Choline as an Essential Feed Supplement

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Abstract

Feed formulation technique, component content, and nutrient requirements, based on the needs and developmental stages of animals, significantly influence the efficiency and well-being of ruminants. Disease may result from an excessive or unbalanced quantity of nutrients or constituents. Choline, a rediscovery of vitamin B_4 that is usually found in phospholipids, is essential for a number of biological processes in cows and chickens. It is a quaternary amine that plays a number of crucial metabolic roles, such as methyl group production for biosynthesis, cell signaling, and lipid metabolism. Choline can be synthesized *de novo*, however this is insufficient to fulfil needs. Choline must be obtained by food. Phospholipid production is one of the essential biological processes that choline supports. It is a donor of methyl groups, acetylcholine, and intracellular messenger molecules. Commercial feeds supplemented with choline chloride at amounts deemed safe for the intended animals. Nonetheless, there is a little margin of safety when compared to the usage level in pigs and poultry.

Keywords: Broiler; Dairy; Fatty liver; Feed conversion ratio; Phosphatidylcholine; Rumen-protected choline.

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Introduction

Choline

Ox bile, or "chole" in Greek, was the source of the first isolation of choline ($C_5H_{14}NO^+$). Adolph Strecker made the discovery in 1864, and in 1866, it was chemically synthesised. He deduced that the platinum salt of material derived from ox and pig gall was an ammonium base. Wurtz was the first to create choline chemically by heating trimethylamine and ethylene oxide in an acidic environment. Choline's most notable structural characteristic is its physiologically active methyl groups, which enable it to function as a labile methyl donor and play a crucial part in the oxidation of homo-cysteine to betaine, which then forms methionine (Gregg et al., 2022).

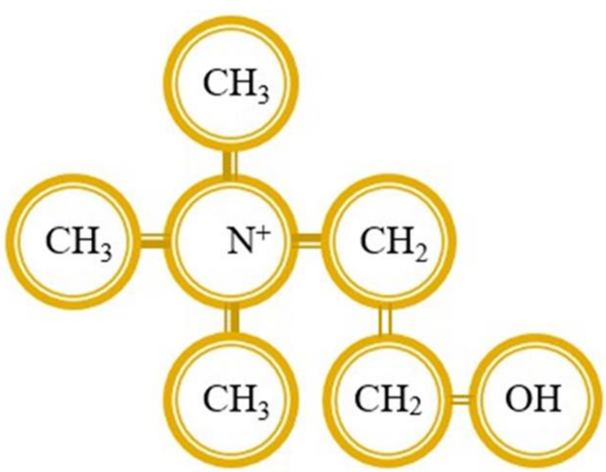

Fig. 1: Choline Structure made in powerpoint

The methyl group of choline in poultry is accessible following its hepatic conversion to betaine. One micronutrient that dissolves in water is choline. It is occasionally categorized as a natural chemical and placed in the vitamin B group. However, because of its high nutritional content, it is regarded as an important nutrient and has nothing to do with vitamins (Alagawany et al., 2016). Trimethylamine 2-hydroxyethyl, a quaternary ammonium base, is resilient to prolonged heating and is soluble in alcohol and water but insoluble in ether and chloroform (Figure 1). Since the body synthesises choline, it is not a vitamin. It is a component of acetylcholine, a nervous system neurotransmitter, and complex lipids found in cell membranes, including phosphatidylcholine (PC) and sphingomyelin (Blanco & Blanco, 2017).

Choline has three vital metabolic functions: first, it is a component of phospholipids; second, it prevents fatty liver; and third, it is a precursor to the creation of acetylcholine. In addition to its non-essential metabolic roles as a interchangeable methyl group, choline also helps broiler chicks avoid perosis and fatty liver disease. Regarding the methylation function, betaine can be used in substitution of choline in growing hens, however it cannot take the place of choline in preventing perosis.

Choline is frequently added as choline chloride to broiler diets because of its significance. However, because it raises the amount of free water in the mixture, which raises the reactive potential, this substance is extremely hygroscopic and may cause the loss of water-soluble vitamins added to premixes. Additionally, because the end product may form lumps, this leads to operational issues in the feed mill (Farina et al., 2017).

Requirement

Conflicting findings have been found in the literature on the effects of adding more choline to diets based on maize and soy bean meal on the developmental efficiency of broilers. Additional dietary choline was found to both decrease feed intake and enhance feed conversion ratio (FCR) when Met was administered at sufficient doses. It also increased feed consumption without changing FCR. Dietary choline lower than the required level significantly lowers feed intake and growth, as shown by (De Lima et al., 2018).

According to the National Research Council's guideline, broilers need 1,472 mg/kg of choline for weight increase and 1,424 mg/kg for feed consumption throughout the starter and finisher phases, respectively. According to the most recent authors, there was no discernible impact of adding 100 mg/kg of choline to the diet on the weight distribution of albumin and yolk, egg size, or egg output. Growth characteristics were enhanced when broiler diets were supplemented with 0.4% choline. According to a different research by (Emmert & Baker, 1997) adding 2000 mg/kg of choline chloride to grill meals had a beneficial impact on the chicks' body weight increase. Methionine, a sulphur amino acid, is essential for reproduction as well as for the development, metabolism, and repair of all tissues. Given its association to choline deficiency as a methyl donor and alternately, the amount of methionine in an animal's diet is significant. Although choline supplements can be taken in along with methionine, they won't replace the essential methionine needed for protein synthesis if the diet doesn't provide homo cystine (Ross et al., 2013).

Since it is usually impossible to cause a choline shortage in birds older than eight weeks, the choline requirement of developing chicks decreases with age. (Igwe et al., 2015) noted that the rate-limiting step in the production of choline for young birds appears to be the methylation of aminoethanol to methylaminoethanol.

Sources

The symptoms of choline shortage in commercial broilers seem to be uncommon since soybean meal, a prominent feed ingredient for broiler chickens, provides an excellent supply of bioavailable choline. It gives seafood its distinctive smell and is present in fish in high proportions.

The herbal choline (Ch)-based products on the market are polyherbal mixtures that have a variety of effects on animal health, such as nephroprotective, antioxidant, antiparasitic, antimicrobial, and anti-inflammatory qualities. They also contain betaine or significant choline sources in the form of phosphatidylcholine and phosphatidylserine (Baldissera et al., 2019). According to reports, methionine, which is not broken down in the rumen, and rumen-protected choline (RPC) may work together as bioactive substances to shield ruminants against illnesses, particularly those that affect them during the peripartum (Zhou et al., 2016). Choline and methionine polyherbal mixes have been assessed and categorised as nutrients having nutraceutical qualities (Mendoza et al., 2020). In the RPC, the chelated minerals are absorbed intact in the intestine after passing through the rumen; at the site of utilisation, the chelates that accomplish blood plasma are released undamaged (Panel, 2011). The hypothesis of this study was that choline and chelated mineral supplementation enhances productive performance in sheep without harming the environment or ruminal microbes (Ley-de Coss et al., 2024).

Lower dietary concentrations of rumen non-degradable choline chloride have been shown to enhance feed breakdown and daily weight gain (DWG) in beef cattle and goats (Habeeb et al., 2017). By transferring non-esterified fatty acids (NEFA) from the liver to other tissues, RPC most likely preserved liver function. It is crucial to keep in mind that herbal additions are plant combinations or certain plant parts that have the largest concentration of physiologically active compounds that affect ruminal fermentation and improve output. For example, it has been demonstrated that herbal combinations containing phosphatidylcholine work in concert with methionine to enhance the health and productivity of dairy cows (Mendoza et al., 2020). It has been demonstrated that synergy with methionine enhances dairy cow health and productivity. Furthermore, natural products possess antioxidant activity that improves animal health and productive development, inhibits bacterial growth, modifies metabolic pathways, and enables the prevention and treatment of illnesses (Kholif & Olafadehan, 2021). Additionally, it has been shown that the rumen's microbial community breaks down dietary choline, suggesting that the dosage should be increased. Nonetheless, the application of secured choline to dairy cattle has demonstrated a favourable impact on milk output (Liu et al., 2019).

Deficiency

Choline deficiency causes perosis and growth retardation among young poultry. The main clinical symptom of choline shortage in chicks and turkeys is perosis, however bob white quail exhibit bent legs and swollen hocks. Pinpoint haemorrhages surrounding the hock joint are the initial sign of perosis, which is followed by an evident flattening of the tibiometatarsal joint. The bird becomes comparatively motionless when the Achilles tendon gradually separates from its condyles. According to certain research, choline is necessary for the phospholipids essential for the proper development of the bone's cartilage matrix, which helps avoid perosis. It's likely that adult hens produce enough choline to fulfil their needs for producing eggs (Pour et al., 2014).

Choline Metabolism

Lecithin hydrolysis in the intestinal lumen is linked to choline. Lecithin in the diet can be hydrolysed by enzymes found in intestinal mucosal cells and pancreatic secretions. The ileum and jejunum absorb choline mostly through a carrier mechanism that is reliant on salt and energy (Lu et al., 2023). Choline was absorbed by ileal cells in the guinea pig almost three times more quickly compared to jejunal cells. The transport system's preferred placement in ileal cells confirms previous findings in hamster and rat cells.

Choline that has been absorbed is mainly carried through the lymphatic circulation as lecithin attached to chylomicra; plasma lipoproteins mainly carry it to the tissues as phospholipids. All tissues contain choline, which is an essential part of phospholipids found in all kinds of membranes. Choline is accumulated by all tissues, although the liver, kidney, mammary gland, placenta, and brain absorb it most crucially. Mammary cells' absorption of choline allows this tissue to isolate choline about 70 times more than maternal blood. Through the successive methylation of phosphatidyl ethanolamine by phosphatidyl ethanolamine-N-methyltransferase, the majority of species are able to synthesise choline, as lecithin. Enzymes that employ S-adenosylmethionine (SAM) as the methyl donor are truly responsible for this action. Male rats exhibit modest choline synthesis activity, whereas chicks do not exhibit it until about 13th week of life (Holdorf et al., 2023).

Choline and Fatty Liver

By reducing fatty acid production, a sufficient dose of choline enhances mitochondrial energy metabolism and lipid metabolism. Because a lack of choline hinders the integration of FAs in phosphatidylcholine (PC), it increases their availability for the production of triacylglycerol (TAG) and diacylglycerol (DAG), which favours the buildup of TAG in muscle cells. Choline affects fat metabolism by regulating the expression of genes related to intracellular transport of fat and FA generation (acetyle CoA carboxylase and fatty acid synthase) (Moretti et al., 2020). Choline shortage resulted in liver fattening and hepatocyte loss in some experimental animal models, heart-related illnesses, anomalies in bone formation, and altered kidney functioning (Biswas & Giri, 2015).

The negative metabolic effects of the high-calorie diet in chicken farming are reduced when herb and lipotropic supplements are added to the feed (Saeed et al., 2017). To lessen the liver fattening syndrome, Lcarnitine, vitamin B12, and vitamin E are therefore frequently given to the poultry diet. The study by Jiang et al. (2014) shown that grill cholesterol may be decreased by choline chloride. Fatty liver disease is a metabolic disease that is commonly found in the poultry business these days, particularly in chickens raised in cage farming systems. because caged birds are unable to move sufficiently to expend the calories they consume.

Rats given diets lacking in choline showed a significant rise in hepatic TAG buildup. Hepatic production and secretion of VLDL depend on the dynamic synthesis of phosphatidylcholine (PC), which is obtained from choline (Zenobi et al., 2020). Choline condensation with diacylglycerol and phosphatidylethanolamine methylation using S-adenosylmethionine as a methyl donor are the two processes for PC production. It has been hypothesised that ruminant species may be choline insufficient and hence more prone to fatty liver due to the widespread choline breakdown by the rumen microbial community. it is believe that giving ruminants choline supplements would provide a sufficient supply of choline and spare methyl donors like methionine, which would improve PC synthesis and apolipoprotein assembly. However, feeding rumen-protected choline is the sole efficient method of increasing choline flow to ruminant intestines (Cooke et al., 2007).

Due to a negative nutritional balance, dairy cows in the early stages of lactation mobilise their bodily reserves, mostly adipose but also muscular tissue. The periparturient period's mobilisation of adipose tissue raises blood fatty acid concentrations, which frequently results in the onset of fatty liver. (Arshad & Santos, 2022) demonstrated that in nursing dairy cows, hepatic lipidosis above 4% to 7% triacylglycerol on a moist tissue base was linked to decreased survival, health, and productive performance. Interventions like dietary changes to treat or mitigate hepatic lipidosis are therefore desirable since they may lower the likelihood of fatty liver while simultaneously improving dairy cow health and productivity. Since rumen-protected choline works well, dietary choline is a dietary intervention to reduce the risk of fat influx into the liver.

Up to 50% of dairy cows may develop mild to serious fatty liver as a result of the widespread breakdown of fat depots caused by unfavorable nutritional balance in the latter weeks of pregnancy and the initial weeks of lactation. Because the bovine liver exports lipoproteins slowly, it is believed that fatty liver in periparturient dairy cows is caused by the liver's considerable intake of fatty acids and subsequent reesterification to triacylglycerols. Hepatic fatty acid extraction increased significantly from 19 days before to calving to 11 days post-calving, a difference of around 2.28 mol/d (Reynolds et al., 2003). This rise most likely results from the alteration in lipolysis that occurs when lactation begins, which puts cows at risk for fatty liver. The levels of choline and its byproducts in plasma are at their lowest during the first weeks of lactation, when cows experience negative nutrient balance (Imhasly et al., 2015). In prepartum cows, supplementing with rumen-protected choline (RPC) raised plasma concentrations of choline metabolites (Brown et al., 2023). Enhancing prepartum choline level may lower the probability of fatty liver and enhance postpartum health and breastfeeding efficiency (Arshad et al., 2020).

Choline and Brain Function

The bio-availability of choline in the diet affects both general health and the cognitive processes in the brain. Because the precursor of acetylcholine influences cholinergic neurotransmission and contributes to epigenetic modifications through methyl metabolism through betaine and homocysteine reduction, it plays a part of sustaining cell membranes and myelination during the formation of phospholipids. Specifically, the frontoparietal cortex's attentional regulation and the hippocampus's memory functions are influenced by the basal forebrain cholinergic system (Solari & Hangya, 2018). Additionally, tasks connected to anxiety include cholinergic neurotransmission in the amygdala (Sharp, 2019). Its impact on brain acetylcholine levels has been linked to various cognitive processes mediated by multiple brain regions (amygdala, hippocampus, prefrontal cortex, etc.) and brain circuits, in addition to its function in cell membrane maintenance and epigenetic processes (Gámiz & Gallo, 2021).

Glycerophosphocholine (GPC) therapy for an extended period of time in old rats increased the total amount of muscarinic M1 receptors to levels seen in the striatum and hippocampus of young rats. GPC dramatically increased K^+-stimulated intra-synaptosomal Ca^{2+} oscillations in pure synaptosomes obtained from the hippocampus in young but not elderly rats. In male rat hippocampus, cortical, and striatal slices, repeated injections of GPC markedly enhanced the basal production of [3H]inositol monophosphate. In cortical synapto-neurosomes, GPC consistently enhanced receptor-stimulated phosphatidylinositol hydrolysis. GPC reduced the cell death program's execution and improved neurones' resistance to ischaemic damage in a rat model of acute cerebral ischaemia. In vitro tests in astroglial cell cultures have demonstrated that GPC promotes proliferation, which is in line with these findings (Kansakar et al., 2023).

Heat Stress in Poultry

The broiler sector frequently deals with heat stress, especially in the summer. Heat stress can change carcass features, raise mortality, and have a detrimental effect on growth performance (Liu et al., 2020). Because betaine has osmoregulatory properties that can assist reduce cellular dehydration, it is believed to offer protection against heat stress. Betaine can be immediately oxidised from choline. The effects of substituting choline and betaine for dietary Methionine in Ross 308 broilers subjected to heat stress were assessed by Mahmoudi et al. (2018). These authors suggested that choline and betaine can be used in place of Met in heat-stressed broilers since they found no changes in the average daily feed intake or body weight increase between birds given either choline, betaine, or an amalgamation of the two. Although it has been noted that adding betaine to broiler diets is more effective than adding choline at raising betaine concentrations in the liver, where choline is metabolized to betaine, Gregg et al. (2023) found that broilers fed diets complemented with either betaine or choline had comparable plasma betaine concentrations. This implies that since both choline and betaine increase the amount of betaine in the blood, they may have similar metabolic advantages.

Choline and Other Nutrients

For animals, choline is a necessary nutrient in the absence of extra methionine and folate in the diet. Transmethylation processes and dietary choline can both satisfy the choline requirement. Choline is recognised to have two different kinds of functions: those of choline itself and those of a methyl donor. S-adenosyl-methionine, a metabolite of methionine, and betaine, a metabolite of choline, are the two main methyl donors in animal metabolism (Selvam et al., 2018). Regarding their roles in methyl group supplying, choline and methionine are equivalent. Because choline is heavily broken down in the rumen of adult ruminants, dietary choline makes up a negligible portion of the choline body pool. Additionally, methyl group metabolism is typically conservative, with a high rate of completely novel methyl group synthesis through the tetrahydrofolate system and a relatively low rate of methyl catabolism. Choline is still not readily available in the diet of dairy ruminants, but milk produces a lot of methylated substances, and the tetrahydrofolate pathway's precursors are limited, particularly when lactation starts. Choline may therefore be a limiting component for high-yielding dairy cows' ability to produce milk (Pinotti et al., 2002).

Conclusion

Rumen-protected choline (RPC), a choline supplement for ruminants, has been shown to increase immunological function, postpartum DMI, milk supply, and milk energy output, as well as decrease hepatic triglyceride buildup. The mobilisation of liver fat in the nature of lipoproteins into extra-hepatic tissues, where they may be deposited or metabolised, is caused by the well-known lipotropic factor choline. Better growth, an improved FCR, and a lower lipid content in the liver, abdomen, and carcass are the results of this process, which redirects excess fat energy in the direction of muscle protein amplification rather than body fat synthesis.

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