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Betaine plays many roles in broiler diets

Betaine has many important functions in the health and performance of broiler chickens, especially under conditions of heat stress.

Betaine is a trimethyl derivative found in living organisms in deserts and low rainfall areas. It acts as an osmolyte to help maintain cellular water balance and as a methyl donor through methionine recycling. Increased water retention due to the osmolytic effect of betaine increases the volume of the cell, thereby increase the anabolic activity, integrity of cell membrane and overall performance of the bird.

The osmolytic property of betaine permits cellular adaptation to adverse osmotic environments noticed in hot and humid climates. Vertebrates, including poultry, have limited ability to synthesise betaine in sufficient quantity. In plants, it is synthesised and accumulated to protect against salt and temperature stress.

In practical poultry nutrition, betaine can play a role in improving performance and carcass composition, reducing litter moisture as well as helping to overcome coccidiosis and stress.

Metabolism and functions

Betaine in the purified form is absorbed by the mid-jejunum in chicks. Absorption of betaine is more rapid than choline or methionine. Choline and methionine are associated with plasma lipoprotein, whereas betaine remains in a free state in the plasma. Choline must be transported from the cytosol into the mitochondria where it is oxidised to betaine, which is transported to the cytosol. However, the efficiency of converting choline to betaine is reduced by polyether ionophore anticoccidials by interfering with mitochondrial membrane transport of the compound. The methyl group from betaine can be transferred to homocysteine to yield methionine via betaine-homocysteine methyl transferase. However, this reaction does not supply additional methionine to the cell, as the homocysteine is synthesised from methionine.

Betaine acts as a methyl donor and an osmolytes that assists in cellular water homeostasis. Dietary supplementation of betaine may decrease the requirement of methyl donors like methionine and choline. Betaine contributes methyl groups for the synthesis of carnitine via S-adenosyl methionine. Carnitine is required for transport of long-chain fatty acids across the mitochondrial membrane for oxidation. Betaine increases the concentration of S-adenosyl methionine and homocysteine in liver, which facilitates in-vivo methionine synthesis by utilising methyl groups from a single carbon pool. In chicks, betaine donates a methyl group (CH₃) to homocysteine for the synthesis of methionine approximately three times more efficiently than choline. However, adequate concentration of cysteine is required to achieve the beneficial effects of betaine supplementation. Inadequate dietary concentration of cysteine may affect the activity of betaine by reducing the concentrations of homocysteine for methionine formation.

The osmo-protective property of betaine may be due to the dipolar zwitterions and its high solubility in water. Osmolytes are important during cellular dehydration. Betaine minimises water loss from cells against a prevailing osmotic gradient between cell and its surrounding environment. Betaine accumulation results in an increased water-binding capacity of the intestinal cells and it promotes changes in the structure of the gut epithelium that increase gut surface area. Betaine

stimulates cell proliferation in the intestinal tissue, particularly the mucosal membrane. The enlarged gut wall epithelium may increase the surface for nutrient absorption. Reduced gut pH and intestinal villi height with betaine (hydrochloride) supplementation in the stomach may improve the digestibility of methionine and other nutrients.

Nutrient utilisation

Betaine was reported to improve apparent digestibility of lysine, protein, fat and carotenoids and in-vitro methionine uptake in broilers challenged with coccidia. Improved cell integrity and surface area of gastrointestinal lumen with betaine supplementation appeared to enhance the digestibility of dietary nutrients. Dietary supplementation of betaine increased the activities of several hormones in serum such as luteinising hormone, follicle stimulating hormone, triiodo-thyronine, thyroxine, oestradiol and progesterone in laying hens. Increased activities of the hormones and mucosal surface area and cell integrity might have led the cell to an anabolic state and helped in cell multiplication and metabolic activity. Improved surface area and vitality of gut mucosa might have increased secretion of digestive enzymes and absorptive area in the intestine.

Methyl donor activity

Betaine contains three methyl groups in its structure and donates these in several metabolic reactions. As a result, betaine can spare compounds such as methionine, choline and folic acid, thus betaine supplementation may reduce the need for supplementation of these nutrients. On a molecular weight basis, betaine contains about 3.75 and 0.90 times the methyl groups of methionine and choline, respectively. The first methyl group is donated to homocysteine in its enzyme-induced conversion to methionine in the liver. The other two-methyl groups are supplied to one-carbon pool, which will be handled by folic acid. Methyl tetra hydrofolate can also donate methyl group to homocysteine for methionine synthesis.

Osmolytic activity

Betaine functions as an osmolyte by most body tissues, including the liver. It helps to maintain osmotic equilibrium in small intestine epithelium by maintaining water balance in hyper-osmotic conditions like non-specific diarrhoea and coccidiosis. Under heat stress and dehydration, sodium ions (Na⁺) will be moved from the cellular fluid in to the cell. The higher the concentration of Na⁺, the greater is the inhibition of nutrient uptake by the cell. Higher concentrations of potassium (K⁺), magnesium and phosphorus within the cell also inhibit the activity of enzymes necessary for metabolism of nutrients.

To maintain normal enzyme activity, function and volume, cells raise the intracellular concentrations 'organic osmolytes' such as methyl amines, choline and betaine. In birds, myo-inositol, betaine and taurine are also major physiological organic osmolytes. Betaine prevents dehydration by increasing water-holding capacity of the cell. Utilisation of betaine as an osmolyte is more beneficial than inorganic electrolytes in terms of energy expenditure in osmo-regulation and compatibility with the cell organelles. The stability of mucosal cell structure increased and the movement of water from the mucosal cell decreased even at higher osmotic pressure in the gut lumen of birds fed a betaine-supplemented diet.

Betaine supplementation also reduces the energy required for osmoregulation by reducing the activity of the 'Na/K' and 'calcium pump' by 64 and 73%, respectively. This primarily uses adenine triphosphate (ATP) as an energy source.

The concentration of electrolytes increases within the cell under dehydration. To regulate the desired concentration of water within the cell, K⁺ is pushed in to the cell against concentration gradient. To pump any ion against concentration gradient, one molecule of ATP is required. Higher concentrations of electrolytes in the cell are known to inactivate enzymes and proteins. The higher concentrations of the electrolytes bind with active sites of enzymes and thereby deactivate them. Movement of betaine across the cell membrane does not require energy and will not interfere with cell ecosystem or cell metabolism. Betaine in feed or drinking water can control osmoregulatory conditions including diarrhoea, catharsis, diuresis and ascites.

Improved performance

The influence of betaine supplementation on performance of broilers primarily depends on the concentrations of other labile methyl groups in diet and magnitude of stress to the bird. Betaine supplementation was ineffective in influencing the bird's performance in diets with either adequate or severe deficiency of methionine. However, improvement in

bodyweight, breast meat yield, feed conversion and decreased abdominal fat pad weights with betaine supplementation have been reported. The results of our recent study indicate significant improvement in feed efficiency in broilers fed betaine (800mg/kg) either sub-optimal concentrations of methionine compared to those fed no betaine, irrespective of the concentration of the amino acid.

Reducing litter moisture

During intestinal stress conditions (including diarrhoea), the absorption of Na⁺ and chloride ions (Cl⁻) decreased through the intestinal villus membrane. This results in hyperosmolar solution in the intestinal lumen. Betaine supplementation increases intestinal mucosal cell integrity and allows the cells to function normally. This helps to optimise nutrient digestibility and reduce their excretion. Litter moisture content reduced at 6 days from 46 to 27% after feeding betaine in water (2.5g/litre). The dose of betaine to control diarrhoea in poult was 0.15-1.5g/kg bodyweight. Betaine is also reported to influence positively water balance in broilers exposed to coccidia and to reduce faecal moisture content.

Better carcass characteristics

Betaine has methionine-sparing activity and is involved in synthesis of carnitine. Thus, it has a role in protein and fat metabolism, respectively, and can alter carcass composition. Betaine reduces protein turnover, which results in higher nitrogen retention, which in turn has a positive effect on accretion of protein in muscle (carcass leanness). Betaine enhances lipid catabolism via its role in carnitine synthesis and leads to low carcass fat deposition.

The effect of betaine on abdominal fat deposition and carcass yields is inconsistent, depending on many other dietary factors.

Our recent data indicate significant improvement in breast meat yield with betaine supplementation (800mg/kg) to diets containing different concentrations of methionine compared without betaine supplementation, irrespective of methionine concentration. At higher concentrations of methionine (2.4% of crude protein), betaine had no effect on breast meat yield of commercial broilers.

Controlling coccidiosis

Effects of betaine as an osmolyte are clear when exposed to gut osmotic disorders. Coccidiosis decreases villus height and jejunal crypt:villus ratio, and increases the osmolarity in duodenum. The beneficial effects of betaine on birds infected with coccidiosis may be due to its osmolytic activity as well as increased phagocytic activity in the gut mucous membrane. Betaine (0.1%) decreased the osmolarity of duodenum and increased the number of leukocytes in the epithelium and lamina propria of chicks with coccidia infection. Betaine increased phagocytosis of coccidia by macrophages and nitric oxide release from heterophils and macrophages.

The efficacy of certain anticoccidial compounds can be modulated by dietary betaine supplementation. Growth of *Eimeria acervulina* was reduced in chicks fed diets containing betaine (0.075%) plus salinomycin (66mg/kg) compared to those fed salinomycin only. Other anticoccidials like polyether ionophores interfere with conversion of choline to betaine.

Counteracting stress

Stress leads to release of more number of reactive oxygen species (ROS) in the system. These impair the cell structure, membrane integrity and ion pump in the gut lumen. Cell dehydration leads to disturbances in cell metabolism and its enzyme activities. Feed intake leads to movement of intracellular water in to the gut lumen, which causes shrinkage of the gut mucosal epithelium. Disturbance in cell structure impairs nutrient absorption, cell membrane transport and certain intracellular metabolic processes (metabolism of amino acid, ammonia, carbohydrates and fatty acids). In extreme circumstances, mucosal cell shrinkage may leads to disruption of intestinal mucosal integrity, which may permit the entry of pathogens and toxins in to the blood.

Betaine increases cytoplasmic osmotic pressure in stressed cells and tolerance to temperature and ionic disturbance. Accumulation of conventional osmolytes like K⁺ in the cell may lead to disturbance in activity of cell enzymes. Accumulation of betaine protects the cells from osmotic stress and allows them to continue normal metabolic activities

under stress conditions that would otherwise inactivate the cell. Betaine supplementation during heat stress reduces the heterophil:lymphocyte ratio, which is an indicator of stress in poultry.

Dose

The concentration of betaine required to supplement a broiler diet largely depends on the concentration of other labile methyl groups (methionine, choline, folic acid), environmental temperature, intestinal integrity, coccidial challenge and the anticoccidial used. The response of betaine was greater than methionine when added to diets containing low levels of methionine (75% of the US National Research Council recommendation, 1994). Typically, betaine can be added at 0.05-0.08% in broiler diet. Benefits on coccidiosis lesion scores have been noted at 0.05% but osmolyte activity increases as dose of betaine increases. During diarrhoea, when the osmotic balance is disturbed, the effective dose to control diarrhoea ranged from 0.15-1.5g/kg bodyweight.

Generally, the recommended concentration of betaine in the feed is 500-750g/tonne. Utilisation of betaine may be reduced at higher concentration (>800g/tonne).

Conclusions

Betaine is a natural osmolyte found in plants and animals grown in low rainfall areas. Its major functions in animals are as an osmolyte and methyl donor. Its osmolytic properties are useful to help maintain the gut mucus membrane during heat stress and digestive disorders. As a methyl donor, it is involved in the synthesis of methionine. Betaine is also reported to improve breast meat yield in broilers.

Chart 1: Effects of betaine and methionine on feed conversion of 21-day old broilers

Chart 2: Effects of betaine and methionine on breast meat yield in 42-day old broilers

Chart 1: Effects of betaine and methionine on feed conversion of 21-day old broilers

Chart 2: Effects of betaine and methionine on breast meat yield in 42-day old broilers

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