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Review

Ameliorative effects of betaine and ascorbic acid administration to broiler chickens during the hot-dry season in Zaria: A review

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This review highlights the huge challenges heat stress pose to profitable production of broiler chickens during the hot-dry season. It also enumerates the negative effects of heat stress due to excess production of reactive oxygen species (ROS) in broiler chickens. It emphasizes that administration of betaine and/or ascorbic acid is highly beneficial to broiler chickens, subjected to high ambient temperature and high relative humidity, characteristic of hot-dry season in the Northern Guinea Savannah zone of Nigeria. In conclusion, supplementation of betaine and ascorbic acid to broiler chickens during the hot-dry season may improve health and production, decrease mortality and increase their productivity.

Key words: Broiler chickens, lipid peroxidation, betaine, ascorbic acid.

INTRODUCTION

The hot-dry season in the Northern Guinea Savannah zone of Nigeria is thermally stressful to poultry (Sinkalu and Ayo, 2008). Meteorological factors, such as high ambient temperature and high relative humidity, exert adverse effects on poultry production (Chen et al., 2013). They are known to cause heat stress in poultry during the hot-dry season (Rhoads et al., 2013). It is considered that animals are under heat stress when there is an imbalance between heat production within the body and heat loss. Reactive oxygen species (ROS) are produced in excess of what the body can cope with under heat stress condition (Kikusato and Toyomizu, 2013). Exposure of broiler chickens to acute heat stress depresses the mitochondrial respiratory chain activity, which, in turn, leads to the excess production of ROS, and, consequently, induces lipid peroxidation (Yang et al., 2010). The increased ROS production induced by chronic heat stress occurs in the mitochondria of skeletal muscle cells through the elevation of membrane potential due to increase in oxygen consumption, especially at the initial phase of heat exposure (Azad et al., 2010b). This causes continuous lipoperoxidation of polyunsaturated fatty acids, and consequently, the destruction of cell membranes (Sunil-Kumar et al., 2011).

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The production of broiler chickens under heat stress conditions results in reduction of feed intake (Azad et al., 2010a). The decrease in live performance of birds reared under high ambient temperature, exceeding the thermo-neutral zone of the birds, is due to decrease in feed conversion to meat (Lagana et al., 2007). Heat stress damages the intestinal barrier in broilers due to oxidative stress (Gu et al., 2012), and negatively influences the welfare of broilers kept under pre-slaughter conditions (Vieira et al., 2011). It induces a rise in serum corticosterone concentration, mortality, and a reduction in the percentage of phagocyticizing macrophages. It causes mild multi-focal acute enteritis, demonstrated by an increase in concentration of lymphocytes and plasmocytes in the *lamina propria* of the jejunum (Quinteiro-Filho et al., 2012).

Antioxidant supplementation reduces the negative consequence of ROS activity such as ascites syndrome in broilers (Rajani et al., 2011). Betaine is an oxidative by-product of choline which serves as an osmo-regulator and is a substrate in the betaine-homocysteine methyltransferase reaction, which links choline and betaine to the folate-dependent one-carbon metabolism. Betaine is an important source of one-carbon units (Ueland, 2011). It has osmo-protective property and is a donor of methyl group (Hruby et al., 2005). Betaine is used by cells to defend against changes in osmolarity (Klasing et al., 2002).

Betaine supplement may stimulate protection of intestinal epithelium against osmotic disturbance; improve digestion, absorption and nutrient utilisation in broiler chickens (Mahmoudnia and Madani, 2012). Ascorbic acid is a potent antioxidant, as evidenced by the capacity to increase the level of enzymatic and non-enzymatic antioxidants of heat-stressed broiler chickens (Ismail et al., 2013). Ascorbic acid supplementation improves immunity of broiler chickens under heat stress conditions (Motasem, 2012).

The aim of the present review was to evaluate the ameliorative effects of betaine and ascorbic acid administration to broiler chickens during the hot-dry season in Zaria, located in the Northern Guinea Savannah zone of Nigeria.

POULTRY INDUSTRY IN NIGERIA

Agriculture, including poultry production is the most important sector of the Nigeria economy, providing employment for about 75% of the populace (CBN, 2007). In Nigeria, poultry production is a major contributor to animal protein. Nigeria has poultry population of 114.3 million, comprising 82.4 million chickens and 31.9 million other poultry, including pigeons, ducks, guinea fowls and turkeys (Abdullahi et al., 2006). The predominant systems of poultry production in Nigeria are subsistent and commercial systems. The commercial system is further sub-divided into small - (100 to 20,000 birds), medium - (20,001 to 50,000 birds) and large - (> 50,000 birds) scale poultry farming. These birds are kept under intensive system of management at a stocking density of 22 to 25 birds/m^2 (Dafwang, 2002). However, subsistent farming comprises indigenous breeds that are allowed to roam about to scavenge for feeds (Adeyemo and Onikoyi, 2012). In the tropical and subtropical regions of the world, including Nigeria, production performance of broiler chickens is adversely affected by high ambient temperature (Cahaner and Leenstra, 1992). Heat stress results in decreased feed intake, feed efficiency, body weight and flock activities.

These factors consequently result in increased mortality, increased pulse, respiratory and panting rates (Ubosi, 2001; Yunusa, 2002). Adverse effects of heat stress may result in 100% mortality in poultry farms in Nigeria (Obeng, 1985). Heat stress in broiler chickens has been associated with increased generation of ROS (Lin et al., 2006), ameliorated by antioxidants (Surai, 2006). Antioxidants such as ascorbic acid, singly or in combination with vitamin E, has been used to ameliorate the adverse effects of heat and transport stresses in Northern Guinea Savannah zone of Nigeria, during the hot-dry season in laying chickens (Ajakaiye et al., 2010) and broiler chickens (Onu, 2009).

POULTRY PRODUCTION AND ITS CHALLENGES

Production of chickens (*Gallus gallus*) for human consumption dates back to 4000 years ago. Since then, there has been a continuous selection for specific desired traits through selective breeding of parent stock to achieve the desired results (Kalmar et al., 2013). *G. gallus* is the major ancestor species, but *Gallus sonneratii* has also contributed to the genetic make-up of the modern domestic chicken. Furthermore, the knowledge of gene sequencing has accelerated the identification of causal mutations, determining major morphological differences between wild *Gallus* and domestic breeds (Job et al., 2011). The advantages of poultry production are ease of management, high turn-over, fast returns on investment, and its wide acceptance for human consumption (Haruna and Hamidu, 2004). Domestic chickens are also considered an important biological model for research in the biomedical field (Rubin et al., 2010).

The poultry enterprise is becoming complex as a result of the rapid strides in technology, changing market dynamics and growing scale of production. Due to some factors, starting from the procurement of chicks to their final disposal, entrepreneurs are faced with numerous constraints (Swu et al., 2012). Factors such as acute heat stress at marketing age, especially in broiler chickens raised in open houses with poor ventilation impairing heat exchange, result in economic losses (Hassan and Reddey, 2012). Some considerations should be given to the microclimate within the broiler houses as birds experience heat stress (Lallo et al., 2012). Heat stress is one of the most important environmental stresses confronting poultry production worldwide. Understanding and controlling environmental conditions are crucial to successful poultry production and welfare (Lara and Rostagno, 2013). Some of the challenges faced in poultry production, especially in developing countries, include poor government support and management practices, high mortality and cost of feed (Amos, 2006). Evidence has shown that the critical issues of low production and inefficiency in resource allocation and utilisation in poultry production have adversely affected farmers in Nigeria (Ezeh et al., 2012). Population, urbanization and rising incomes are expected to double the demand for livestock products, including broiler meat in developing countries (Mammo, 2012). There is a shift in emphasis to broiler chickens for poultry meat, from spent layers (laying birds which have reached the end of egg production) in developing countries (Oluyemi and Roberts, 2000). There have also been significant improvements in poultry meat production in Nigeria due to efforts made in the use of improved breeds for production and the intensification of management systems of poultry (Ikani and Annalte, 2000). Poultry meat is affordable because it is relatively cheap for purchase by consumers (Damisar and Hassan, 2009). Broiler production is profitable because it has a positive net return on investment (Heidari et al*.,* 2011), whereas broiler meat has gained wide acceptance because it is a healthier alternative to red meat (Shini et al., 2010).

RELATIONSHIP BETWEEN ENVIRONMENTAL FACTORS AND THE WELFARE OF BROILER CHICKENS

The town of Zaria (11°, 12$^{/}$; 7°E, 38$^{/}$E) is located in the Northern Guinea Savannah zone of Nigeria. It has annual ambient temperature, ranging between 18.0 ± 3.7 and 31.8 ± 3.2°C, and has harmattan (the cold-dry period of the year) (November-February), hot-dry (March-May) and rainy (June-October) seasons (Ayo et al., 2011; Dzenda et al., 2013). The meteorological factors, such as ambient temperature and high relative humidity (particularly during the hot-dry season), directly influence production of broiler chickens (Genc and Portier, 2005). During hot conditions, characterized by high ambient temperature, relatively humidity and radiant energy, there is a decrease in the ability of animals to dissipate heat. This initiates compensatory and adaptive mechanisms to return the body to homeostasis (Daramola et al., 2012). When hot conditions persist, the difference between ambient temperature and body temperature of broiler chickens decreases, causing a reduced rate of sensible heat loss, which further results in mortality due to hyperthermia (Azoulay et al., 2011).

It is necessary to assess the environmental parameters of rearing broilers because they affect their performance (Kumar et al*.*, 2011). For instance, heat stress, resulting from high ambient temperature and relatively humidity negatively affects poultry performance in the tropical and subtropical regions of the world (Sohail et al., 2010). The temperature-humidity index, an index of thermal comfort integrating the effects of ambient temperature and relative humidity (Purswell et al., 2012), is used to evaluate the degree of thermal stress in livestock (Dikmen and Hamsen, 2008).

THERMO-NEUTRAL ZONES OF BROILER CHICKENS

The thermo-neutral zone is the range of ambient temperature, which does not affect regulatory changes in metabolic heat production or evaporative heat loss in birds (Kingma et al., 2012). In the tropics, the diurnal ambient temperature fluctuations usually exceed the thermo-neutral zone of chickens, resulting in heat stress (Dei and Bumbie, 2011). Ambient temperatures outside the thermo-neutral zone of birds, irrespective of age, may negatively affect their energy balance and fitness (Ardia, 2013).

Metabolic disorders such as ascites and sudden death syndromes may occur in broilers reared above the temperature of thermal comfort in the first week of life of the birds (Fernandes et al., 2013). Broiler chickens subjected to heat stress show elevated corticosterone levels and lower levels of thyroid hormones (Mahmoud et al., 2014). Elevated temperature negatively affects production, reproductive potential, immune responses and health status of livestock (including broilers) (Nardone et al*.,* 2010). Holik (2009) reported that the thermo-neutral zone for poultry in the tropics is between 18 to 24°C and between 12 to 26°C in temperate regions, while Kingori (2011) showed that the most favourable temperature range for poultry is between 12 to 26°C. Broiler chickens exhibit different behavior in response to daily variations in the thermal environment. Wing-spreading and beak-opening are some important adaptations to thermal environments (Fernandes et al., 2013). Since adaptation of animal (including birds) to their thermal environment requires regulation of body temperature, measurement of that adaptation through the energy the animal expends, provides an indicator of the extent and energy cost of adaptation (Nienaber et al., 2009).

RESPONSES OF BROILER CHICKENS TO HEAT STRESS

The state of well-being of animals may be assessed by the health, physiological and behavioral responses (Earley et al*.,* 2010). An increase in oxidative damage and alterations in amino acid concentrations in the diencephalon may contribute to the physiological, behavioral and thermoregulatory responses of heat-exposed chicks (Chowdhury et al., 2014). Behavioral responses such as posture, orientation, shelter seeking, huddling and dispersion are some means by which broilers seek to regulate their body temperature under hot ambient conditions (Kadzere et al., 2002). Heat tolerance in broilers may be enhanced by increasing sensible heat loss, which is determined by the difference between surface temperature and ambient temperature. It is more useful than the evaporative heat loss, which causes dehydration (Yahav et al., 2005). In addition to the damages that occur at cellular level due to oxidative stress, a number of signaling pathways, consisting of certain proteins (for example: apoptosis signal-regulating kinase 1, c-Jun NH_2-terminal protein kinase, signal transducers and activators of transcription) are modulated by heat shock protein 90 to improve tolerance to stress (Pandmini and Rani, 2011). Biochemical responses may be used to evaluate welfare of broiler chickens under hot conditions (Wang et al., 2013b). Heat tolerance in chickens may be assessed using biochemical parameters, especially during the early period of heat stress, owing to the close association between heat tolerance and biochemical indices (Run-Shen et al., 2011). Elevated ambient temperature is a limiting factor to poultry production in hot regions (Melesse et al., 2011). Though broiler chickens, to some extent, may acclimatize to some levels of oxidative stress, resulting from heat stress (Pamok et al., 2009), they experience some organ damage due to lipid peroxidation caused by hyperthermia (Mete et al., 2012).

Physiological responses to heat stress, which may be determined by their genetic make-up (Felvet-Gant et al., 2012), include decrease in antioxidant capacity, increased respiratory rate and rectal temperature (Ali, 2010). Heat stress decreases feed consumption (Chowdhury et al., 2012) and, consequently, reduces weight gain and growth. This further constitutes a major challenge in broiler production in the tropics (Widjastati and Hernawan, 2012). Heat stress also causes high water and electrolyte excretion, which impairs the ability for heat dissipation and alters acid-base homeostasis (Sayed and Downing, 2011).

Certain hormones like glucocorticoids and catecholamines are released in response to stressful conditions to enable the body cope with stress (Mostl and Palme, 2002). Two regulators of neuronal hormone regulators, arginine-vasotocin and corticotrophin-releasing adreno-corticotrophic hormones (ACTH), in addition to plasma corticosterone are also involved in stress responses (Cornell et al., 2013). High-affinity mineralocorticoid receptors ensure the maintenance of homeostasis, while the low-affinity glucocorticoid receptors mediate the recovery from stress. Hence, it is important to maintain balance between these systems for cellular homeostasis, performance and health (Dekloet, 2004). Glucocorticoids cross the blood-brain barrier to interact with certain receptors, located mainly at the hippocampus and the frontal lobes, consequently influencing learning and memory (Lupien et al., 2007). Acute heat stress activates corticotrophic-releasing hormone, resulting in impairment of memory consideration (Roozendaal et al., 2002). Increased plasma corticosterone may also down-regulate testosterone and progesterone concentration in plasma of chickens, impairing reproduction in broiler breeders (Rettenbacher et al., 2013). Finally, heat stress may result in redistribution of body resources (such as protein and energy) at the expense of growth, reproduction, production and health, to ensure survival (Gupta et al., 2013).

BIOMARKERS OF HEAT STRESS IN BROILER CHICKENS

Modern commercial broilers appear to have a compromised immune status, higher mortality and lower resistance to stresses, like heat stress (Khan et al., 2012). Heat stress induces hyperthermia in poultry (Syafwan et al., 2011). The health status of animals may be evaluated by measuring haemotological parameters (Talebi et al., 2005). Skin temperature, measured by thermography could be used as an index of welfare for domestic birds (Marelli et al., 2012). Erythrocyte osmotic fragility (EOF) may be used as an indirect measure of lipid peroxidation (Minka and Ayo, 2013). Heterophil/lymphocyte ratio is used as an indicator of heat stress (Prieto and Campo, 2010). The EOF is an important biomarker of oxidative stress, which may be utilised as a biomarker for heat stress in laying hens (Sinkalu et al., 2014). It may be used in broiler chickens to diagnose oxidative stress, having been demonstrated to serve as a biomarker of transport-induced oxidative stress, under high ambient temperature conditions, and as a reliable method for diagnosis of oxidative stress in quails (Minka and Ayo, 2013) and rabbits (Ayo et al., 2014). Furthermore, high levels of cortisosterone and heat-shock protein 70 may indicate levels of heat stressed (Zulkifli et al., 2009), and could result in high intensity levels of fear responses, evidenced by long tonic immobility in heat-stress broiler chickens (Al-Aquil et al., 2009).

REACTIVE OXYGEN SPECIES AND THEIR ROLES IN HEAT STRESS IN BROILER CHICKENS

In the eukaryotic cells, mitochondria are the site of aerobic energy production. Electron transfer from respiratory substrates is coupled to oxygen to produce ATP; however, this transfer may lead to the formation of oxygen radicals and other (ROS) (Venditti et al., 2013). ROS are also generated in the mitochondria of skeletal muscles of heat-stressed broiler chickens (Azad et al., 2010a; Kikusato et al., 2010). The continuous generation of ROS and the inability to manage their negative burden result in oxidative stress and cellular damage due to lipid peroxidation, occurring in the membranes (Singh et al., 2013). Disease ensues due to a decrease in immune function of the body (Ambrozova et al., 2011). The ROS-mediated damages of erythrocyte membrane results in haemolysis (Eroglu et al., 2013), which is responsible for erythrocyte fragility (George et al., 2012).

Damage to the cytoskeleton is common in neuronal cell death and is an early event in oxidant-induced cell injuries (Tiogo et al., 2011). Oxidative stress causes depletion in energy, accumulation of cytotoxic mediators and cell death (Lee et al., 2009). Excessive ROS production is involved in the pathogenesis of contractile dysfunction in heart-failure (Kubio et al., 2011) and in carcinogenesis (Quan et al., 2011), due to the fact that cancer cells (like in Marek's disease) require elevated ROS levels to maintain their high multiplication rate (Sosa et al., 2013). It is also implicated in intermittent hypoxia-induced hypertension (Del Rio et al., 2010).

REACTIVE OXYGEN SPECIES SIGNALING AND THEIR ROLE IN THE BODY

ROS, which can be generated by the activities of mitochondrial respiratory chain, nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, xanthine oxidase, lipoxygenase, uncoupled nitric oxide synthase and myeloperoxidase enzymes, play both physiological (such as cell growth and stress adaptation) and pathological roles (such as cellular damage and attenuation of cell function) at different levels (Sugarmura and Keaney, 2011). ROS are regarded as signaling molecules, propagating information regarding cellular pathways and the overall redox and cell metabolic activities in the mitochondria (Ghouoleh et al., 2011). ROS, under pro-oxidant conditions, are regarded as essential triggers and modulators of cell-signaling and cell behavior. Hence, antioxidant compounds may interfere with cell signal transduction by interrupting ROS at critical levels of signaling pathways (Lee et al., 2009; Leonarduzzi et al., 2010).

Thus ROS, hitherto considered a toxic by-product of aerobic respiration, are now known to be cardinal factors in cell-cell signaling because they play numerous signaling roles from bacteria to mammalian cells (Mittler et al., 2011). ROS signaling explains the mechano-transduction of calcium ion (Ca^{2+}) discharge in the heart, both in healthy and pathological states, depending on the rate of discharges. This offers the possibility for new therapies (Prosser et al., 2011). The interaction of the sphingosine - 1- phosphate and its receptors controls the assembling of progenitor cells through the stimulation of ROS signaling on bone marrow stromal cells, haematopoietic progenitors and stromal cell-derived factor 1 release (Golan et al., 2012).

ANTIOXIDANT SYSTEM OF THE BODY

In response to oxidative stress, organs and tissues possess distinct antioxidant systems. The knowledge of antioxidant defense systems serves as a guide for establishing the most effective nutrient supplementation to reduce oxidative stress. Such approach enhances bird's health and welfare, product quality, and increase economic returns of broiler production (Panda and Cherian, 2013). The body protects itself against the negative effects of ROS by two mechanisms, namely: through the regulation of membrane permeability and its antioxidant potentials (Lushchak, 2011). The copper-zinc superoxide dismutase enzyme is an important cellular defense against ROS (Klooppel et al., 2010). The tumor necrotic factor-α raises the basal levels of glutathione by up-regulating γ-glutamyl cystein synthetase synthesis and stabilising potentials in cells (Persson and Vainikka, 2010).

The suppression of nuclear factor erythroid 2-related factor 2 (Nrf 2), an important transcription factor in antioxidant regulation system, occurs during oxidative stress in poultry (Kim et al., 2012), as evidenced by changes in levels of activities of superoxide dismutase, catalase, glutathione and thiobarbituric acid-reactive substances (Liu et al., 2013). The skeletal muscle mitochondria of broilers produce superoxide anions during heat stress (Mujahid et al., 2005). The life-span of erythrocytes, which may function in antioxidant defenses, decreases by 50%, when the cells are exposed to excessive ROS production. This may be due to protein and/or amino acid degradation (such as tryptophan) in their cytoskeleton (Olszewska et al., 2012). It may further be due to post-translational modification of proteins, destroying the fate and functions of the erythrocytes (Pandey and Rizvi, 2013).

ANTIOXIDANT SUPPLEMENTATION IN BROILER CHICKEN PRODUCTION

The amelioration of hyperthermia in poultry, due to heat stress, could be achieved by reducing the thermal load via increasing the dissipation potentials, reducing heat production levels or altering the daily malproduction pattern (Syafwan et al., 2011). Supplementations with anti-stress agents in poultry are used to alleviate negative effects of stressors, especially heat stress (Pandurang et al., 2011).

Antioxidants decrease the deterioration of meat quality due to lipid peroxidation and stabilize meat oxidation after slaughter (Yasin et al., 2012). They also improve erythrocytic indices of broiler chickens subjected to heat stress (Majekodunmi et al., 2013).

a) Ascorbic acid as an antioxidant

It has been demonstrated that supplementation with L-ascorbic acid, both singly and in combination with dl-tocopherol acetate, is beneficial to heat-stressed layer hens (Ajakaiye et al., 2011). Ascorbic acid may be supplemented at 40 mg/bird/day in drinking water to reduce significantly the impact of heat stress and improve the productivity of broiler chickens (Vathana et al., 2002), due to its ability to improve the breast meat of broilers under heat stress (Abioja et al., 2010). During heat stress, endogenous ascorbic acid, produced by the kidneys of birds is not sufficient to mitigate the negative effects of the stress.

The adverse effects, resulting from heat stress, include reduction in immunity, feed intake, weight gain, egg production, number of chicks per hen, hatchability of fertile eggs, and of egg and carcass quality. It may also cause mineral imbalance, increase in panting and mortality, hence, necessitating the administration of supplemental ascorbic acid (Abidin and Khatoon, 2013). It has been shown that the body temperature, which is the net effect of heat production and heat loss, is reduced in chickens administered with ascorbic acid during exposure to high environmental temperature (Mckee and Harrison, 2013).

The physiological and biochemical potentials of ascorbic acid, an electron donor, are due to its ability to donate one or two electrons, making it a potent reducing agent and an antioxidant (Du et al., 2012). Its supplementation alleviates the negative effects of oxidative stress (Sujatha et al., 2010). Ascorbic acid has been demonstrated to decrease lipid peroxidation, and it improves protein concentration and iron status of broilers (Wang et al., 2011).

Glutathione activity is important for the maintenance of ascorbic acid metabolism by regulating the expression of ascorbic acid transporter and function (Mardones et al., 2012). Its supplementation to broiler chickens enhances the metabolic response to heat stress (Imik et al., 2013); improving performance and decreasing antioxidant status due to heat stress (Sahin, 2003). 2-0-α-Glucopyranosyl-L-ascorbic acid, a derivative of ascorbic acid protects dermal fibroblast from oxidative stress and cellular senescence. Therefore, it may be used as an anti-ageing agent (Taniguchi et al., 2012).

b) Betaine administration in livestock production

Betaine, a trimethyl derivative of glycine, is present in animal tissues. As a methyl group donor (Dilger et al., 2007), it is involved in transmethylation reactions as it donates its labile methyl group during metabolism. Betaine, widely found in animals, plants (wheat bran, spinach), microorganisms and seafood (from marine invertebrates) is known to protect cells, protein and enzymes from environmental stress (like high ambient temperature, low water and high salinity), because it is an osmolyte (Craig, 2004). It is also a metabolite of choline degradation and exerts an osmoregulatory role in cells (Hruby et al., 2005; Ratriyanto et al., 2009); especially in intestinal cells during heat stress (Metzler-Zebeli et al., 2009). As an osmolyte, betaine regulates water balance, resulting in the stability of tissue metabolism, especially in the gastro-intestinal tract (Lipinski et al., 2012). Betaine decreases lipid peroxidation in the breast muscles of broiler chickens, and, hence, the quality of broiler meat (Alirezaei et al., 2012). It may also exert free-radical-scavenging ability against lipid peroxidation, as well as maintaining myocardial energy (ATP) status via sustaining the enzyme activities in the Krebs cycle (Ganesan et al., 2007).

Betaine supplementation reduces the abdominal fat and facilitates the even distribution of lipid in geese (Su et al., 2009). The effects of betaine on fat may be due to its influence on mRNA expression and the promoter CpG dinucleotide methylation profiles of chicken's lipoprotein lipase gene (Yi et al., 2009; Xing et al., 2011). It further influences levels of plasma homocysteine, which could be used as a marker of methyl deficiency (Lever and Slow, 2010). Plasma homocysteine is reduced with betaine administration (Atkinson et al., 2009). In the transfer of its methyl group, methioine, a key intermediate, is converted to S-adenosyl methionine, and subsequently, to homocysteine. Homocysteine and methionine accumulate during methyl-donor deficiency (like in betaine deficiency), making the metabolites potentially toxic to the body (Waldroup et al., 2006). It also induces expression of spot-14 (S_{14}), which responds to thyroid hormones, located in hepatic nuclei, and functions to relay hormone and nutrient-related signals to genes involved in lipid metabolism (Su et al., 2009).

Methionine is a limiting amino acid in poultry (Kalbande et al., 2009). It is involved in vital functions such as methylation reactions of DNA (Swennen et al., 2011) and histones (Tesseraud et al., 2011). Osmolytes, like betaine, decrease inflammatory responses due to hyperosmolarity. This is because a high osmolytic state triggers pro-inflammatory cytokine release and inflammation (Brocker et al., 2010). Betaine also prevents the up-reglation of HSP 70 (Oliva et al., 2011). Osmolyte accumulation is necessary for the viability of cells of renal medulla. This is because renal medulla is exposed to diverse ionic and osmotic compositions in their environment, which may result in ROS production (Rosab-Rodriguez and Valenzaela-Soto, 2010). Betaine, also known as N,N- dimethylglycine, may be included at 1 to 10 g/kg of feed without inducing toxicity or impairing performance in broilers (Kalmar et al., 2012).

PHYSIOLOGICAL ROLES OF METHYLATION PROCESS IN THE WELL-BEING OF BROILER CHICKENS

The expression of HSP is influenced by high temperature, which may be strongly associated with the DNA methylation pattern in the HSP70 promoter (Gan et al., 2013). HSPs are methylated in response to stress. Methly donors, like methionine and betaine increase development of breast muscle as evidenced by the expression of myostatin, Myf_5, and Mef_{2B} genes (Wen et al., 2014). Traits for growth are vital in the poultry industry, and they have been shown to be related to DNA methylation of chicken muscle (Hu et al., 2012). DNA methylation down-regulates the expression of a growth factor receptor responsible for tumor formations (Luo et al., 2013). Furthermore, brain-derived neutrotropic factor, which determines the susceptibility or resistance of chickens to Marek's disease, plays some roles in neuronal survival, cholesterol metabolism, cell differentiation and tumor formation (Yu et al., 2009). Tumor formation in chickens could be mediated by epigenetic alterations and genetic variation via the modification of DNA methylation, catalysed by DNA methyltransferase (Yu et al., 2008; Luo et al., 2012).

Generally, DNA methylation is the key factor of gene suppression (Useni et al., 2009). It functions in gene silencing by methylation of specific gene promoter sequences of the host genome against retrovirus and transcriptional suppression of transgenes (Jang et al., 2013). The difference in the expression of gene-mediated epigenetic processes could result in broad phenotypic expression in animals. DNA methylation may influence the extent to which the gene expression varies and also the modification of epigenetic mechanism (Nätt et al., 2012).

Furthermore, methyl-donor deficiency results in liver steatosis and, consequently, in a metabolic syndrome due to hypomethylation of the organic cation transporter PGC-1α, reduced binding with peroxisome proliferators-activated receptor γ (PPAR-γ), co-activator-α and hepatic nuclear oxidation. This links methyl donor deficiency and epigenomic deregulation of energy metabolism (Pooya et al., 2012). Such deficiency may also result in increased risk of cardiovascular diseases due to hyper-homocysteinemia. Consequently, it increases prohibin and decreases α-crystallin β, which indicate mitochondrial injury and stress to the endoplasmic reticulum (Martinez et al., 2013). It is conceivable that the negative effects of heat stress on the sustainable growth of broiler production in the tropical and subtropical regions may be alleviated by betaine administration in drinking water (Mahmoudnia and Madani, 2012).

CONCLUSION REMARKS

Poultry production in the Northern Guinea Savannah zone of Nigeria is important in meeting the high demand for safe and wholesome poultry meat in Nigeria, and indeed Africa. Owing to high ambient temperature and high relative humidity, which induce heat stress, broiler chicken production is greatly hampered, especially during the hot-dry season. This is because heat stress increases production of oxidants, causing oxidative stress and lipid peroxidation of cell membranes. During heat stress, broilers respond physiologically and behaviorally to combat the negative effects of the stress. This channels useful energy of the birds to coping with heat stress by attempting to return the body to homeostasis at the expense of weight gain and, consequently, production. Heat stress causes decreases in feed intake, conversion of feed to meat, poor weight gain and high mortality, resulting in huge economic losses.

The administration of potent antioxidants, such as ascorbic acid and betaine, ameliorate the negative effects of heat stress. The properties of ascorbic acid as an electron donor, and betaine, as methyl donor and an osmolyte, make their administration to broiler chickens, raised during the hot-dry season, beneficial in heat stress alleviation.

It is concluded that supplementation of betaine (1 to 10 g/kg of feed) and ascorbic acid (40 mg/bird/day in drinking water) to broiler chickens during the hot-dry season may improve health and production, decrease mortality and increase their productivity. It is recommended that further studies be conducted to elucidate the molecular and genetic mechanisms underlying the responses of broiler chickens to oxidative stress due to heat stress, with the aim of combating its negative effects.

Conflict of Interests

The author(s) have not declared any conflict of interests

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