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Asian Journal of Animal and Veterinary Advances

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Asian Journal of Animal and Veterinary Advances 10 (9): 461-475, 2015
ISSN 1683-9919 / DOI: 10.3923/ajava.2015.461.475

Dietary Essentiality I: Coenzyme Q10 Conditionally Essential-Review

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ABSTRACT

The essentiality of nutrients keeps on changing with the advancement in nutritional research and genetic gain. The genetic gain especially in poultry sector is very high which results in increase in nutrient requirement of both the essential and non-essential nutrients. For the rapid growth the requirement of essential nutrients reaches many folds which are in direct relation with the performance, but the requirement for non-essential nutrients is an indirect one. Most of the dispensable amino acids, vitamin C, carnitine, etc. which are being synthesized endogenously are now a days unable to meet the birds requirements that warrants the dietary supply. Another important nutrient is coenzyme Q10 (CoQ10) which endogenously synthesized is now gaining much attention as a supplement for fast growing broilers. The CoQ10 can be termed as multi-functionary as each and every cell in the body needs this but quantity is being high for very active organs like heart, lungs, liver, kidney, etc. They are essential for cellular oxidative phosphorylation and regenerative antioxidant. The supplementation of CoQ10 improved the feed efficiency with reducing the electron leaks from mitochondria and increases total antioxidant capacity. For this property, CoQ10 is widely used in human medicine especially persons suffering from cardiac, neurological disorder, hypercholesterolemic condition and also even in cancer. The CoQ10 in poultry draws first attention when it is found to reducing the ascites mortality in marketable broilers. Thereafter, the advantages of CoQ10 is started to exploit with much attention to ascites, feed efficiency, cholesterol lowering effect nutraceutical and nutrigenomic property both in poultry and swine industry.

Key words: Broiler, coenzyme Q10, essential, oxidative phosphorylation, ubiquinone

INTRODUCTION

The nutritional research is extending into a new era where an already proven fact of dietary non-essentiality is being revised into different categories like semi, conditionally essential nutrients. The once termed as non-essential amino acids are now recommended as dietary requirement of nutritionally non-essential amino acids, arginine, glutamine, proline to name few of them (Wu *et al*., 2013). Similarly, endogenous synthesis of vitamin C is a well-known fact but however, during the periods of stress (metabolic or thermal) the exogenous supplementation of this vitamin resulted in very good performance and survivability in poultry. The resultant of extensive

genetic research resulted in higher and more efficiently growing pig and poultry varieties which are entering the market on a regular basis. These genetic changes require an overall change in nutritional approach towards establishing the nutrient requirements.

Poultry breeders are working on the objective of increasing a minimum of one egg per generation in case of egg type chicken and reducing one day in attaining market weight per year in broilers. As result, the number eggs laid during a laying period of 240 eggs over 30 years before has rose to 325 eggs now. Whereas, it took twelve weeks to achieve a body weight of 2.3 g in 1950, which is now being achieved within 6 weeks in meat birds (Duncan, 2001). Feeding and management for this level of production had to be developed concurrently to exploit the full genetic potential for growth. To achieve this performance, nutritionist attempt to increase the density of the nutrients in the diet.

This increase in energy density and feed intake along with reduced transit period resulted in loss of nutrient period. To counteract this feed enzymes like non-starch polysaccharide degrading enzymes, proteases, phytase, probiotics, acidifiers, etc. are being routinely incorporated in both chicken and swine industry. All these attempts are concerned about transferring the nutrients from the feed into the cells with the supposition that all the absorbed nutrients are utilized without much wastage. But in order to utilize the absorbed nutrients the endogenous system should be elevated.

Since, dietary energy constitutes the major cost of broiler diet every attempts to improve the efficiency of energy utilization and minimizing the energy wastage will help in improving the profitability of broiler production. The various systems are involved in transfer of nutrients to its metabolic pathways, especially in energy utilization of oxidative phosphorylation pathway in mitochondria where coenzyme Q10 is playing an important role as an electron carrier.

Coenzymes are cofactors essential for a large number of enzymatic reactions which takes place in the body. Coenzyme Q10 (CoQ10) also known as ubiquinone was first isolated from the beef heart mitochondria in 1957 during an investigation of the mitochondrial electron transport system (Crane *et al*., 1957). The fundamental role of CoQ10 in the mitochondrial respiratory chain and in oxidative phosphorylation was determined by Mitchell (1975) for which he was awarded the Nobel Prize in Chemistry in 1978 (Bliznakov *et al*., 2004). The CoQ10 is an endogenously synthesized lipophilic compound present in all living cells (ubiquitous in nature), hence it is also designated as ubiquinones (Lenaz and Esposti, 1985). Coenzyme Q10 (CoQ10) is a lipid-soluble compound involved in mitochondrial adenosine triphosphate (ATP) synthesis-bioenergetics and reduces the pulmonary hypertension syndrome and ascites mortality (Geng *et al*., 2004a).

The CoQ10 does various roles along with its three important functions in the body, namely as an electron carrier in respiratory chain, antioxidant (Kaikkonen *et al*., 1997) and cell signalling and gene expression (Ernster and Dallner, 1995). These functions are having practical applications in clinical practice and its use as food/feed supplementation (Krizman *et al*., 2012). Supplementing coenzyme Q10 is known to provide health benefits, much like nutraceuticals even in healthy individuals (Ramasarma, 2012) and individuals with metabolic disorders like oxidative phosphorylation disorder (Marriage *et al*., 2004). The CoQ10 also maintains membrane fluidity (Fato *et al*., 1984) and protects membranous phospholipid against peroxidation (Takayanagi *et al*., 1980) and in plants photosynthesis (Redfearn, 1966). Normal respiratory rate requires the maintenance of a high CoQ10 concentration and even a small decrease was deleterious (Battino *et al*., 1990). With all these introductory background a review on usefulness and possible opportunity for coenzyme Q10 in poultry feeding has been attempted.

IS COENZYME Q10 A VITAMIN?

The CoQ10 is similar to vitamin K in its chemical structure but it is not considered a vitamin because it is synthesized in the body (Bhagavan and Chopra, 2006; Wang *et al*., 2015). All the fat soluble vitamins (A, D, E and K) possess isoprene units in their structures. Likewise coenzyme Q is also having an isoprenoid (seen A, D, E and K), a quinone structure (as in vitamin K) and cyclized chromenol (vitamin E). A definition to which a molecule is considered as a vitamin is as follows: an organic compound with small molecular weight, not to be synthesized in the body and supplemented through the diet; the absence of this will leads to a deficiency syndrome; converted to an active coenzyme form required for metabolic activity. With day to day findings makes CoQ nearly fit into the typical definition for a vitamin. Being endogenously synthesized by all animal tissues might rule them out for a vitamin status. But vitamin D_3 and vitamin C is endogenously synthesized from cholesterol and glucose respectively, still given the vitamin status, hence CoQ10 might be termed as vitamin Q as expressed by folkers. Supplementing coenzyme Q provides health benefits to the likes of nutraceuticals (Ramasarma, 2012).

CHEMISTRY OF COENZYME Q10

The CoQ10 is 2, 3-dimethoxy-5-methyl-6-decaprenyl-1, 4-benzoquinone (Wang *et al*., 2015). It contains 10 isoprene units the predominant from in both mammals and birds, whereas CoQ9 (nine isoprene units) is predominant in rodents (Battino *et al*., 1990). Due to its lipophilic nature and higher molecular weight (863 Da), the oral bioavailability of CoQ10 is low (Krizman *et al*., 2012). Following absorption, it is taken up by the liver for incorporation into Very Low Density Lipoprotein (VLDL) particles before released into circulation (Bhagavan and Chopra, 2006). Kaikkonen *et al*. (1997) reported an elevated Q10 content in VLDL and Low Density Lipoprotein (LDL) fraction by 160% following dietary supply. To counteract the problem of low bioavailability, currently different types of carriers like lipid emulsion of solid triglyceride, tocopherol succinate and phospholipids (Ultrasome®) (Amselem, 1999), different cyclodextrins (Fir *et al*., 2009) and gel form (UbiQGel®) (Natural Medicines Comprehensive Database, 2003) are being tried with great success.

BIOSYNTHESIS OF UBIQUINONE

The CoQ10 is endogenously synthesized in all human and animal cells (Elmberger *et al*., 1987). Two pathways involved in CoQ10 biosynthesis in the body. The biosynthesis of polyprenyl side chain occurs through the mevalonate pathway. This reaction starts with acetyl-coenzyme A and ends up with farnesyl pyrophosphate (FPP). This FPP also acts as a substrate for the biosynthesis of isoprenylated proteins, dolichol and cholesterol. However, the quinone head is either synthesized from the amino acid tyrosine or phenylalanine (Turunen *et al*., 2004).

Ramasarma (1968) summarized the major findings of coenzyme Q10 as below:

- Coenzyme Q is distributed throughout all cell components
- Unlike vitamin K and E, exogenous CoQ absorbed into liver and not in other tissues
- All the tissues in the body have the capacity to independently synthesis the CoQ, but this capacity is less during developing early embryonic tissues
- The mevalonate pathway used by animals, plants and fungi for the synthesis of CoQ but not used by some bacteria and also for synthesis of vitamin K in mycobacteria
- In liver accumulation of CoQ occurs due to lower catabolism or enhanced synthesis under conditions like deficiency of vitamin A, cold stress exposure and excess thyroid secretion

- Excesses of CoQ in liver either by endogenous synthesis or by absorption, has negative feedback mechanism to inhibit its own synthesis which also leads to low serum cholesterol content as de novo synthesis of cholesterol shares the same biosynthetic pathway

Presently, coenzyme Q10 has been produced by chemical synthesis, semi-chemical synthesis or microbial conversion and is commonly available. Humans or animals fed non-vegetarian diet will have higher CoQ10 intake and its absorption varies with the amount and uptake increases with increase in fat content. The absorption of reduced form is more than the oxidized CoQ10 and with its large molecular weight about 60% of intake excreted through the faeces (Zlatohlavek *et al*., 2012). The yeast fermentation technique which involves with inclusion of B-vitamins in their culture is the major form of industrial CoQ10 synthesis. Recently, CoQ10 is available as feed grade powder form for swine and poultry but in gel form for human preparations (Ioana *et al*., 2009; Lambrechts and Siebrecht, 2013).

COENZYME Q10 ON BROILER PERFORMANCE

Supplementing CoQ10 at 20 and 40 mg kg^{-1} feed increased the body weight gain upto 21 days of age in broilers maintained at higher altitude (Huang *et al*., 2011). But the gain in body weight was not reported between 21 and 42 days of age which was suggested as an interaction effect between the age of the bird and longer duration of supplementation could have weaken the beneficial effects of CoQ10. To address this issue, Krizman *et al*. (2012) supplemented CoQ10 (5 mg day^{-1}) for different periods namely 0, 10, 20, 30 and 40 days and observed higher weight gain on continuous usage for 40 days than other short term feeding periods. Through these studies that supplementation of CoQ10 has beneficial effect on growth rate but it is subjected to dose and duration i.e., high dose (20 or 40 mg kg^{-1}) for short term (21 days) feeding or low dose (5 mg kg^{-1}) for long term (40 days) feeding. The reason for weakened effect might be the explanation given in point six by Ramasarma (1968). Gopi *et al*. (2014a) fed the broilers with three energy levels (normal, low and high), three levels of CoQ10 (0, 20 and 40 mg kg^{-1} feed) found higher body weight gain, better feed efficiency with less feed cost per kilogram weight gain was observed in high energy group supplemented with 20 mg of CoQ10 kg^{-1} diet. Fathi (2015) had improved feed efficiency in broilers when fed them with CoQ10 at 40 mg kg^{-1}.

However, similar effect couldn't be observed when the birds reared under higher environmental temperature with Temperature Humidity Index (THI) around 33.05°C (Gopi, 2013) against the previously mentioned study of THI around 25.08°C. Supplementation of CoQ10 at 20 and 40 mg kg^{-1} in broiler ration did not improve the growth rate or Feed Efficiency (FE) (Geng *et al*., 2004a). But, Geng *et al*. (2007) observed higher weight gain by CoQ10 at 40 mg kg^{-1} feed either from day one or 10th day of age with no effect on the feed intake and feed efficiency. The CoQ10 at 200, 400 and 800 mg kg^{-1} had neither produced significant effect on the body weight nor feed efficiency on growing white leghorn chicken (Honda *et al*., 2010). Nakamura *et al*. (1996) supplied CoQ9 (the predominant form in rodents) at 200 mg kg^{-1} in broiler diet which resulted in increased survival rate due to low ascites mortality but the body weight and feed efficiency at 56 days were not affected.

Production score is an index used to assess the productivity in broiler chicken. The higher the production score more the return to the producers can get. This index was proposed by Suzuki and Shibata (1989), which takes average body weight, survival rate, market age and feed efficiency into consideration. The CoQ9 supplementation resulted in higher production score over the unsupplemented birds. Similarly, Gopi (2013) observed higher score at 20 mg kg^{-1} but the score dropped to the control in 40 mg kg^{-1} feed supplemented group.

Gopi *et al*. (2014a) found that supplementation of 20 mg CoQ10 kg^{-1} reduced the cost of feeding broilers but not at 40 mg CoQ10 kg^{-1} feed. He explained that this cost benefit was due to higher body weight gain, lower feed intake resulted in better feed efficiency.

COENZYME Q10 ON ASCITES HEART INDEX (AHI) AND ASCITES MORTALITY

In fast growing broilers, the impact of ascites mortality is very high (after 5 weeks of age) as the farmers are not only losing the bird they are incurring the feeding and rearing cost by the time. Feed restriction or skip-a-day feeding is followed in broiler during finisher phase to avoid the problem of ascites which results in poor body weight and feed efficiency. Few researchers are suggesting that ascites might be due to bird's inability to endogenously synthesize the CoQ10 demand. To counter act this, CoQ10 was used, in fact the importance of CoQ10 was felt when Nakamura *et al*. (1996) observed a reduction in ascites mortality in broilers when fed with CoQ10. Then the term Ascites Heart Index (AHI) comes into prominence which gives more information about the susceptibility of the bird's to ascites. Ascites Heart Index (AHI), a sensitive index of pulmonary hypertension which based on the relative ratio of the right ventricle to the total ventricle (Burton *et al*., 1968). The AHI was further made into more useful tool by Cawthon *et al*. (2001), who graded broilers with AHI value of less than 0.27 without any fluid accumulation in abdomen as normal and those birds having AHI value more than 0.30 with fluid accumulation are pulmonary hyper tensioned and prone to ascites mortality. The relative heart weight of birds receiving CoQ10 at 20 mg kg^{-1} of diet was higher (Azuma *et al*., 1985; Geng *et al*., 2004a, b, 2007, Gopi, 2013). Fathi (2015) observed as a reduction in AHI ratio at 40 mg kg^{-1}. However, Huang *et al*. (2011) reported lower heart weight with respect to percentage of body weight when broilers fed with 20 and 40 mg of CoQ10. Ascites mortality in broilers was reduced around 75% by CoQ10 supplementation at both 20 and 40 mg kg^{-1} of diet (Geng *et al*., 2004a, b, 2007). But at 40 mg kg^{-1} of diet supplementation the incidence of leg problem was high (Geng *et al*., 2004a). This reduction in ascites mortality (around 40%) was observed when broiler fed CoQ9 (Nakamura *et al*., 1996). These studies imply that CoQ either 9 or 10 isoprene units are able to reduce the broiler's mortality due to ascites.

COENZYME Q10 ON LIPID METABOLISM

Clinical human and animal studies suggested that dietary CoQ10 supplementation improved the cholesterol metabolism in mammals. Krizman *et al*. (2012) recorded nearly 10% lower cholesterol concentration in heart tissue of broilers when supplemented with CoQ10. The CoQ10 supplementation decreased plasma total cholesterol concentration in humans (Cicero *et al*., 2005) and rats (Modi *et al*., 2006). The CoQ10 was reportedly able to suppress the hepatic cholesterogenesis in rats (Omkumar *et al*., 1992) and in hens (Kamisoyama *et al*., 2010).

In an experiment with layer chicks by Honda *et al*. (2010) recorded reduced hepatic total cholesterol, plasma cholesterol and Very Low Density Lipoprotein (VLDL) cholesterol concentration by supplementation of CoQ10 at 400 and 800 mg kg^{-1} feed. However, the plasma HDL, LDL cholesterol and total bile acids were not influenced by CoQ10 supplementation. The reduction in cholesterol level was due to decreased enzymatic activity of 3-hydroxy-3-methylglutaryl coenzyme A reductases (HMGR) in the liver, but it had no influence on the enzymatic activity of 3-hydroxy-3-methylglutaryl coenzyme A synthetase (HMGS). In contrast, the activity of HMGR was increased in the observations of Schroepfer (2000) and Espenshade and Hughes (2007). Dietary CoQ10 supplementation suppressed hepatic cholesterogenesis in laying hens (Kamisoyama *et al*., 2010). Kamisoyama *et al*. (2010) observed a decrease in egg yolk cholesterol concentration by 7-10% on CoQ10 supplementation.

In long term CoQ10 feeding trial Honda *et al*. (2010) observed reduced cholesterol synthesis with suppression in cholesterol catabolism resulting in return of hepatic cholesterol to normal level. However, long term (0-42 days) supplementation of CoQ10 at 20 and 40 mg kg^{-1} reduced the levels of serum total cholesterol and serum LDL-cholesterol (Schmelzer *et al*., 2011; Gopi, 2013). The reduction in serum LDL-cholesterol due to CoQ10 supplementation was attributed to the action of reduced form of CoQ10(H_2) which induces characteristic gene expression patterns, which are translated into reduced LDL-cholesterol level in human subjects. However, there were no reports of increase in the HDL-cholesterol levels (Honda *et al*., 2010; Gopi, 2013).

The CoQ10 reduced cholesterol metabolism in the plasma of patients with myocardial infarction (Singh *et al*., 2003) and in diabetic rats (Modi *et al*., 2006). The CoQ9, a major coenzyme Q in rats, decreases plasma total cholesterol concentration and suppresses hepatic cholesterogenesis (Krishnaiah and Ramasarma, 1970).

COENZYME Q10 ANTIOXIDANT PROPERTIES

Under the present intensive system of poultry production especially in tropics, stresses due to environment, metabolic, managemental, etc. are inevitable, resulting in lower productivity, less nutrient retention, decreased serum and tissue vitamins level, Humoral Immunity (HI) and molecular changes like protein, nucleic acid denaturation and lipid peroxidation. Increased Reactive Oxygen Species (ROS) metabolites compromises cell membrane integrity (Cawthon *et al*., 2001) with resulting in drip loss in muscles (Huang *et al*., 2011) affect keeping quality of muscles. Different nutrients and additives (like use of synthetic amino acids, low heat increment nutrients, vitamin C, E and minerals-selenium, zinc and magnesium or additives gensein, melatonin, essential oils are tried with varied success to counter act these stresses (Gopi *et al*., 2014b). Aside from its role in mitochondrial bioenergetics, ubiquinone also affects membrane fluidity (Fato *et al*., 1984) and protects membrane phospholipids against peroxidation (Takayanagi *et al*., 1980). The CoQ10 in its reduced form possesses free radical scavenging and increases total antioxidant capacity (Forsmark-Andree *et al*., 1997; Armanfar *et al*., 2015). The CoQ10 are preferred over α-tocopherol (Tang *et al*., 2001) as CoQ10 enhances the activity of other enzymatic and non-enzymatic antioxidants. The serum vitamin E level was increased by CoQ10 at 20 mg kg^{-1} as observed in works by Ernster and Dallner (1995) and Gopi (2013). As CoQ10 shows the property of regenerating the oxidized (inactive) α-tocopherol to reduced (an active form of vitamin E) (Constantinescu *et al*., 1994). Serum or liver malonaldehyde (MDA) is a product of lipid peroxidation and serves as biomarker for oxidative damage in lipids (Geng *et al*., 2004b; Mujahid, 2007; Gopi, 2013; Fathi, 2015). This suggested the protective action on lipid peroxidation in liver mitochondria (Ramirez-Tortosa *et al*., 2008) by CoQ10.

Superoxide dismutase (SOD) activity was increase in accordance with CoQ10 supplementation in broilers (Geng *et al*., 2004b; Huang *et al*., 2011) and in rats (Lakomkin *et al*., 2005). An increase in hepatic SOD and anti-ROS capacity in broilers was observed by CoQ10 supplementation (Geng *et al*., 2004b). The supplementation of CoQ10 increases the SOD activity by antagonizing Nitric Oxide (NO) inactivation; thereby making more NO availability for the biological function which leads to extracellular SOD gene-expression (Tiano *et al*., 2007). The reduced glutathione and glutathione peroxidase activity were also increased by CoQ10 at 20 mg kg^{-1} (Lakomkin *et al*., 2005; Huang *et al*., 2011; Gopi, 2013). This synergistic action of CoQ10 is possible as it acts as a primary regenerating antioxidant (Quiles *et al*., 2004). However, supplementation at 40 mg kg^{-1} of diet resulted in no effect on serum vitamin E and SOD levels. This ineffectiveness of CoQ10 at 40 mg kg^{-1} of diet is due to the auto-oxidation of CoQ10 resulting in higher production of

mitochondrial Reactive Oxygen Species (ROS) (Turrens *et al*., 1985) which leads to oxidative stress in the body. The development of auto-oxidation was observed in birds fed higher level of CoQ10 for prolonged duration.

COENZYME Q10 ABSORPTION AMONG BODY TISSUES

The content of CoQ10 in different body tissues are well studied in human subjects and not enough studies in farm animals or birds. The highest concentration of CoQ10 was found in the most active organs like heart, kidney and liver (Ernster and Dallner, 1995). The CoQ10 concentration depends on a balance between inputs and outputs. Inputs are the level of CoQ10 which is endogenously synthesized plus dietary supply and the output are the usage by oxidative stress and cellular metabolism (Lenaz *et al*., 1990). An adult human body has approximately 2 g of CoQ10, where a daily replacement of 0.5 g should be done by both endogenous synthesis and dietary means (Kalen *et al*., 1989, Bliznakov and Wilkins, 1998). Therefore, an average body CoQ10 content turnover rate was around 4 days (Ernster and Dallner, 1995) and dietary supply becomes essential with impairment in endogenous synthesis. The body content of CoQ10 decreased rapidly after the age of 40 years in humans with reduced biosynthesis (Kalen *et al*., 1989). The CoQ10 supplementation reversed the reduced circulating CoQ10 concentrations in statin-treated subjects as statin inhibits the pathways involved in both cholesterol and CoQ10 supplementation (Nawarskas, 2005; Fedacko *et al*., 2013). Various authors recommended daily intake of CoQ10 about 30-100 mg for healthy people over 40 years and 60-1200 mg for those undergoing an adjunctive therapy in some medical conditions (Jones *et al*., 2002, Bonakdar and Guarneri, 2005, Challem, 2005). The CoQ10 level in human tissues vary with inappropriate nutrition, smoking and different medical conditions cardiomyopathy, diabetes and neurological disorder conditions (Elsayed and Bendich, 2001; Quinzii *et al*., 2007; Fotino *et al*., 2013; Madmani *et al*., 2014).

Similarly in broiler chicken, the concentration of CoQ10 among different body tissues recorded by Pravst *et al*. (2010), are heart 92.3-192 mg kg^{-1}, liver 116.2-132.2 mg kg^{-1}, thigh 24.2-25 mg kg^{-1}, breast 7.8-17.1 mg kg^{-1}, wing 11.0 mg kg^{-1} and whole chicken 14-21 mg kg^{-1}. Among the organelles larger amount of CoQ10 is found in mitochondria of heart cells (92.3-282.0 mg kg^{-1}), followed by liver (22.7-132.2 mg kg^{-1}) of cattle, swine and chicken. Being lipophilic the vegetable oils especially rape seed and peanut oils have high content (63.5-77.0 mg kg^{-1}) of CoQ (Pravst *et al*., 2010). This again proved that CoQ10 is required more by tissues that are very active.

In the body CoQ 10 mainly present in reduced form (ubiquinol) except in the lungs and brain where the oxidized form is predominant (Aberg *et al*., 1992; Cohen, 2015). Ubiquinone (oxidized state) is reduced to ubiquinol (reduced state) either during or following absorption in the intestine and with about 95% of circulating CoQ10 exists in ubiquinol form (Bhagavan and Chopra, 2006). So their activity is not affected which form (reduced or oxidized) it is consumed. The CoQ10 level in food ingredients was found to be reduced by 14-32% on frying but boiling did not have any effect on CoQ10 level (Weber *et al*., 1997).

Lenaz *et al*. (1991) and Wen *et al*. (1999) observed an increase in hepatic mitochondrial membrane CoQ10 content in rats with exogenous CoQ10 supplementation. About 1.6-fold increase in plasma concentration of CoQ10 was recorded by Krizman *et al*. (2012) following CoQ10 supplementation in broilers. This fold increase resulted in increased CoQ10 in heart (11.3%), breast (45%), wings (25%) and legs (16%) of chicken. Cooke *et al*. (2008) and Gopi *et al*. (2014a) recorded an increase in muscle CoQ10 at 20 mg kg^{-1} content with reduction in muscle cholesterol content but were not at 40 mg of CoQ10 kg^{-1} of diet. Krizman *et al*. (2012) also proposed that for production of functional food chicken, supplementation of CoQ10 could be considered in future as CoQ10 in

muscles are more bioavailable than other synthetic forms. The unresponsiveness at higher level of supplementation (40 mg kg^{-1}) is due to negative feedback mechanism operating in birds wherein CoQ10 biosynthesis could have reduced due to higher exogenous supply as explained by (Lenaz *et al*., 1990).

The CoQ10 to cholesterol index (QCI) is increasingly used as a measure for assessment of meat quality. Krizman *et al*. (2012) used QCI as a reliable indicator of oxidative status and the possible oxidative stresses induced by different food ingredients and consider them as oxidant foods. In simple terms, muscles with higher oxidative stress due to either metabolic activity or food would results in reduction of QCI value. The QCI value was higher in 20 mg kg^{-1} supplemented group as a suggestive of low oxidative stress (Gopi, 2013). The auto-oxidation (Turrens *et al*., 1985) of CoQ10 at 40 mg of CoQ10 kg^{-1} increased muscle metabolic activity leading reduced QCI value.

Due to its antioxidant property, CoQ10 supplementation will be helpful in reducing drip loss during meat storage. Huang *et al*. (2011) observed that supplementation with CoQ10 at 40 mg kg^{-1} diet improved breast muscle yield and reduced the drip loss in broilers. The reduction in muscle drip loss was attributed to the reduced reactive oxygen metabolites thereby, improving the cell membrane integrity and improved water retention.

COENZYME Q10 ON BLOOD PICTURE

In CoQ10 deficiency chicks and turkey pullets (Larsen *et al*., 1969) and in monkeys (Farley *et al*., 1967) supplemented CoQ4 and found maintaining a normal level of haemoglobin (Hb) and Packed Cell Volume (PCV) and in anaemic monkeys it improved the haemopoietic activity (Fitch *et al*., 1965). The CoQ10 showed hematopoietic activity by prolonged hematopoietic response in the peripheral blood and bone marrow in children having marasmus or kwashiorkor (Majaj and Folkers, 1968). However, in healthy broiler CoQ10 supplementation did not affected the PCV percent (Geng *et al*., 2004a, b; Asadi *et al*., 2013; Gopi, 2013) and also with CoQ9 supplementation (Nakamura *et al*., 1996). The Erythrocyte Osmotic Fragility (EOF %), reflects the degree of erythrocyte membrane extensibility and erythrocytes cell geometry (Gharaibeh *et al*., 1993). A lower EOF percentage indicates higher membrane extensibility and protection of the cellular structure from osmotic damage. Ubiquinol ($CoQ10H_2$) which exists mostly in blood is known to be serving as an antioxidant to erythrocyte membrane. A reduction in EOF percentage in broiler when fed with CoQ10 at 20 and 40 mg kg^{-1} of diet (Geng *et al*., 2004b; Gopi, 2013). However, this effect was more pronounced for short term feeding (0-28 days) as reported by Geng *et al*. (2004b) and at 20 mg kg^{-1} only by Gopi (2013). This variation in response was related to the age influence on the absorption and auto-oxidation of CoQ10 (Zhang *et al*., 1995) in rats. The CoQ10 supplementation did not alter the serum calcium, phosphorus and potassium levels but at 40 mg kg^{-1} of diet CoQ10 supplementation increased the serum sodium level (Gopi, 2013). This increase in the serum sodium level due to CoQ10 supplementation is attributed to the protective effect and electrolyte retention by CoQ10 on the kidney tissue (Aly, 2012). Broilers fed CoQ10 had lower blood glucose level which was reported to be due to improvement in the β-cell functions which enhances insulin sensitivity and could reduce the insulin requirement for diabetic patients (Hodgson *et al*., 2002). Low or deficient level of CoQ10 was reported in diabetes mellitus type II patients. The CoQ10 supplementation was able to reduce the blood glucose level in those patients (Ates *et al*., 2013; Mohammadi *et al*., 2013; Alam and Rahman, 2014; Shen and Pierce, 2015). The antioxidants possess the ability to restore the endoplasmic reticulum function and β-cell function preservation in diabetes induced mice (Han *et al*., 2015) which could be the reason for reduction in blood glucose level due to CoQ10. However, another hypothesis was proposed for the positive

effect of CoQ10 is the glycerol-3-phosphate dehydrogenase (G3PD) shuttle. As G3PD is the rate-limiting in mitochondria can impact β-cell function in pancreas (Giroix *et al*., 1991; Ostenson *et al*., 1993; Sener *et al*., 1993; Fernandez-Alvarez *et al*., 1994). This G3PD activity was impaired diabetes condition (type II). The increase in CoQ10 concentration in mitochondria following supplementation optimized G3PD activity in β-cell (McCarty, 1999).

COENZYME Q10 IN EGG TYPE CHICKEN AND IMMUNE SYSTEM

Very few works had been carried out with CoQ10 supplementation in egg type chicken. Dietary CoQ10 supplementation did not have any effect on egg production and feed efficiency (Kamisoyama *et al*., 2010). Hens fed diets containing CoQ10 had heavier eggs with Albumen Height (AH) and Haugh Unit (HU) remain unaffected. However, lower shell weights, density, thickness, higher occurrence of blood and meat spots were observed (Tercic *et al*., 2011). Kamisoyama *et al*. (2010) fed CoQ10 at 800 mg kg^{-1} feed to layers for 28 days and reported dietary CoQ10 decreased cholesterol concentration in the egg yolk at 21 and 28 day of the experiment. Bliznakov *et al*. (1970) found 48 h after an intravenous injection of an emulsion of CoQ10 at 750 μg rat^{-1}, the phagocytic activity in rats was highly enhanced. Bliznakov (1978) showed an increased resistance by animal models to bacterial, viral and protozoal infections and chemically-induced neoplasia. This clearly explained that administration of CoQ10 also enhanced resistance through stimulation of host defense system by increasing cellular energy availability. Hogenauer (1981), recorded macrophage potentiating activity by CoQ10 in immune suppressed mice which provided protection against lethal infections. An increase in immunoglobulin G (IgG) level was recorded by Folkers *et al*. (1982) by oral capsules of CoQ10 to cardiovascular disease, diabetes mellitus and cancer in human subjects. In broilers, Gopi (2013) reported an increase in HI titre against NewCastle Disease Virus (NDV) at 21 days of supplementation. This increase in titre value due to CoQ10 supplementation is attributed to its antioxidant activity.

CONCLUSION

The coenzyme Q10 was first discovered in 1957 but their use in poultry had gained importance only after its protective role in ascites mortality in broilers. The beneficial effects of the CoQ10 is coming out on daily basis in human subjects and it is gaining importance in poultry feeding with more emphasis is being paid to ascites and feed efficiency. However, the potential benefits of CoQ10 can be exploited as cholesterol lowering agent, immune-modulator, nutraceutical, nutrigenomic compound and in development of CoQ10 enriched meat and egg products which could offer more oral bioavailability as a lipid emulsion.

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