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Betaine: A potential feed additive for poultry sector

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Abstract
Present review summarizes the potential effects of betaine supplementation in poultry. In last few decades, the poultry sector has adopted intensive system of rearing to achieve cope up with global food and nutrient shortages. Betaine, a timethylglycne, is mainly known as methyl donor. Betaine can be choice of methyl donor over Choline, methionine and folic acid. Betaine is a powerful osmolyte, a potent antioxidant that can be useful in alleviating heat stress conditions in poultry. Betaine is an excellent carcass modifier which increases lean meat production in poultry and improves meat quality by delaying postmortem changes in meat. Thus, Betaine can be potent feed additives for poultry farming.

Keywords: Potential, feed, poultry, sector, farming

Introduction
Poultry sector has grown tremendously during last few years and it has shifted towards intensive production system. Intensive production system is profitable but it is difficult to manage as it demands better growth performance in stress free conditions. In the current global climatic scenario, environmental heat stress in tropical countries like India is a major challenge as it negatively affects growth rate and production performance of poultry (Singh *et al.,* 2022) [41]. Heat stress also increases oxidative stress which also increases reproductive tract problems and mortality rate which ultimately leads to huge economic damages to poultry owners (Shakeri *et al.,* 2018) [37]

A feed additive seems to be most economical and sustainable way to cope up with intensive production and heat stress in animals. Different types of feed additives are normally used in livestock rearing. However, looking to global environmental issues feed additives that can be beneficial in intensive production and heat stress are gaining interest among researchers i.e., Antioxidants, methyl donors etc. Methyl donors are emerging area of interest due to its wide range of effects to cope up against heat stress conditions in poultry (Deshpande *et al.,* 2020) [13].

Chemical structure of betaine
Betaine is a zwitter ion having a positively charged trimethyl ammonium and a negatively charged carboxyl group (Singh *et al.,* 2022) [41]. Betaine, a trimethyl derivative of glycine, is small molecule, highly soluble and neutral in nature. Chemically, it is termed as N, N, N-trimethylammonioacetate (Alagawany *et al*., 2022) [2].

Sources
Scheibler discovered and isolated betaine from sugar beet (*Beta vulgaris*) in 1869. Betaine Sugar beets are the primary sources of betaine but it is also found in high levels in lucerne, wheat, ground nut meal, microorganisms and certain aquatic vertebrates (Singh *et al.,* 2022; Zhao *et al*., 2018) [41, 52] . Betaine can be synthesized in body through metabolism of choline or can be of dietary origin (Zhao *et al.,* 2018; Willingham *et al.,* 2020) [52, 48]. Betaine can be added to the poultry diet in dry powder, a liquid or in a drinking water (Alagawany *et al.,* 2022) [2].

Physiological role of betaine

Currently importance of natural plant based extracts is gaining attention in poultry farmers. Betaine is a byproduct of sugar beet processing industry and abundantly available in plant kingdom. Betaine can be a potential feed additive that can improve production performance of poultry (Dunshea *et al.*, 2019; Rao *et al.*, 2011) [14, 30].

Role of betaine as methyl donor

Methyl donors and the methionine cycle

The term "methyl donor" typically refers to a chemical compound or molecule that can transfer a methyl group (-CH_3) to another molecule during various biochemical reactions. A methyl group is a simple chemical unit composed of one carbon atom bonded to three hydrogen atoms (Cronje, 2016) [11]. Folate, choline and betaine are important methyl donor that play important role in methionine regeneration following transmethylation where the transfer of methyl group from the activated form of methionine (S-adenosylmethionine) to S-adenosylhomocysteine (Sharma *et al*., 2006) [39]. S-adenosylhomocysteine, further changed into homocysteine, which can either be remethylated to methionine utilizing methyl groups derived from betaine, or irreversibly removed from the cycle by transsulfuation to cysteine, choline or tetrahydrofolate, a folate derivative (Cronje, 2016) [11]. S-adenosylmethionine coordinates the partitioning of homocysteine between remethylation and trassulphuration which inhibits two remethylation enzymes 1) Methyltetrahydrofolate reductase (MTHFR) and 2) betaine homocysteine methlytransferase (BHMT), and activates the transsulfuration enzymes, cystathione b-synthase (Cronje, 2016; Selhub and Miller, 1992) [11, 36].

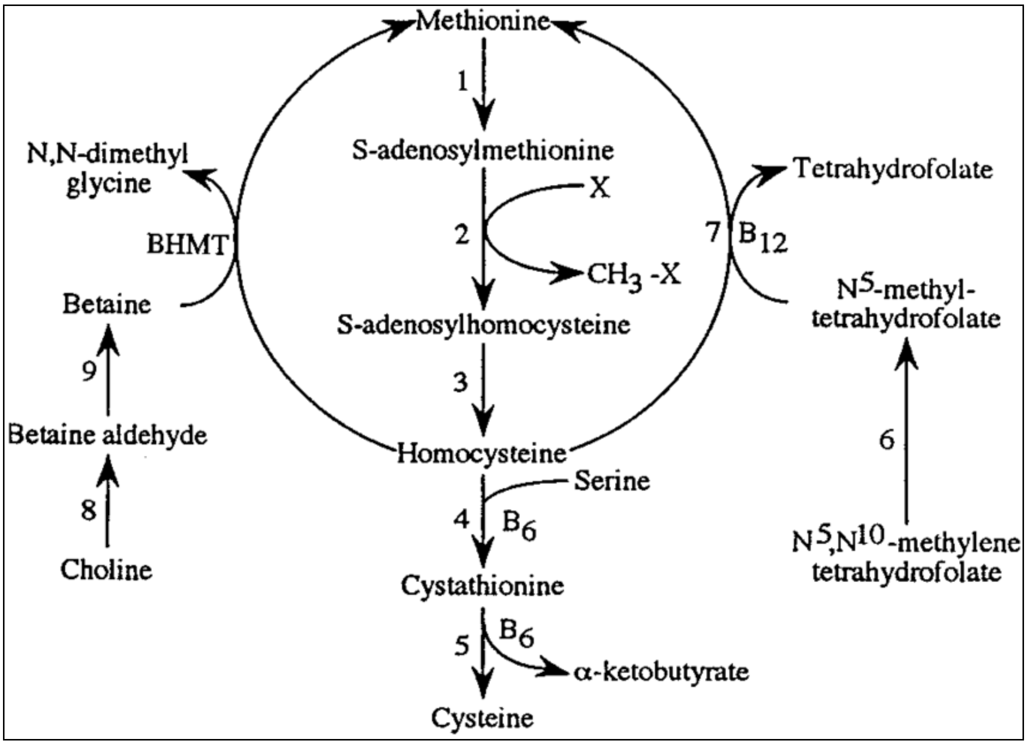

Fig 1: The methionine cycle (Source; Rao, *et al.*, 1998) [31]

Insufficient methyl groups for remethylation will cause increase buildup of toxic homocysteine. Transmethylation regulates DNA expression, protein synthesis, muscle contraction, hormone signalling, neurotransmission, protein synthesis, cell division and maintains integrity of cell membrane. Notably, methylation processes also impact the proliferation of macrophages and lymphocytes (Sharma *et al*., 2006) [39].

Betaine directly used in the transmethylation cycle, spares methionine and reduces toxic homocysteine. Betaine donates its methyl group to homocysteine and converts to methionine (Singh *et al.*, 2022) [41] and this reaction is dependent up on betaine homocysteine methyltransferase (BHMT). Due to its aminoacid and methyl donor functions betaine is directly involved in energy and protein metabolism (Eklund *et al*., 2005 Craig, 2004) [15, .9]

Role of Betaine in Heat Stress

Betaine is a natural heat stress substance used in poultry sector. In hot climatic condition, heat stress leads to oxidative damage, which reduces feed intake, growth, production and performance of poultry (Cronje, 2016) [11]. During heat stress blood flow is redistributed to periphery and causes compensatory decrease in blood flow to the gut, compromising gut health and allowing the endotoxins to enter into the bloodstream and triggering an inflammatory response (Cronje, 2005) [10]. Oxidative stress activates Tumor necrosis factor (TNF) which causes an increase in intestinal permeability due to loosening the bonds which hold enterocytes altogether (Al-sadi *et al.*, 2013) [4]. Further, heat stress also induces fatty degeneration of liver by increasing the plasma fatty acids concentrations (Itoh *et al.*, 1998) [23]. Dietary betaine supplementation has alleviated the negative effects of heat stress and improved oxidative status of animals (Wen *et al.*, 2019) [47]. In broilers, supplementing with betaine reduced the levels of free fatty acids in the blood and found improved growth rate and FCR during heat stress (He *et al*., 2015) [20]. Osmotic changes at cellular level during heat stress causes dehydration. Osmoregulatory property of betaine may help in maintaining celluar integrity and cell hydration during heat stress (Mahmoudnia and Madani, 2012). Dietary betaine supplementation in poultry diets helps to cope up heat stress by maintaining the cellular water and ionic balance (Saeed *et al.*, 2017) [34].

Role of betaine in prevention of fatty liver disease

Excess triglyceride buildup in the livestock animal's liver is the direct cause of fatty liver disease (FLD). In FLD, mobilization of fatty acids from adipose tissue in more quantities that cross capacity of the liver to oxidize fatty acids. FLKS is caused by excess energy consumption (Julian, 2005) [24] and FLHS appears to be caused by excess energy intake in combination with high concentration of estrogen, which is secreted during egg laying to stimulate mobilization (Hansen and Walzem, 1993) [19]. Excess fatty acids cause a variety of metabolic stresses, which activate c-Jun N-terminal kinase (Rocha and Folco, 2011) [33] and Insulin-receptor substrate is inactivated by c-Jun N-terminal kinase, which reduces the sensitivity of muscle and fat tissue to insulin (Crojne, 2016; Tarantino and Caputi, 2011) [11, 45]. Moreover, c-Jun N-terminal kinase inactivates Adenosine monophosphate-activated protein kinase (AMPK) which increases the accumulation of fat in the liver because AMPK stimulates fatty acid oxidation and inhibits fatty acid synthesis (Daval *et al*., 2006) [12].

Adenosine monophosphate-activated protein kinase (AMPK) inhibits Acetyl-CoA carboxylase, the enzyme that converts acetyl-CoA into malonyl-CoA. Inhibiting malonyl-CoA synthesis results in 1) decreased fatty acid synthesis and 2) increased fatty acid oxidation is because reduced concentrations of malonyl-CoA increase the activity of carnitine: palmitoyl-CoA transferase-1, which facilitates the entry of long-chain fatty acyl CoA into the mitochondria, where their oxidation takes place (Crojne, 2016) [11]. Additionally, by enhancing mitochondrial biogenesis, AMPK encourages the oxidation of fatty acids (Daval *et al*., 2006) [12].

Betaine activates AMPK which decrease the concentration TNF, stimulate fatty acid oxidation and decrease the concentration of triglycerides in liver which are main causative factor for FLD (Song *et al*., 2007) [42]. Betaine decreased hepatic concentrations of the lipogenic enzyme, acetyl CoA- carboxylase. Betaine completely prevented liver fat accumulation with improved antioxidant status in layers when a high-fat diet was consumed (Chen *et al.*, 2011) [8].

Role of Betaine as Osmolyte

Betaine is most effective osmolyte amongst other organic osmolytes, i.e. proline, glycine, glutamine due to its dipolar zwitterion (Singh *et al*., 2022) [41] and its high solubility in water (Eklund *et al.,* 2005) [15]. Betaine reduces vascular perfusion and prevents water loss from ECF (extra cellular fluid) during hyperthermia by binding and holding with water molecules. Betaine minimizes epidermal dehydration via sweating. It also improves kidney electrolyte balance (Hammer and Baltz, 2002) [18]. By regulating cytoplasmic osmotic pressure and permits cells to control the surface tension of water and stabilizes protein structure with its function (Willingham *et al*., 2020) [48]. In addition, betaine has anti-apoptotic effects that promote the proliferation of cells in a hyperosmotic medium (Alfieri *et al*., 2002) [3]. As betaine enhances intestinal cell proliferation, the enlarged cell's epithelium could increase the nutrient absorption surface and increase feed conversion efficiency in water salinity stressed broilers (Honarbakhsh *et al*., 2007) [21]. Diarrhoea control in flock is important in reducing susceptibility to infection and reducing the atmospheric ammonia level. Further, osmoregulatory properties of betaine helps to reduces excessive droppings and wet litter in mitigating heat stress in poultry (Ratriyanto *et al*., 2017) [32].

Role of betaine as carcass modifier

Betaine is generally called as carcass modifier due to it's growth promoting and lipotropic effects (Gholami *et al.,* 2015) [22]. Normally after slaughtering pH of meat is a decrease due to lactic acid accumulation. Betaine supplementation reduces lactic acid accumulation leading to sluggish decline pH and results in reduced protein denaturation, decreases the water loss of the meat and thus prevents meat quality deterioration (Eldamrawy *et al.,* 2023; Matthews *et al*., 2001) [16, 27]. Betaine increases buffering capacity of the cells by promoting effect on muscle creatine content which maintains phosphate with in the muscle cells and there by delaying the post mortem pH drop due to accumulation of lactic acid (Pettigrew & Esnaola, 2001) [29].

Due to lipotrophic effect on meat and increase muscle yield betaine is also termed as 'carcass modifier'. Betaine contributes to reduction in fat accumulation in the carcass (Partridge, 2002) [28] by provoking the oxidative catabolism of fatty acids through carnitine synthesis which directly reduces carcass fat content (Abd El-Ghany and Babazadesh, 2022) [1]. An effect of betaine on carcass leanness mainly depends up on age, sex and genetics of the animal. Increase in the muscle yield with Betaine supplementation may result from its methyl group donor activity, which is essential for the synthesis of methionine, cysteine, lecithin, and glycine for protein synthesis (Abd El-Ghany and Babazadesh, 2022; Yang *et al*., 2016) [1, 49].

Role of betaine in prevention of coccidiosis

Coccidiosis is an important enteric protozoan parasitic disease of poultry that causes diarrhea and high mortality leading to economic losses (Abd El-Ghany and Babazadesh, 2022) [1]. Ionophore coccidiostats as such disturb the osmotic balance of the gut which may be attenuated by dietary betaine supplementation (Eklund *et al*., 2005) [15]. Dietary betaine supplementation directly inhibits coccidial infection via inhibition of developmental stages of *Eimeria* spp. and indirectly by improving intestinal gut health in cooccidiosis affected birds (Eldamrawy *et al.,* 2023; Matthews *et al*., 2001) [16, 27]. Betaine improved performance parameters in broiler chickens exposed to *Eimeria (E.) acervulina* infection (Matthews and Southern, 2000) [26]. Further, betaine supplememtation also decreased the intestinal crypt-to-villus ratio and intenstinal lesions in broilers suffering from coccidiosis (Eldamrawy *et al.,* 2023; Amerah and Ravindran, 2015) [16, 5].

Table 1: Effects of betaine supplementation on performance of poultry

Species	Optimum Betaine level	Betaine effect	Reference
Broiler chicken	2 gm/kg	↑ FI* ↑ BW* ↓ FCR* ↑Dressing percentage* ↑ Lymphocyte*	Chand *et al.*, 2017 [7]
Yellow feather broiler	0.5 gm/kg	↑ BWG* ↑ FI*	Sun *et al.*, 2019 [44]
Broiler	1 gm/kg	↑ ADG* ↓ FCR* ↑ Serum TG* ↑ Cholesterol*	Ghasemi *et al.*, 2020 [17]
Broiler	1 gm/kg	↑ ADWG*	Shakeri *et al.*, 2020) [38]
Yellow feather broiler	1 gm/kg	↑ ADG* ↓ ADFI* ↓ FCR**	Song *et al.*, 2021 [43]
Broiler	2 gm/kg	↓ Cholesterol** ↓ Hepatic MDA* ↓ Hepatic SOD*	Saleh *et al.*, 2023 [35]
Broiler	2 gm/kg	↑ BW** ↑ WG** ↓ FCR*	Eldamrawy *et al.*, 2023 [16]
Broiler	0.06% betaine / liter of DW	↑ BW* ↑ FI* ↓ FCR* ↑ Carcass wt* ↓ TG** ↓ LDL**	Yeasmin., 2023 [50]
Broiler	3 gm/kg	↑ TAC** ↑ SOD** ↓ MDA**	Eldamrawy *et al.*, 2023 [16]
Laying hen	6 gm/kg	↑ Egg production* ↑ Egg weight* ↑ Feed intake* ↓ Broken & shell-less egg*	Shin *et al.*, 2018 [40]
Laying hen	1 gm/kg	↑ Body weight**	Attia *et al.*, 2016 [6]
Laying hen	0.5 gm/kg	↑ Egg weight* ↑ Egg mass* ↑ Yolk color score*	Zaki *et al.*, 2023 [51]
Laying hen (Starter phase)	0.18 gm/kg	↑ Feed intake* ↑ Weekly body weight**	Wahid *et al.*, 2021 [46]
Laying hen	1 gm/kg	↑ Body weight**	Attia *et al.*, 2016 [6]

* Significant level ($p<0.05$) ** Significant level ($p<0.01$)

Conclusions

From the present review, it can be concluded that dietary betaine supplementation has wide applications in poultry sector. Betaine supplementation can have heat ameliorative effects and can be effectively used as growth promoter, carcass modifier and anti-coccidiostat and potent antioxidant by reducing ROS. Thus, betaine can be an effective additive for poultry sectors.

References

1. Abd El-Ghany WA and Babazadeh D. Betaine: A Potential Nutritional Metabolite in the Poultry Industry. Animals. 2022;12:2624. https://doi.org/10.3390/ani12192624
2. Alagawany M, Elnesr SS, Farag MR, El-Naggar K, Taha AE, Khafaga AF, *et al*. Betaine and related compounds: Chemistry, metabolism and role in mitigating heat stress in poultry. J Therm. Biol. 2022;104:103168.
3. Alfieri RR, Cavazzoni A, Petronini PG, Bonelli MA, Caccamo AE, Borghetti AF, *et al*. Compatible osmolytes modulate the response of porcine endothelial cells to hypertonicity and protect them from apoptosis. J. Physiol. 2002;540(2):499-508.
4. Al-Sadi R, Guo S, Ye D, Ma TY. TNF-α modulation of intestinal epithelial tight junction barrier is regulated by ERK1/2 activation of Elk-1. Am. J Pathol. 2013;183(6):1871-1884.
5. Amerah AM, Ravindran V. Effect of coccidia challenge and natural betaine supplementation on performance,

nutrient utilization, and intestinal lesion scores of broiler chickens fed suboptimal level of dietary methionine. Poult. Sci. 2015;94(4):673-680.
6. Attia YA, Abd El-Hamid AE, Abedalla AA, Berika MA, Al-Harthi MA, Kucuk O, *et al*. Laying performance, digestibility and plasma hormones in laying hens exposed to chronic heat stress as affected by betaine, vitamin C, and/or vitamin E supplementation. SpringerPlus. 2016;5:1619.
7. Chand N, Naz S, Maris H, Khan RU, Khan S, Qureshi MS. Effect of betaine supplementation on the performance and immune response of heat stressed broilers. Pak. J. Zool. 2017;49(5):1857-1862
8. Chen WL, Wei HW, Chiu WZ, Kang CH, Lin TH, Hung CC, *et al*. Metformin regulates hepatic lipid metabolism through activating AMP-activated protein kinase and inducing ATGL in laying hens. Eur. J Pharmacol. 2011;671(1-3):107-112.
9. Craig SA. Betaine in human nutrition. Am. J Clin. Nutr. 2004;80(3):539-549.
10. Cronje P. Heat stress in livestock-The role of the gut in its aetiology and a potential role for betaine in its alleviation. Recent Advances in Animal Nutrition in Australia. 2005;15:107-122.
11. Cronje PB. Essential role of methyl donors in animal productivity. Anim. Prod. Sci. 2016;58(4):655-665.
12. Daval M, Foufelle F, Ferré P. Functions of AMP-activated protein kinase in adipose tissue. J. Physiol. 2006;574(1):55-62.
13. Deshpande A, Singh SV, Somagond YM, Sheoran P, Naskar S, Chahal VP. Physio-biochemical responses and growth performance of buffalo heifers to betaine supplementation during hot humid season under field conditions. Indian J Anim. Sci. 2020;90(3):416-423. DOI: 10.14202/vetworld.2022.1657-1664
14. Dunshea FR, Oluboyede K, DiGiacomo K, Leury BJ, Cottrell JJ. Betaine improves milk yield in grazing dairy cows supplemented with concentrates at high temperatures. Anim. 2019;9(2):57.
15. Eklund M, Bauer E, Wamatu J, Mosenthin R. Potential nutritional and physiological functions of betaine in livestock. Nutr. Res. Rev. 2005;18(1):31-48.
16. Eldamrawy SZ, Abd-Elghany IA, El-Rayes TK. Effect of betaine supplementation on growth performance, carcass characteristics and antioxidants status of broilers. J. Sustain. Agric. Envir. Sci. 2023;2(3):38-44.
17. Ghasemi HA, Nari N. Effect of supplementary betaine on growth performance, blood biochemical profile, and immune response in heat-stressed broilers fed different dietary protein levels. J Appl. Poult. Res. 2020;29(2):301-313.
18. Hammer MA, Baltz JM. Betaine is a highly effective organic osmolyte but does not appear to be transported by established organic osmolyte transporters in mouse embryos. Molecular Reproduction and Development: Gamete Res. 2002;62(2):195-202.
19. Hansen RJ, Walzem RL. Avian fatty liver hemorrhagic syndrome: A comparative review. Adv. Vet. Sci. Comp. Med. 1993;37:451-468.
20. He S, Zhao S, Dai S, Liu D, Bokhari SG. Effects of dietary betaine on growth performance, fat deposition and serum lipids in broilers subjected to chronic heat stress. Anim. Sci. J. 2015;86(10):897-903.
21. Honarbakhsh S, Zaghari M, Shivazad M. Can exogenous betaine be an effective osmolyte in broiler chicks under water salinity stress? Asian-Australas. J Anim. Sci. 2007;20(11):1729-1737.
22. Gholami J, Qotbi AA, Seidavi A Meluzzi A, Tavaniello S, Maiorano G. Effects of *in Ovo* Administration of Betaine and Choline on Hatchability Results, Growth and Carcass Characteristics and Immune Response of Broiler Chickens. Italian J Anim. Sci., 2015;14:1-7.
23. Itoh F, Obara Y, Rose MT, Fuse H, Hashimoto H. Insulin and glucagon secretion in lactating cows during heat exposure. Anim. Sci. J. 1998;76:2182–2189. DOI:10.2527/1998.7682182x
24. Julian RJ. Production and growth related disorders and other metabolic diseases of poultry–a review. Vet. J. 2005;169(3):350-369.
25. Mahmoudnia N, Madani Y. Effect of betaine on performance and carcass composition of broiler chicken in warm weather-A review. Int. J Agric. Sci. 2012;2(8):675-683.
26. Matthews JO, Southern LL. The effect of dietary betaine in *Eimeria acervulina*-infected chicks. Poult. Sci. 2000;79(1):60-65.
27. Matthews JO, Southern LL, Higbie AD, Persica MA, Bidner TD. Effects of betaine on growth, carcass characteristics, pork quality, and plasma metabolites of finishing pigs. J. Anim. Sci. 2001;79(3):722-728.
28. Partridge G. Betaine from sugar beet gives an energy boost. Pig. Int. 2002;32:21.
29. Pettigrew JE, Esnaola MA. Swine nutrition and pork quality: A review. J Anim. Sci. 2001;79(suppl_E): E316-42.
30. Rao SV, Raju MV, Panda AK, Saharia P, Sunder GS. Effect of supplementing betaine on performance, carcass traits and immune responses in broiler chicken fed diets containing different concentrations of methionine. Asian-Australas. J Anim. Sci. 2011;24(5):662-669.
31. Rao P, Timothy A, John F, Garland D, Millian N, Zigler S. Betaine-homocysteine Methyl Transferase is a Developmentally Regulated Enzyme Crystallin in Rhesus Monkey Lens. The J Biol. Chem. 1998;273;30669-30674.
32. Ratriyanto A, Indreswari R, Nuhriawangsa AMP. Effects of Dietary Protein Level and Betaine Supplementation on Nutrient Digestibility and Performance of Japanese Quails. Brazilian J Poult. Sci. 2017;19:445-453.
33. Rocha VZ, Folco EJ. Inflammatory concepts of obesity. International journal of inflammation; c2011.
34. Saeed M, Babazadeh D, Naveed M, Arain MA, Hassan FU, Chao S. Reconsidering betaine as a natural anti-heat stress agent in poultry industry: A review. Trop. Anim. Health Prod. 2017;49:1329-1338.
35. Saleh AA, El-Tahan HM, Shaban M, Morsy WA, Genedy S, Alzawqari MH, *et al*. Effect of dietary supplementation of betaine and organic minerals on growth performance, serum biochemical parameters, nutrients digestibility, and growth-related genes in broilers under heat stress. Poult. Sci. 2023;102(11):103051.
36. Selhub J, Miller JW. The pathogenesis of homocysteinemia: interruption of the coordinate regulation by S-adenosylmethionine of the remethylation and transsulfuration of homocysteine. Am. J Clin. Nutr. 1992;55(1):131-138.
37. Shakeri M, Cottrell JJ, Wilkinson S, Ringuet M, Furness JB, Dunshea FR. Betaine and antioxidants improve growth performance, breast muscle development and

ameliorate thermoregulatory responses to cyclic heat exposure in broiler chickens. Anim. 2018;8(10):162.
38. Shakeri M, Cottrell JJ, Wilkinson S, Le HH, Suleria HA, Warner RD, *et al*. Dietary betaine reduces the negative effects of cyclic heat exposure on growth performance, blood gas status and meat quality in broiler chickens. Agric. 2020;10(5):176.
39. Sharma P, Senthilkumar RD, Brahmachari V, Sundaramoorthy E, Mahajan A, *et al*. Mining literature for a comprehensive pathway analysis: a case study for retrieval of homocysteine related genes for genetic and epigenetic studies. Lipids Health Dis. 2006;5:1-9.
40. Shin JE, Kim JH, Goo D, Han GP, Pitargue FM, Kang HK, *et al*. Effect of dietary supplementation of betaine on productive performance, egg quality and jejunal tight junction-related gene expression in laying hens raised under hot environmental conditions. Livest. Sci. 2018;214:79-82.
41. Singh SV, Deshpande AD, Somagond YM. Betaine: A potent feed additive for amelioration of adverse effect of heat stress in livestock and poultry. Indian J Anim. Res. 2022;92(3):277-282.
42. Song Z, Deaciuc I, Zhou Z, Song M, Chen T, Hill D, *et al*. Involvement of AMP-activated protein kinase in beneficial effects of betaine on high-sucrose diet-induced hepatic steatosis. Am. J Physiol. Gastrointest. Liver Physiol. 2007;293(4):G894-902.
43. Song Y, Chen R, Yang M, Liu Q, Zhou Y, Zhuang S. Dietary betaine supplementation improves growth performance, digestive function, intestinal integrity, immunity, and antioxidant capacity of yellow-feathered broilers. Ital. J Anim. Sci. 2021;20(1):1575-1586.
44. Sun CY, Liu WC, Xiao M, Zhao ZH, An LL. Effects of graded levels of betaine supplementation on growth performance and intestinal morphology in indigenous young yellow feather broilers. Pak. J Zool. 2019;51(6):2323-2328.
45. Tarantino G, Caputi A. JNKs, insulin resistance and inflammation: A possible link between NAFLD and coronary artery disease. World J Gastroenterol. 2011;17(33):3785-3794.
46. Wahid ZA, Ratriyanto A, Prastowo S. The effect of betaine supplementation on performance of laying hens in the tropical climate during the starting period. In IOP Conference Series: Earth and Environmental Science IOP Publishing. 2021;902(1):012043.
47. Wen C, Chen Y, Leng Z, Ding L, Wang T, Zhou Y. Dietary betaine improves meat quality and oxidative status of broilers under heat stress. J. Sci. Food Agric. 2019;99(2):620-623.
48. Willingham BD, Ragland TJ, Ormsbee MJ. Betaine supplementation may improve heat tolerance: Potential mechanisms in humans. Nutr. 2020;12(10):2939.
49. Yang Z, Wang ZY, Yang HM, Zhao FZ, Kong LL. Response of growing goslings to dietary supplementation with methionine and betaine. Br. Poult. Sci. 2016;57(6):833-841.
50. Yeasmin T, Jaman MA, Uzzal H, Gausur MR. Impact of betaine on the performance and specific haemato-biochemical parameters in heat-stress exposed broiler chickens. J. Istanbul Vet. Sci. 2023;7(3):154-162.
51. Zaki A, Jiang S, Zaghloul S, El-Rayes TK, Saleh AA, Azzam MM, *et al*. Betaine as an alternative feed additive to choline and its effect on performance, blood parameters, and egg quality in laying hens rations. Poult. Sci. 2023;102(7):102710.
52. Zhao G, He F, Wu C, Li P, Li N, Deng J, *et al*. Betaine in inflammation: mechanistic aspects and applications. Front. Immunol. 2018;9:1070.