AgroVet Alliance

SCAN ME

CREAMINO

ENERGY FOR HEALTHY GROWTH

Creamino® – The creatine source for animal nutrition

TECHNICAL INFORMATION

alzchem group

Creatine – a lost nutrient in modern animal nutrition

Creatine (Cr) is a key component in the intra-cellular energy metabolism of vertebrates. Its phosphorylated form Phosphocreatine (PCr) prevents low levels of cellular energy by re-phosphorylating ATP from ADP and transporting high energy phosphates within the cell (Wyss and Kaddurah-Daouk, 2000). Creatine can be supplied by endogenous de-novo synthesis and via exogenous supply in food or feed. This way, the body ensures sufficient Cr levels in its cells. However, supplementation of Cr to diets of humans or animals has been shown to improve performance and health by optimising the Cr status (Wyss and Kaddurah-Daouk, 2000). Also, since Cr is predominantly found in muscle (meat) it is logically a component of an omnivore's diet. The use of animal derived products is decreasing continuously in both animal and human nutrition. Therefore, supplementing Cr to these diets is crucial to maintain the natural Cr supply.

Due to its superior processing properties, guanidinoacetic acid (GAA) is the best Cr source for animal nutrition. Being the direct metabolic precursor, GAA's only fate is the synthesis of Cr (Wyss and Kaddurah-Daouk, 2000). The active ingredient in Creamino® is GAA.

Recent research shows that compared to their natural diets both swine and poultry lack Cr in their typical industrially produced diets. The inclusion rates of relevant Cr contributors like fish meal or meat and bone meal are too low to reach the natural levels (Galler et al., 2022; Fig. 1). By adding Creamino® to these diets one can restore the natural exogenous Cr supply and enhance the Cr levels in the body to ultimately support the animals reaching their genetic potential.

Endogenously, Cr is synthesised from the three amino acids arginine (Arg), glycine (Gly), and methionine (Met). Firstly, Arg and Gly are converted to GAA predominantly in the kidneys. Subsequently, GAA is methylated by S-Adenosyl-Methionine in the liver and transported to the target tissues via the bloodstream. The predominant occurrence of Cr is in skeletal muscle (~95%), but it is also prevalent in all other tissues (Wyss and Kaddurah-Daouk, 2000).

(Wyss and Kaddurah-Daouk, Physiological Reviews, 2000;
Galler et al., Proceedings of the Society of Nutrition Physiology, 2022)

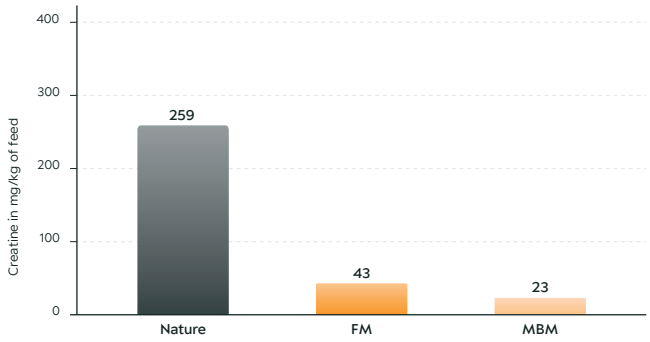

Fig. 1. **Creatine supply in swine feed.**
Nature: feeding habits in the wild, FM: diets containing 3.5%-4.0% of fishmeal, MBM: diets containing 5.0%-10.0% meat and bone meal); (Galler et al., 2022, modified).

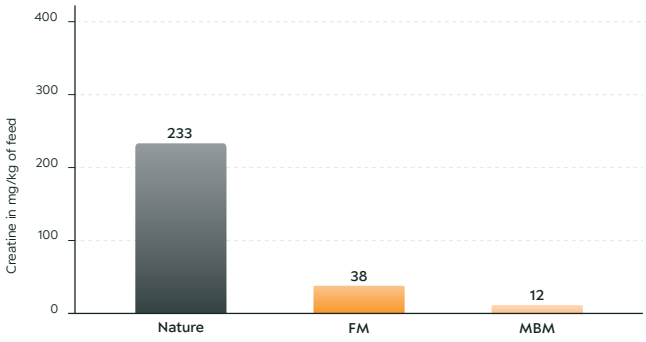

Fig. 2. **Creatine supply in broiler feed.**
Nature: feeding habits in the wild, FM: diets containing 3.5%-4.0% of fishmeal, MBM: diets containing 5.0%-10.0% meat and bone meal); (Galler et al., 2022, modified).

Physiological role of Creatine

Creatine is a crucial part of the intracellular energy homeostasis directly interacting with adenosine triphosphate (ATP). Briefly, ATP is the main source of energy, the "energy currency", in the cell. It is produced in the mitochondria (the cell's powerhouse). The full potential of ATP production is reached in aerobic conditions with sufficient oxygen for oxidative phosphorylation using glucose or fatty acids. The ATP storage is very limited and usually depleted within two seconds (Marshal et al., 2022).

Figure 3 explains the central role Cr plays as an intra-cellular shuttle and storage system to the high energy phosphate bond of ATP. The enzyme Creatine Kinase (CK) catalyses the transfer of ATP's high energy phosphate bond to Cr inside the mitochondrial membrane to form PCr, which then diffuses to the cytoplasm [1]. Two thirds of total Cr pool are PCr, while one third remains as free Cr. PCr interacts with phospholipids and exerts membrane protective effects by providing readily available energy. It is stored in the cytoplasm and donates its high energy phosphate bond to adenosine diphosphate (ADP) to replenish ATP instantaneously independent of the mitochondrial respiration [3 and 4]. This reaction, again, is catalysed by (cytoplasmic) CK. CK and PCr/Cr are also involved in glycolytic pathways to support the ATP production from glycolysis in the cytosol [2] (Walliman et al., 2011).

The balance of ATP/ADP which is obviously directly linked to the PCr/Cr-ratio under short-term energy depletion regulates the overall cellular energy homeostasis. When ATP is depleted, AMP (adenosine monophosphate) is accreted and the adenosine monophosphate protein kinase (AMPK) is activated.

AMPK is a member of the metabolite sensing protein kinase family and functions as a metabolic fuel gauge. AMPK ultimately inhibits anabolic pathways and activates the catabolic pathways involved in carbohydrate, fatty acid and protein metabolism to restore the ATP levels (Aschenbach et al., 2004).

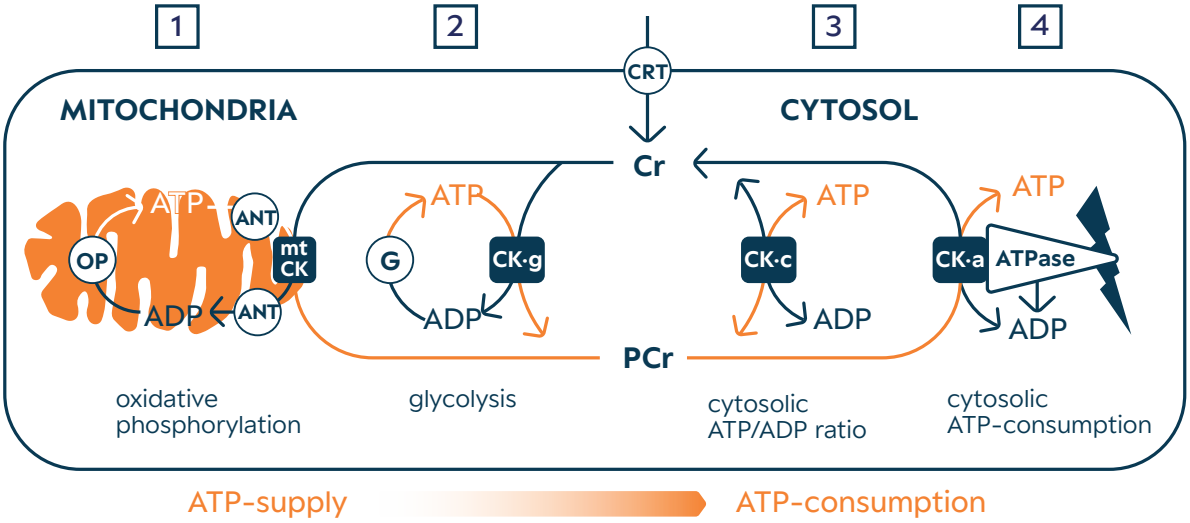

Fig. 3. The physiological intra cellular role of Creatine (Walliman et al., 2011, modified).

GAA has direct antioxidant and protective effects on mitochondria in broilers (Khalil et al., 2021). The same effects were reported in humans subjected to chronic fatigue, post viral fatigue syndrome and long COVID when Cr monohydrate was supplemented (Marshall et al., 2022).

(Wallimann et al., Amino Acids, 2011; Marshall et al., Nutrients, 2022; Aschenbach et al., Sports Med., 2004)

Creamino® – premium German quality from Alzchem the creatine experts

Alzchem's four European sites produce fine chemicals of highest quality for many applications. The company is backward integrated in Germany-based raw materials. Our products start from a Calcium carbide-/Calcium cyanamide base with derivatives not only making products but also providing raw materials for other products. The resulting production stream is highly efficient with far less waste than a system producing only a single product. Having our manufacturing in Germany ensures our employees and our customers of a higher standard of social, safety and environmental care than may be practiced in some areas of the world. Alzchem is very committed to reducing the carbon footprint and environmental impact of its entire production system. We have identified the major contributors and constantly work to reduce their impact. Many of Alzchem's products help our customers reduce their environmental impact as well. For instance, due to its consistent improvement of feed conversion, products like Creamino® help increase the resource efficiency of animal production.

Evaluation of Creamino® (GAA) as an energy source in the diets of modern broilers

(BUTOLO ET AL., PSA, 2022)

In this study, GAA was evaluated for its potential energy sparing effect in broiler diets reduced by 100 kcal of AME_N/kg of feed.

The study was carried out at the experimental farm of Granja Regina, located in Brazil. A total of 1200 Ross AP 95 one-day-old male chickens were allotted to three treatments, with eight replicates of 50 chickens each. The experimental design was completely randomised. The trial comprised five feeding phases. The first four phases lasted one week each and the last phase lasted 12 days. The treatments were: Positive control (PC) with these levels of metabolizable energy (kcal AME_N/kg of feed): Pre-initial: 2900; Initial: 3150; Fattening 1: 3200; Fattening 2: 3250; Final: 3250; Negative control (NC) (-100 kcal/kg in each phase, as compared to PC) and NC + 0.06% of GAA (NC + GAA). Body weight gain (BWG), feed intake (FI), feed conversion ratio (FCR) were determined.

Results indicated that during the whole period, reduction in dietary energy (NC) led to a decrease of performance (BWG and FCR) when compared to the PC ($p<0.05$). When GAA was added to the NC (NC + GAA), performance was improved and reached same levels as the PC group (Fig. 4, 5.).

It was concluded that the addition of 0.06% GAA compensated a dietary energy reduction of 100 kcal AME_N/kg feed without affecting performance of modern broilers. This implies that expensive energy donors in feed can be reduced and thereby feed costs can be lowered.

RESULTS: GROWTH PERFORMANCE

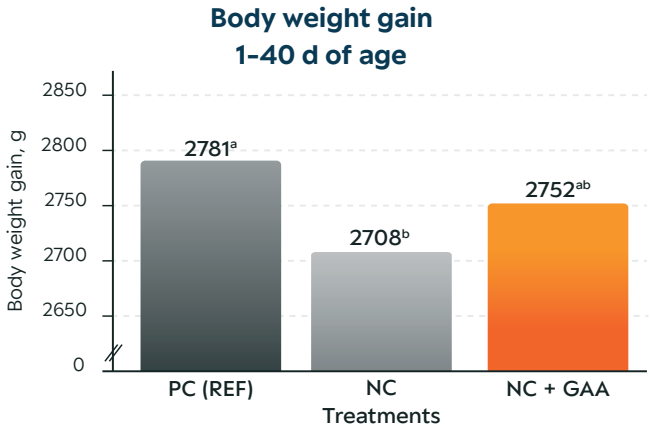

Fig. 4. Effects of GAA on body weight gain of broilers up to 40 days of age compared to a positive and negative control.

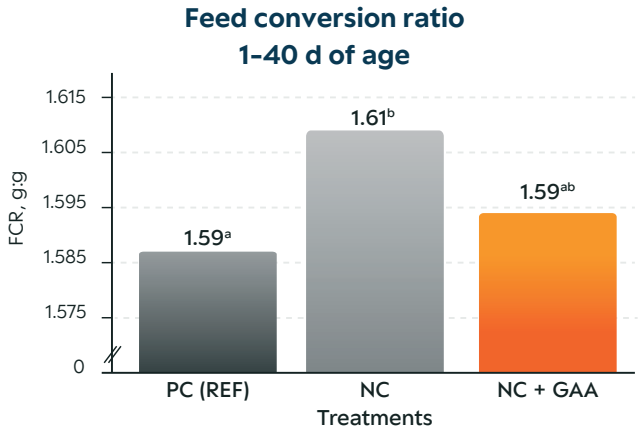

Fig. 5. Effects of GAA on feed conversion ratio of broilers up to 40 days of age compared to a positive and negative control.

Effect of Creamino® (GAA) on productive and economic parameters of broiler chicken

(RIVERA ET AL., IPPE, 2022)

The objective of this study was to evaluate if the supplementation of GAA on top or with an energy matrix, improves or equalizes the productive and economic parameters in broilers, respectively.

The study was carried out on the experimental farm of the Italcol Company located in the department of Santander-Colombia and lasted for 35 days. 1088 Ross 308 AP male chickens, one day old, with an initial weight of 42.5 ± 1.05 grams, were used, and distributed over 4 treatments, with 8 repetitions of 34 chickens per treatment. The experimental design was completely randomized. The treatments were: Control; Negative Control (-80kcal AME_N/kg), GAA on top (0.06%); GAA matrix (Negative Control + 0.06% GAA). The treatments were fed during grower and finisher periods.

The feeding consisted of three phases. The productive figures feed consumption, live weight and feed conversion were measured and the European Efficiency Index (EEI) was calculated.

Overall results indicated that at day 35, when we compared the group supplemented with 0.06% of GAA considering an energy matrix of 80 kcal/kg with the control group, we found that the GAA group obtained 21 grams more per chicken and had a by 2 points lower FCR. When we compared the group supplemented with 0.06% of GAA on top with the control group, we found that the GAA group obtained 59 grams more per chicken and 4 points less in feed conversion.

In conclusion, the use of GAA both matrixed at 80 kcal/kg and on top, improves the productive and economic efficiency in broilers at 35 days of age.

RESULTS: GROWTH PERFORMANCE AND ECONOMICS

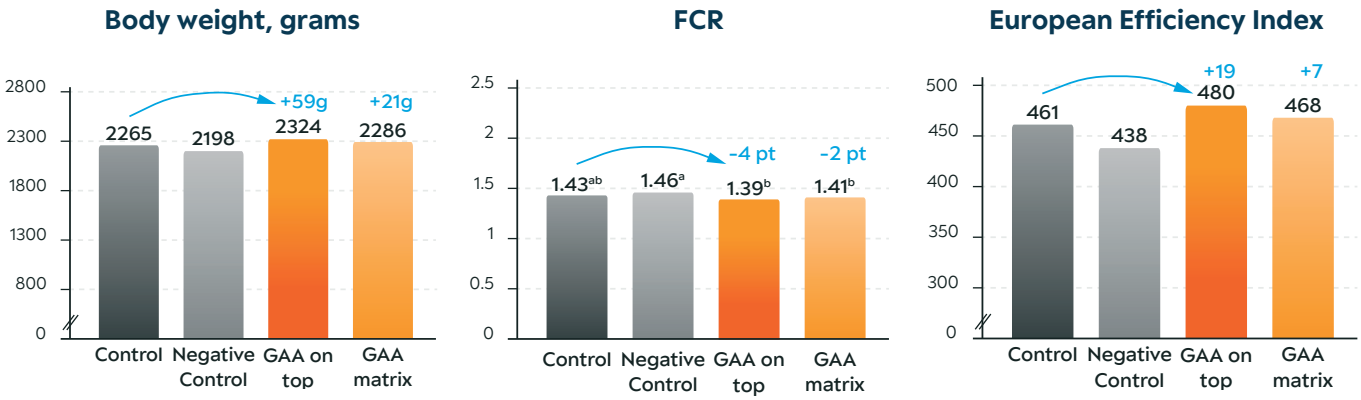

Fig. 6. Effects of GAA on economic parameters in broilers up to 35 days of age when supplemented on top or with an energy matrix.

Effect of Creamino® (GAA) on the performance of broilers exposed to mild heat stress

(CUSTOMER TRIAL- BELGIUM 2022)

The objective of this study was to investigate the effect of using the combined matrices of GAA (-50 kcal AME_N/kg and 0.67% Arg) at the rate of 0.06% in broiler diets during the grower and finisher phases. The birds were exposed to mild heat stress during the finisher period.

In a commercial facility in Belgium, a total of 720 Ross 308 broilers were divided into two equal groups. Each group has 9 replicates/40 birds per replicate. The treatments were: Control group: fed with diets as recommended by Aviagen meanwhile, Creamino® group: was fed as control group but supplemented with GAA at the rate of 0.06% using the following matrix value for energy (-50 kcal) and Arg (0.67% Arg) in the grower and finisher periods only. During the finisher phase, birds were subjected to mild heat stress (28 °C and 60% relative humidity). Both groups were fed the same diet during the starter period.

Results showed that no significant difference was detected in both average daily gain and average daily feed intake in all feeding phases. Meanwhile, feed conversion ratio was significantly improved in the grower and finisher phase, and over both periods together ($p < 0.05$) (Fig. 7.).

In conclusion, GAA supplementation at the rate of 0.06% using combined matrices (50 kcal and 67% Arg) reduced the feed cost and improved feed conversion ratio in the grower and finisher period (mild heat stress), and cumulatively.

RESULTS: GROWTH PERFORMANCE

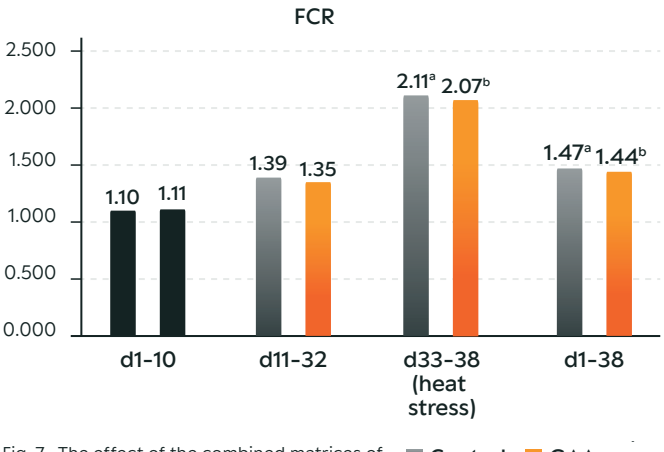

Fig. 7. The effect of the combined matrices of GAA for -50 kcal and 0.67% Arginine sparing on the feed conversion ratio of broilers.

Metabolic programming of broilers by Creamino® (GAA) supplementation in broiler breeders

(REICHER ET AL., POULTRY SCIENCE, 2020)

Metabolic programming is a nutritional intra-uterine and/or early postnatal stimulus at a critical period of development that has a significant lasting effect on future animal performance.

In this study, the molecular effects of GAA supplementation on creatine transporter (CRT) expression and Cr synthesis was evaluated. Twelve 47-weeks-old Cobb 500 broiler breeder hens were randomly selected and divided into 2 equal-weight treatment groups. The hens were artificially inseminated every 5 days with fresh semen. The control group fed on standard mash feed, meanwhile, the treatment group was supplemented with 0.15% GAA. After 11 weeks of supplementation, at 58 weeks of age, eggs were collected from the 6 hens of each group. Creatine transporter expression in intestine, ovary and oviduct of hens was evaluated at the end of the 15 weeks experimental period. The concentration of Cr in egg yolk and egg albumen was measured. Moreover, CRT was evaluated in embryo intestine on day 17 and 19 and in day-old-chicks. Meanwhile AGAT and GAMT were measured in the liver and kidney.

Overall results indicated that 0.15% GAA supplementation in broiler breeder feed increased GAA absorption potential in the duodenum (Table 1.) and increased Cr transfer potential in the magnum part of the oviduct (Table 2.) leading to an elevation of Cr deposition in egg yolk and egg albumen of hatching eggs (Table 3.). This resulted in decreased CRT expression and Cr synthesis potential in late-term embryo and hatching progeny indicating the high Cr load in day-old chicks which supports the future performance of broiler chickens (Table 4, 5.).

Table 1. Supplementation of 0.15% GAA increased CRT expression in duodenum.

Treatments	Duodenum	Jejunum	Ileum
Control	0.90^{b} ± 0.09	1.46 ± 0.15	1.76 ± 0.29
0.15% GAA	1.80^{a} ± 0.26	1.60 ± 0.15	1.84 ± 0.44

Values are presented as mean fold change ± SEM, GAA, guanidinoacetate.
^{a,b} means with different superscript letters differ significantly ($p < 0.05$).

Table 2. 0.15% GAA increases the CRT expression in the magnum.

Treatments	Ovary	Magnum	Isthmus
Control	1.04 ± 0.13	1.83^{b} ± 0.69	1.12 ± 0.25
0.15% GAA	0.98 ± 0.14	3.88^{a} ± 0.43	0.97 ± 0.30

Values are presented as mean fold change ± SEM, GAA, guanidinoacetate
^{a,b} means with different superscript letters differ significantly ($p < 0.05$).

Table 3. 0.15% GAA supplementation to broilers is leading to an elevation of in creatine deposition in egg yolk and egg albumen of hatching eggs.

	(0.00% GAA)	(0.15% GAA)	P-Value
Creatine concentration in dry albumen (mg/kg)	15.15 ± 0.081	19.10 ± 1.069	<0.01
Total creatine in the albumen (mg)	0.08 ± 0.004	0.09 ± 0.005	<0.05
Creatine concentration in dry yolk (mg/kg)	16.62 ± 0.549	26.80 ± 0.952	<0.01
Total creatine in the yolk (mg)	0.17 ± 0.006	0.25 ± 0.007	<0.01
Total egg creatine (mg)	0.24 ± 0.01	0.35 ± 0.012	<0.01

Table 4. Increased maternal GAA supply reduced the CRT expression in the progeny's small intestine.

Treatments	E17	E19	DOH
Control	0.15 ± 0.01	0.22^{a} ± 0.02	1.58^{a} ± 0.14
Maternal 0.15% GAA	0.12 ± 0.01	0.16^{b} ± 0.01	1.21^{b} ± 0.10

Creatine synthesis gene relative expression in progeny tissues after 15 weeks of maternal GAA supplementation. Examination time points include embryonic day 17 (E17), embryonic day 19 (E19), and day of hatch (DOH). Values are presented as mean fold change ± SEM.
^{a,b} means with different superscript letters differ significantly ($p < 0.05$).

Table 5. Maternal supply of 0.15% GAA affects the expression of AGAT and GAMT in kidneys and liver.

Treatments	Progeny kidney		Progeny liver	
	AGAT	GAMT	AGAT	GAMT
Control	1.03^{a} ± 0.14	1.025 ±0.11	1.02 ± 0.11	1.03^{a} ± 0.12
Maternal 0.15% GAA	0.66^{b} ±0.08	0.98 ± 0.12	1.19 ± 0.14	0.53^{b} ± 0.12

Creatine synthesis gene relative expression in progeny tissues after 15 weeks of maternal GAA supplementation. Values are presented as mean fold change ± SEM.
^{a,b} means with different superscript letters differ significantly ($p < 0.05$).

Effect of Creamino® (GAA) on breast muscle myopathies in broilers

(KHALIL ET AL., ANIMALS, 2021)

This experiment evaluated the effects of GAA supplementation at rate of 0.00%, 0.06%, and 0.12% on the productive performance, breast muscle myopathy (wooden breast, WB) and meat quality of broiler chickens. Results showed GAA supplementation improved FCR (Fig. 8.), reduced the incidence of wooden breast severity (Fig. 9.), increased muscle glycogen and reduced the ultimate pH (Fig. 10.).

In conclusion, guanidinoacetic acid can be used in broiler diets to improve the productive performance without exacerbating pectoral myopathy or affecting meat quality.

RESULTS: FCR

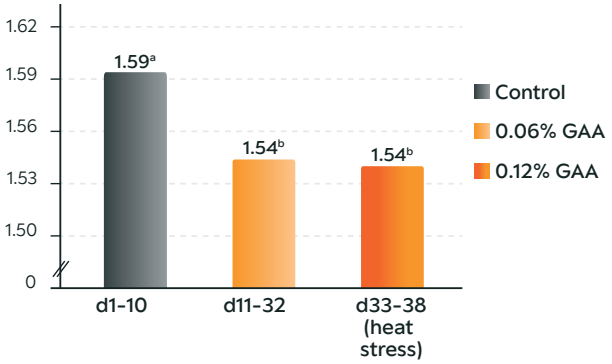

Fig. 8. Effects of GAA supplementation on growth performance up to 42 days of age.

RESULTS: WOODEN BREAST

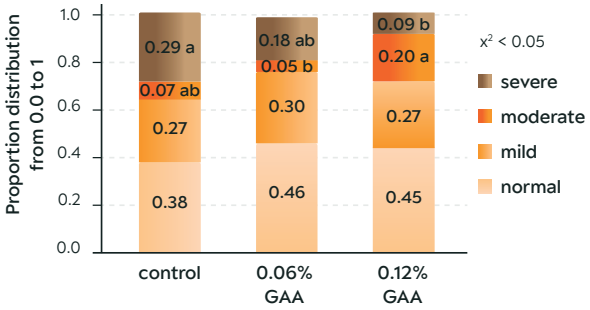

Fig. 9. Effect of GAA supplementation on the proportional distribution of wooden breast of male broiler chicks at 42 days of age.

Figure 9 shows that 0.12% GAA supplementation reduced severe WB by 20% compared to the control group. The attenuation of WB severity score resulted in a higher proportional distribution of lower WB severity scores compared to the control group. Meanwhile, the 0.06% GAA supplemented group reduced severe WB by 11% compared to the control group, which resulted in higher proportional distribution of lower WB severity scores.

RESULTS: CREATINE, GLYCOGEN CONCENTRATION AND PECTORAL MUSCLE PH

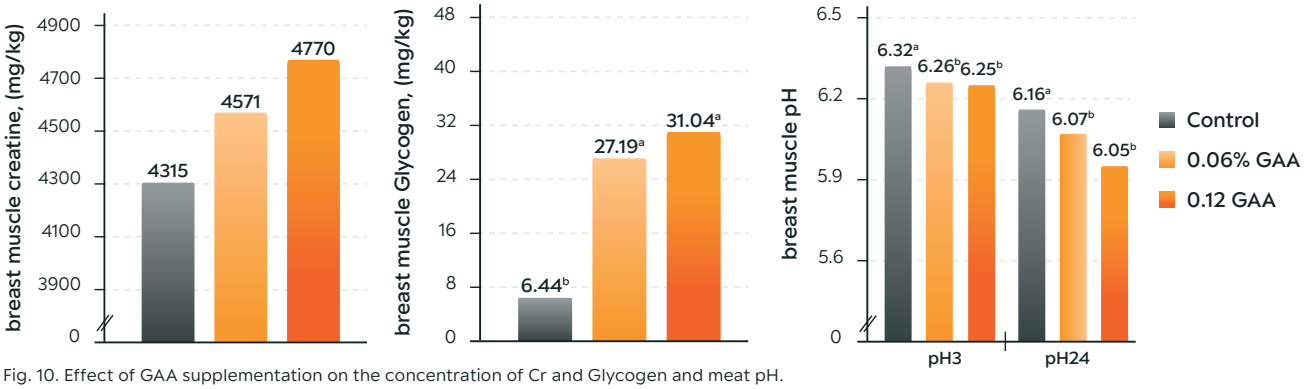

Fig. 10. Effect of GAA supplementation on the concentration of Cr and Glycogen and meat pH.

Figure 10 shows that 0.06% and 0.12% GAA supplementation increased breast muscle Cr contents by 6% and 11%, respectively. It is worth noting that the total Cr contents comprise ~66% PCr and 33% free Cr. The availability of breast muscle glycogen reflects the PCr status to maintain the energy homeostasis. In this study GAA supplementation maintained muscle glycogen at high levels, significantly. Moreover, the availability of muscle glycogen post mortem determined the ultimate pH due anaerobic fermentation and lactic acid build up. Results showed a significant reduction of pH values in GAA groups.

Arginine sparing effect of Creamino® (GAA) in moderately low crude protein broiler diets

(SHARMA ET AL., POULTRY SCIENCE, 2022)

This study aimed at determining the extent GAA could spare Arg in broilers offered moderately low crude protein (CP) diets and if supplemental betaine (as a methyl donor) provided additional benefits. A total of 720 day-old Ross 308 male broilers were assigned into 9 dietary treatments with 8 replicates of 10 birds each. The treatments comprised a normal CP diet (21.5% in grower and 19.7% in finisher), a low CP (-1.5%) diet deficient in Arg, a low CP diet sufficient in Arg, and low CP diets with GAA, where 0.1% added L-Arg was spared by GAA at 50% (0.20% GAA), 100% (0.10% GAA) and 150% (0.067% GAA) with and without 0.1% betaine. The treatments were offered during grower (d 10–24) and finisher (d 25 –42) phases. All diets contained adequate levels of methyl donors (e.g. methionine and choline).

RESULTS: GROWTH PERFORMANCE

11a. Weight gain d 10-42

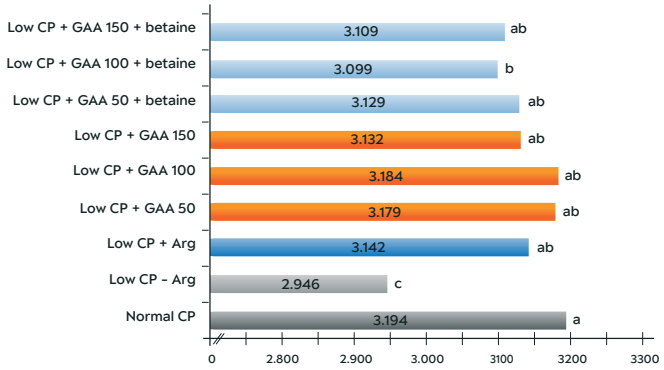

Figure 11a. shows that birds offered a low CP diet deficient in Arg had around 7.8% lower weight gain as compared to those offered a normal CP diet in all the phases. When Arg was added, weight gain increased and became comparable to the normal CP treatment during d 10-42. When GAA spared Arg at 50%, 100% and 150% without or with betaine, weight gain was higher than the Arg deficient low CP treatment and comparable to the low CP + Arg treatment in all the phases. Betaine did not have synergistic effects when added to each level of GAA.

11b. FCR d 10-42

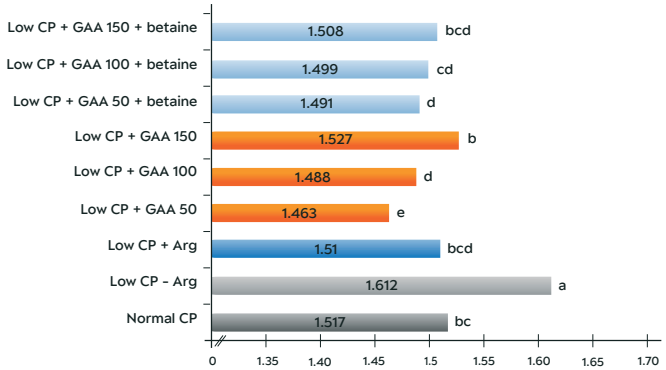

Figure 11b. reveals that over the experimental period, birds offered a moderately low CP diet deficient in Arg had 10 points higher FCR over all phases as compared to those offered a normal CP diet. When Arg was increased to recommended levels, FCR decreased and became comparable to the normal CP treatment. From day 10-42, when GAA spared Arg at 150% FCR was lower than in the low CP - Arg treatment. Sparing 100% and 50% Arg, GAA improved FCR by 5 to 15 points compared to both the low CP - Arg group and the Normal CP group.

Fig. 11. Growth performance of broilers offered low crude protein diets with guanidinoacetic acid and betaine.

In conclusion, GAA can replace up to 150% of Arg in moderately low CP diets. This way GAA can be used to support low CP feeding programs for broilers. Combining betaine as a methyl donor with GAA showed no synergistic effect. Therefore, there was no need for additional methyl donors to convert GAA into Cr.

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