.

Tan, X., W.D. Sun, J.C. Li, J.Q. Pan and X.L. Wang, 2006. Changes in pulmonary arterioles protein kinase Ca expression associated with supplemental L-arginine in broilers during cool temperature exposure. Br. Poult. Sci., 47: 230-236.

Tan, X., W.D. Sun, J.C. Li, J.Q. Pan, Y.J. Liu, J.Y. Wang and X.L. Wang, 2007. L-Arginine prevents reduced expression of endothelial Nitric Oxide Synthase (NOS) in pulmonary arterioles of broilers exposed to cool temperatures. Vet. J., 173: 151-157.

Tayade, C., T.N. Jaiswal, S.C. Mishra and M. Koti, 2006. L-Arginine stimulates immune response in chickens immunized with intermediate plus strain of infectious bursal disease vaccine. Vaccine., 24: 552-560.

van As, P., M.G. Elferink, A.M. Closter, A. Vereijken, H. Bovenhuis, R.P.M.A. Crooijmans, E. Decuypere and M.A.M. Groenen, 2010. The use of blood gas parameters to predict ascites susceptibility in juvenile broilers. Poult. Sci., 89: 1684-1691.

Veldkamp, T., R.P. Kwakkel, P.C.M. Ferket, J. Simons, J.P. Noordhuizen and A. Pijpers, 2000. Effects of ambient temperature, arginine-to-lysine ratio and electrolyte balance on performance, carcass and blood parameters in commercial male turkeys. Poult. Sci., 79: 1608-1616.

Voslarova, E., P. Chlouopek, J. Chloupek, I. Bedanova, V. Pistekova and V. Vecerek, 2011. The effects of chronic intermittent noise exposure on broiler chicken performance. Anim. Sci. J., 82: 601-606.

Wideman, R.F., Y.K. Kirby, M. Ismail, W.G. Bottje, R.W. Moore and R.C. Vardeman, 1995. Supplemental l-arginine attenuates pulmonary hypertension syndrome (ascites) in broilers. Poult. Sci., 74: 323-330.

Witzel, D.A., W.E. Huff, L.F. Kubena, R.B. Harvey and M.A. Elissalde, 1990. Ascites in growing broilers: A research model. Poultry Sci., 69: 741-745.

Williams, R.B., 1999. A compartmentalised model for the estimation of the cost of coccidiosis to the world's chicken production industry. Int. J. Parasitol., 29: 1209-229.

Wu, L.Y., Y.J. Fang and X.Y. Guo, 2011. Dietary L-arginine supplementation beneficially regulates body fat deposition of meat-type ducks. Br. Poult. Sci., 52: 221-226.

Xiang, R.P., W.D. Sun, J.Y. Wang and X.L. Wang, 2002. Effect of vitamin C on pulmonary hypertension and muscularization of pulmonary arterioles in broilers. Br. Poult. Sci., 43: 705-712.

Xiong, M., S. Li, Peng, Y. Feng, G. Yu, Q. Xin and Y. Gong, 2010. Adipogenesis in ducks interfered X. by small interfering ribonucleic acids of peroxisome proliferator-activated receptor γ gene. Poult. Sci., 89: 88-95.

Xu, L., S.G. Wu, H.J. Zhang, L. Zhang, H.Y. Yue, F. Ji and G.H. Qi, 2011. Comparison of lipid oxidation, messenger ribonucleic acid levels of avian uncoupling protein, avian adenine nucleotide translocator and avian peroxisome proliferator-activated receptor-gamma coactivator-1 alpha in skeletal muscles from electrical-and gas-stunned broilers. Poult. Sci., 90: 2069-2075.

Yang, L., G.Y. Tan, Y.Q. Fu, J.H. Feng and M.H. Zhang, 2010. Effects of acute heat stress and subsequent stress removal on function of hepatic mitochondrial respiration, ROS production and lipid peroxidation in broiler chickens. Comp. Biochem. Physiol. C Toxicol. Pharmacol., 151: 204-208.

Yesilbag, D., M. Ern, H. Agel, A. Kovanlikaya and F. Balci, 2011. Effects of dietary rosemary, rosemary volatile oil and vitamin E on broiler performance, meat quality and serum SOD activity. Br. Poult. Sci., 52: 472-482.

Young, V.R. and A.M. Ajami, 2000. Glutamate: An amino acid of particular distinction. J. Nutr., 130: 892S-900S.

Zhang, Z.Y., G.Q. Jia, J.J. Zuo, Y. Zhang, J. Lei, L. Ren and D.Y. Feng, 2012. Effects of constant and cyclic heat stress on muscle metabolism and meat quality of broiler breast fillet and thigh meat. Poult. Sci., 91: 2931-2937.

Zhang, L., H.Y. Yue, S.G. Wu, L. Xu, H.J. Zhang, H.J. Yan, Y.L. Cao, Y.S. Gong and G.H. Qi, 2010. Transport stress in broilers. II. Superoxide production, adenosine phosphate concentrations and mRNA levels of avian uncoupling protein, avian adenine nucleotide translocator and avian peroxisome proliferator-activated receptor-gamma coactivator 1-alpha in skeletal muscles. Poult. Sci., 89: 393-400.

Zhao, J.P., H.C. Jiao, Z.G. Song and H. Lin, 2009. Effects of L-arginine supplementation on glucose and Nitric Oxide (NO) levels and activity of NO synthase in corticosterone-challenged broiler chickens (*Gallus gallus*). Comp Biochem. Physiol. C Toxicol. Pharmacol., 150: 474-480.

Zhou, H., N. Deeb, C.M. Evock-Clover, C.M. Ashwel and S.J. Lamont, 2006. Genome-wide linkage analysis to identify chromosomal regions affecting phenotypic traits in the chicken. II. Body composition. Poult. Sci., 85: 1712-1721.