Review Article

"Bio Choline"- An Alternative to Synthetic Choline in Broiler Production

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Abstract

Choline is present in the feed ingredients as well as synthesized in the body of the broilers. But, this may not be sufficient to meet their requirements for physiological functions, optimum performance and lowering the body fat content. This warrants the exogenous supplementation of choline in diet. This can be done through synthetic choline chloride or through choline present in natural herbs (Bio Choline). The inimitable characteristics of Bio Choline over synthetic choline have been highlighted in this paper. Various studies that compare the performance of broilers fed on synthetic choline chloride vis-à-vis Bio Choline have also been discussed. Bio Choline has proved to be more efficacious in improving the performance of broilers in terms of growth, feed intake (FI) and feed conversion ratio (FCR). Additionally, Bio Choline reduces liver fat and body fat (abdominal fat) better than with choline chloride and thus, prevent occurrence of fatty liver syndrome (FLS) and perosis. Various discrepancies encountered in these parameters have also been discussed.

Key words: Bio Choline, Choline, Fatty Liver, Performance, Perosis

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Introduction

Choline is an essential nutrient for poultry. It participates in the formation of acetylcholine which is an important neurotransmitter (Ferguson *et al*., 2004) and helps in transmission of nerve impulse. It acts as a lipotropic agent by preventing the abnormal accumulation of fat in the liver (fatty livers), by promoting its transportation as lecithin or by increasing its utilization in the liver itself (Wen *et al*., 2014). It acts as a component of membrane phospholipids. Phosphatidylcholine is the most predominant form of phospholipid in body and is made in all nucleated cells *via* choline pathway. It accounts for 35% of the cell membrane

phospholipids and various organelles, like mitochondria and microsomes. Choline also acts as a source of "Biologically labile methyl groups" after being oxidized to betaine. Betaine can further be used to convert homocysteine to methionine *via* transmethylation pathway in the liver. The first step in endogenous choline biosynthesis is "methylation of phosphatidylethanolamine", which allows S-adenosyl-methionine to donate a methyl group and therefore spare choline in mammalian species (Ridgway, 2016). Owing to this, the nutritional requirements of choline and methionine are interdependent, *i.e*. increasing the supply of any one of these nutrients will reduce the requirement of the other. However, poultry have limited capacity to carry out this initial biosynthetic step (Selvam *et al.*, 2018). Therefore, they have higher dietary requirement of choline, especially for young chicks.

The choline is commonly supplemented in broiler diets in the form of choline chloride. However, this product has certain disadvantages as it is highly hygroscopic and may leads to oxidative loss of vitamins in the diet. In addition, this causes the formation of trimethylamine (TMA) in the gastrointestinal tract of the birds. TMA is a short-chain aliphatic amine that is formed from dietary choline in a reaction catalyzed by enzymes within the gut bacteria (Selvam *et al.*, 2018). This metabolite is present in higher concentrations in fish, and thus, responsible for the characteristic fishy odor (Esposito *et al*., 2018). In feedstuffs, choline is present as free choline or in esterified form, including phosphocholine, glycerophosphocholine, sphingomyelin, or phosphatidylcholine (Zeisel *et al*., 2003). Now-a-days, Bio Choline is produced from selected plants that contain high content of choline in esterified form. Esterification has the benefit to provide receptor recognition that improves bioavailability and reduces transformation of choline to TMA (Koujalagi *et al*., 2018). Bio Choline also contains glycerols, phosphatidyl inositol and phosphatidyl serine which play significant role in metabolism, enzymatic modulation and biosynthesis of phosphatidylcholine. Along with PUFA(s) and phospholipids, they optimize fat metabolism and efficient dispersion of liver lipids and produce significant growth response. Thus, it can be used as an important alternative to the synthetic choline chloride in broiler production. The unique features of Bio Choline over synthetic choline have been depicted in Fig.1.

Fatty liver syndrome (FLS) is a condition characterized by excessive fat deposition in the liver. It generally affects fast growing broilers fed with high energy diets and caged layers with an inability to move and exercise freely (Jiang *et al*., 2013). It occurs due to deficiency of methyl group donors in the feed and decreased gluconeogenesis in the liver due to deficiency of biotin in commercial chicken (Jiang *et al*., 2013). Death may occur due to insufficient levels of the key biotin-dependent enzyme "pyruvate carboxylase". Now-a-days, broilers are fed with high energy diet for faster gain in body weight.

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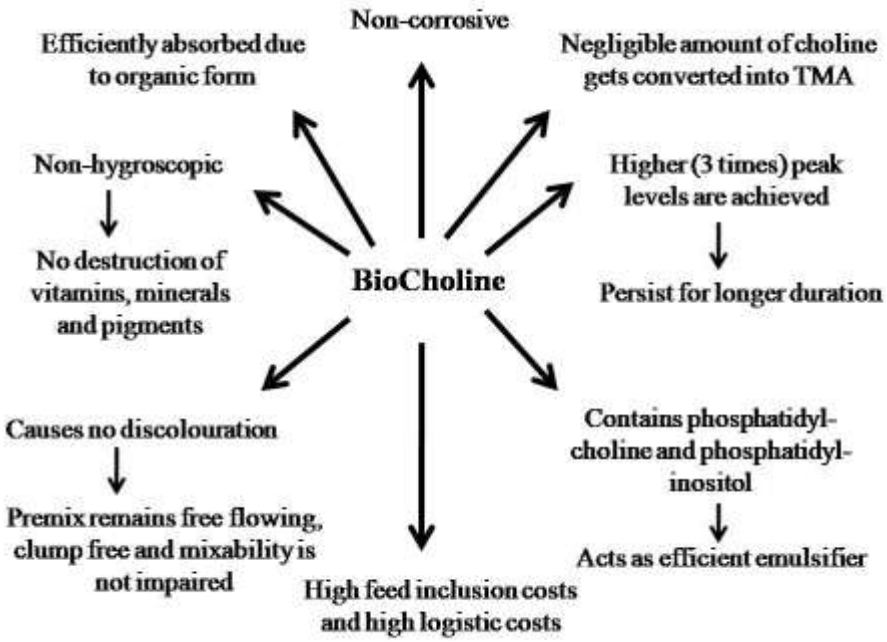

Fig. 1: Advantages of Bio Choline over synthetic choline

This high energy gets converted into fatty acids which require labile methyl groups and dietary emulsifier for digestion and metabolization of lipids. Therefore, the inclusion of choline and biotin in broiler diets is essential. Various studies have revealed that dietary supplementation of Bio Choline is effective in reducing the adverse metabolic consequences of a high energy diet in broiler chicken (Leeson and Summers, 2005). Many researchers have indicated that herbal Bio Choline can replace choline chloride in diets for poultry (Chen *et al*., 2007; Gangane *et al*., 2010). However, metabolic effect of Bio Choline varies according to the dietary composition and metabolic status of the broilers as well as environmental conditions (Azadmanesh and Jahanian, 2014). The main objective of this paper is to discuss the importance of BioCholine over synthetic choline in broiler production.

Mechanism of Action

BioCholine is a unique herbal animal feed supplement that contains non-toxic, natural, stable and highly bioavailable choline in conjugated/esterified form (Phosphatidyl choline, lecithin and equivalents) along with the phospholipids and PUFA(s) (Koujalagi *et al*., 2018). The chemical structure of esterified/conjugated choline of BioCholine resembles with that of synthetic choline. The natural choline conjugates present in BioCholine enters into the biological system and release highly labile methyl groups at the site of action. The labile methyl groups of BioCholine help in energy metabolization and control of fatty liver syndrome.

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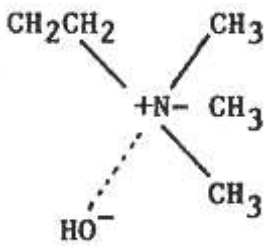
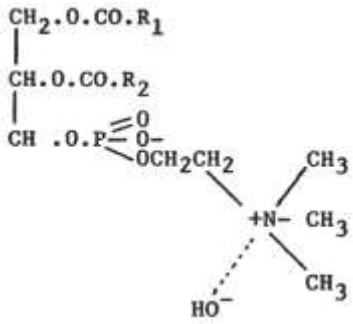


Inorganic Choline



Conjugated Choline

Furthermore, unlike synthetic choline chloride, natural choline conjugates have been reported to promote hepatic expression of the genes encoding mallic enzyme, fatty acid synthase, acetyl-CoA carboxylase, sterol regulatory element binding protein, stearoyl-CoA ($^{\Delta}9$) desaturase 1 and liver fatty acid binding protein (L-FABP) and thereby regulate fat metabolism of broilers.

Molecular Mechanism of Action

The peroxisome proliferator-activated receptors (PPARs) are a group of nuclear receptor proteins that plays an essential role in the regulating cellular differentiation, development and metabolism (Grygiel-Górniak, 2014). There are several types of PPAR receptors i.e. PPAR-α, PPAR-γ and PPAR-δ, each with the specific function. The PPAR-α has implication in fatty acid metabolism and its activation lowers lipid levels (Neschen *et al*., 2007). Besides PPAR-γ and PPAR-δ are also engaged in energy metabolism and lipolysis (Medina-Gomez *et al*., 2007; Sertznig *et al*., 2007). Among these PPAR receptors, PPAR-δ is the least known form that participates in fatty acid oxidation, mainly in skeletal and cardiac muscles (Stephen *et al*., 2004). The BioCholine contains small quantity of phosphatidyl choline and phospholipids that causes the activation of these PPAR receptors and thus, initiates secretion of adiponectin (Berger and Moller, 2002). Adiponectin is a protein hormone that modulates fat, glucose and fatty acid metabolism. Its level is inversely related with body fat percentage as it increases lipolysis and reduced uptake of FFA in the liver and increase their clearance from liver. In this way, BioCholine prevents FLS and keep the level of liver lipids low in broilers.

Effects on Broiler Performance

Several studies have been done to evaluate the effect of BioCholine on the performance of broilers. However, some controversial results have been obtained in broiler depending on source of BioCholine, dietary composition, bird's metabolic status as well as environmental conditions. The nutritional requirements of choline in broilers are based on studies conducted about decades ago, and therefore, they

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need to be updated due significant changes in diet formulation and bird performance since then. Changes in the genetic potential should also be taken into consideration when comparing the nutritional requirements of broilers. The requirement of the choline increases after third week of age in broilers due to higher lean growth during this period (Viola *et al*., 2008). The supplementation of choline at the level of 1000 mg/kg leads to improvement in the FCR and breast yield but, without significant effect on weight Gain (WG) and the carcass yield (Waldroup *et al*., 2006). This was consistent with the study of Pompeu *et al*. (2011), who observed improvement in FCR at 21 days, with linear response for this variable with choline supplementation up to 400 mg/kg in a basal diet containing 1367 mg/kg of choline. Contrary to these findings, Swain and Johri (2011) did not observe any effect of choline supplementation on the performance of broilers at 42 days.

Bioequivalence of BioCholine and Synthetic Choline

The bioavailability and utilization of different choline esters varies, which elucidate the higher efficiency of phosphatidylcholine. The choline in the form of chloride gets transformed trimethylamine by the intestinal bacteria, and immediately excreted (Craciun and Balskus, 2012). On the other hand, there is no or low degradation of phosphatidylcholine in the gastrointestinal tract. The phosphatidylcholine has an indirect emulsifying role in fat digestion. This has been attributed to their ability to increase the bile juice flow, phosphatidylcholine content in the bile juice, and bile cholesterol content (LeBlanc *et al*., 1998). Additionally, Khosravinia *et al*. (2015), reported improvement in body weight and ADG in the broilers fed with BioCholine due to efficient carbohydrate and fat metabolism. However, it had no significant effect on FI and FCR. Increased weight gain with no change in FI and minute improvements in FCR suggest that BioCholine may improve energy utilization (efficient carbohydrate and fat metabolism) in the diet. In contrast, Waldroup *et al*. (2006) observed marginal improvement in FI in birds supplemented with BioCholine. This improvement may occurs due to its medicinal plants ingredients containing a broad spectrum of vitamins, acids and alkaloids and many other active compounds that increases bile flow and improves feed intake.

The vegetal source of choline acts as a replacement of choline chloride in the diet of broilers (Calderano *et al*., 2015). This was consistent with the findings of Kumar (2009) and Dematt̂ Filho *et al*. (2015) that weight gain, FI, FCR and viability of broiler chickens were similar when replacing the choline chloride by a vegetal source of choline in the diets. Although, some studies reported an improvement in weight gain and FCR of birds supplemented with vegetal source of choline (Yu, 2009; Pompeu *et al*., 2011). But, substitution of DL-methionine 99% by a vegetal source of methionine resulted in worse performance of broilers (Dematt̂ Filho *et al*., 2015). This occurs due to lower absorption of plant methionine source used as compared to synthetic methionine. However, some controversial results have been obtained by various

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researchers regarding the effect of choline chloride on birds' performance (Devegowda *et al*., 2011). These variations may occur due to the methionine level in the experimental diets. deSouzaReis *et al*. (2012) stated that there is no need for adding choline to the diet containing methionine and cystine at more than 0.91%. This was supported by the fact that endogenous synthesis of choline in the liver by donating methyl groups by methionine.

Recently, study has been conducted to evaluate the bioequivalence of BioCholine as an alternative to choline chloride in broilers (Farina *et al.*, 2017). They observed that BioCholine improves FCR and reduces feed intake, indicating better dietary fat absorption. This was consistent with the study of Waldroup *et al*. (2006). However, some studies did not find any effect of choline supplementation on FCR (Hassan *et al*., 2005; Calderano *et al*., 2015). These discrepancies may occur due to difference in the level of sulfur amino acid in diet because choline did not affect FCR only in studies where diets contained high levels of these amino acids.

Effects on Occurrence of FLS and Perosis

Fatty liver occurs due to lack of methyl groups in the diet, and not only by choline deficiency. Biotin and choline play an essential role in the transportation of lipids from liver towards the peripheral tissues and organs in the form of lipoproteins, indicating their ability to reduce liver fat (Jahanian and Rahmani, 2008). This was further supported by Waldroup *et al*. (2006), that choline deficiency in quails increases liver fat and later on, supplementing choline to their diet decreased liver fat percentage. The incorporation of BioCholine in the diet of broilers leads to efficient carbohydrate and lipid metabolism (Cengiz *et al*., 2012; Khosravinia *et al*., 2015). Contrary to these findings, Farina *et al*. (2017) reported no effect on liver fat percentage among broilers fed with different sources of choline. It could be due to adequate supply of methyl groups from their diet that contained adequate methionine levels, and due to the dietary inclusion of soybean meal and corn gluten, which contains S-methylmethionine (SMM) that is analogous to S-adenosylmethionine (Augspurger *et al*., 2005).

Perosis or chondrodystrophy mostly occurs in young birds whose diet is deficient in manganese (Mn) or some vitamins like choline, nicotinic acid, pyridoxine, biotin or folic acid. The studies related to the effect of choline on perosis shows contradictory results. According to Fritz *et al*. (1967), 1900 mg choline/kg of diet is required to prevent that disorder. On the other hand, some studies demonstrated that even lower level can dramatically reduce perosis in broilers (Ryu *et al*., 1995). Dietary choline levels of 304 mg/kg in the starter phase, 249 mg/kg in the grower phase, and 243 mg/kg in the finisher phase do not cause fatty liver or perosis in broilers (Farina *et al*., 2017). In addition to the nutrient deficiency, other factors like method of rearing may influence the incidence of perosis in broilers.

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Conclusion

The emergence of herbal choline and the possibility to adding vegetable sources of choline to broiler diets is a novel approach. This development makes organic poultry production more attractive to the farmers and more accessible to the human population. The replacement of synthetic choline by BioCholine improves production efficiency and reduces the need for incorporating costly protein sources in feeding strategies. Thus, it economize the production costs of broilers.

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