DL-Methionine: The first methionine source

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A journey through time

Methionine (Met), a sulfur containing amino acid, is recognized as a vital molecule for the proper metabolic function of animals. In addition to being a building block for proteins (feathers, muscle, enzymes, hormones, among others), it serves as the precursor for other sulfur amino acids and their derivatives, such as cystine, homocysteine, and glutathione, and is the main methyl group donor to epigenetic pathways in the form of S-adenosylmethionine (SAMe).
Methionine was first isolated in 1922 by J. H. Müller, a researcher at Columbia University in New York. However, its formula and structure were only described three and six years later by S. Odake, G. Barger and F. P. Coyne, respectively.
The search for how to produce large amounts of purified methionine for food and feed supplementation was fostered by the discovery of its essentiality in the 1930s and advancements in the petrochemical industry which enabled the production of acrolein, an intermediate product in the synthesis of DL-Met.
Researchers at Degussa AG (now Evonik) followed up these findings during the post-war years. The first technically feasible synthesis of DL-Met was achieved by W. Schwarze, H. Wagner, and H. Schulz as pharmaceutical grade to treat chronic protein insufficiency suffered by soldiers returning home from the war in 1948. Further application of methionine for animal feed came along a few years later in 1953, after animal feeding trials were conducted and showed positive results.
Nowadays, DL-Met is being successfully produced by Evonik at three international hubs (Americas, Europe and Asia) with world-class plants located in Mobile (USA), Antwerp (Belgium) and Singapore, supporting the global demand for this essential amino acid. Additional investments are being made at the Mobile and Singapore production plants with backward integration projects to locally produce methyl-mercaptan, an intermediate in the DL-Met synthesis. These investments allow for more efficient DL-Met production while improving its sustainability value by removing the outsourcing and transportation of this material from other locations to the plant. You can find more information about the backward integration project at Evonik's website or by scanning the QR code.

View Evonik's Press Release
on the backward integration of their methyl-mercaptan plant in Mobile, AL

View Evonik's Press Release
on their second methyl-mercaptan plant in Singapore

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Methionine sources

Since the first synthesis of DL-Met, alternative supplemental sources, such as Methionine Hydroxy Analogue Free Acid (MHA-FA) and Methionine Hydroxy Analogue Calcium salt (MHA-Ca), were developed and are currently offered by several companies around the world. However, these sources differ significantly in their structure and availability to the animals.

Data as early as 1980 has shown that DL-Met, an amino acid per chemical structure, is considered 100% bioavailable to animals, whereas MHA-FA, an organic acid, is considered 63-70% bioavailable relative to DL-Met [1-3]. More recently conducted studies have shown a bioefficacy of around 65% for MHA-free acid (MHA-FA) and calcium salt (MHA- Ca) for all farmed monogastric terrestrial and aqua species under any production condition [4-9]. This means that 100 parts of MHA products can be replaced by 65 parts of DL-Met in feed without impacting performance.

The methodology to determine the relative bioefficacy has been described by Littell et al. [10]. In summary, two (multiple) dose response data sets are analyzed by either linear (slope-ratio) or simultaneous multi-exponential regression (Figure 1). The steepness from the regression equations are related to each other, taking DL-Met as the reference. The resulting coefficient suggests how much DL-Met is needed to replace MHA for the same animal performance, independent of general supplementation and performance levels. In this approach, it has been clearly demonstrated that the maximum achievable performance (asymptote) is similar for both products.

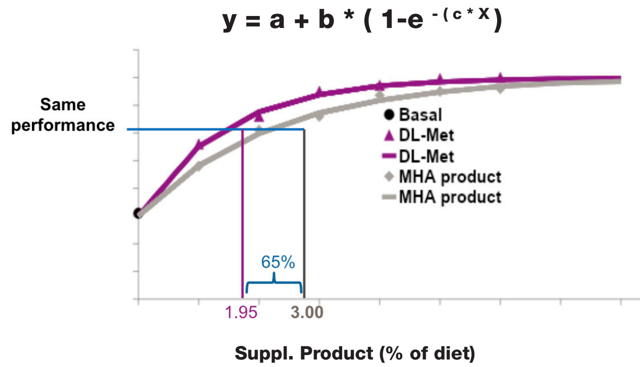

Figure 1: *Simultaneous multi-exponential regression analysis to determine relative bioeficacy.*

In order to validate the multiple-exponential regression approach, diluted DL-Met has also been used as an internal standard. The dilution of MetAMINO® can be done by using 35% of starch, glucose, limestone, or finely grinded grains. With a known concentration of only 65% DL-Met in a premix (65DLM), the simultaneous dose-response trial should reveal a bioefficacy of about 65% relative to pure DL-Met (99% purity). Broiler trials using 65DLM suggested an average bioefficacy of 63%, which was identical to the bioefficacy determined for MHA-FA [11-13]. These results confirmed that the multi-exponential regression analysis is a valid approach to estimate the bioavailability of Met sources and resulted in a similar bioefficacy as liquid MHA-FA. Additionally, 65DLM has been used to facilitate the practical verification of the difference in bioavailability of MHA-FA in field studies conducted under different diet and production conditions. Result of these trials have consistently demonstrated that 65DLM can replace MHA products in a 1:1 ratio, without requiring changes in the feed formulation and yielding similar performance results.

Penn State University:
Another successful Validation study

A recent study comparing MHA-Ca and 65DLM in standard and reduced crude protein (CP) level diets was conducted in collaboration with Penn State University [14]. A total of 3,072 Ross 708 male broilers received diets varying in Met source (none, MHA, or 65DLM) and CP (Standard or 2%-point Reduced), in a 2 × 3 factorial arrangement. Each treatment was fed to 16 replicate floor pens with 32 broilers per pen across a three-phase feeding program from 1 to 42 days. The results have shown that, regardless of dietary CP level, no differences were seen between MHA-Ca and 65DLM for body weight gain and feed conversion ratio (Figure 2).

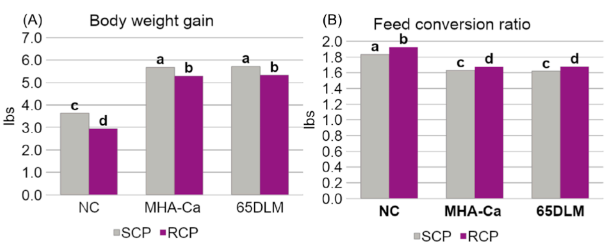

Figure 2: *(A) Body weight gain and (B) feed conversion ratio results from 1 to 42 days. (A) CP level: P<0.001; Met source: P<0.001; Interaction: P<0.001; SEM: 0.016; (B) CP level: P<0.001; Met source: P<0.001; Interaction: P<0.001; SEM: 0.015. NC – Negative control diet, no methionine supplemented; MHA-Ca – methionine hydroxy analogue calcium; 65DLM – 65% DL-Methionine + 35% limestone substituting MHA-Ca in a ratio 1:1; SCP – Standard crude protein diet; RCP – Reduced crude protein diet, 2%-point reduction in CP relative to SCP.*

However, when looking into the processing parameters, it was observed that the chilled carcass weight significantly favored 65DLM, followed by MHA-Ca, and lastly the negative control, without Met supplementation (Figure 3, A). The difference between the non-supplemented birds was visually detected, with the deficient bird being significantly smaller (Figure 3, B).
Similar results were observed for breast weight and yield. In the standard CP diet, the 65DLM

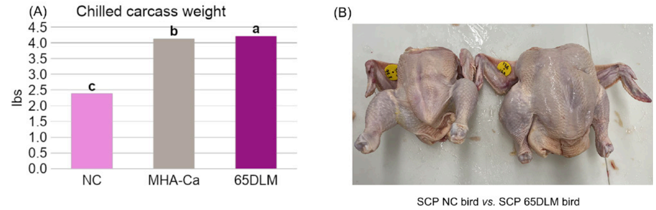

Figure 3: *(A) Chilled carcass weight from 1 to 42 days and (B) chilled carcass visual comparison between standard crude protein negative control bird (left) and standard crude protein 65DLM-fed bird (right). (A) CP level: P<0.01; Met source: P<0.01; Interaction: P=0.120; SEM: 0.212. NC – Negative control diet, no methionine supplemented; MHA-Ca – methionine hydroxy analogue calcium; 65DLM – 65% DL-Methionine + 35% limestone substituting MHA-Ca in a ratio 1:1.*

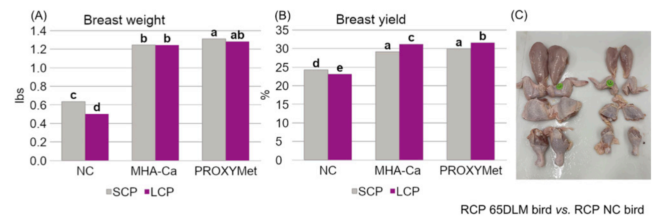

Figure 4: *(A) Chilled carcass weight from 1 to 42 days and (B) chilled carcass visual comparison between standard crude protein negative control bird (right) and standard crude protein 65DLM-fed bird (left). (A) CP level: P<0.01; Met source: P<0.01; Interaction: P=0.120; SEM: 0.212. NC – Negative control diet, no methionine supplemented; MHA-Ca – methionine hydroxy analogue calcium; 65DLM – 65% DL-Methionine + 35% limestone substituting MHA-Ca in a ratio 1:1.*

group had significantly greater breast weight and yield than MHA-Ca, and the negative control showed the lowest values. The same trend was not seen in the reduced CP diet, with no differences between MHA-Ca and 65DLM (Figure 4, A and B). It was also possible to observe that the carcass cuts were substantially smaller in the negative control-fed bird compared to the one fed with 65DLM (Figure 4, C), demonstrating the importance of methionine for proper growth and muscle deposition.
This study is a clear demonstration that 100 units of MHA leads to equivalent body weight gain and feed conversion ratio to 65 units of DL-Met. However, DL-Met showed a potential to improve meat yield, which could be related to greater Met+Cys deposition compared to MHA and its lower bioefficacy.

New meta-analysis confirms historical and recent results

These results are in line with a large number of broiler trials in which 100 units of MHA were compared with 65 units MetAMINO®. A meta-analysis evaluating effect sizes quantified using Hedges'g with 95% confidence interval (difference between DL-Met and MHA groups) of 76 feed conversion ratio responses revealed that none of the feed conversion ratio values analyzed differed between MHA and DL-Met (65 parts DLM, 100% homogeneity among data sets) [15]. Similar results were found for weight gain, which overall confirms that the recommended bioavailability is applicable under any nutritional and production condition without impacting broiler performance but allowing for substantial cost savings.

Contact your Evonik representative if you would like to validate the 100 MHA:65 DLM approach in your operation, with guaranteed results by our experts. Additional studies showing the benefit of using DL-Methionine, as well as a benefit calculator can be found at

metAMINO.Evonik.com.

Calculate your methionine savings

with Evonik's MetAMINO® Calculator, and brush up on academic research and field trial results with the MetAMINO® Atlas

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