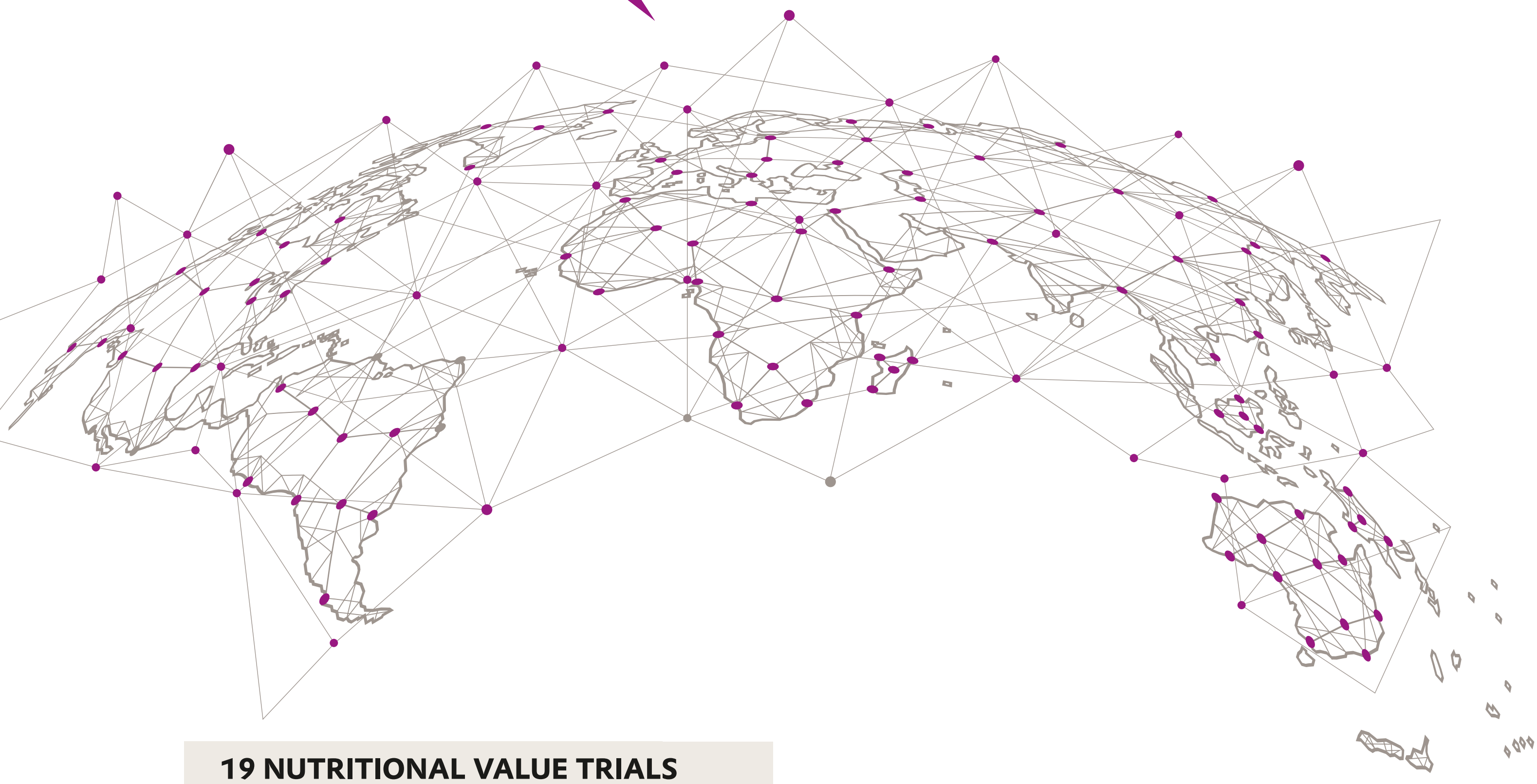
MetAMINO® ATLAS

EDITION 2

BECAUSE IT'S ABOUT

RESULTS



19 NUTRITIONAL VALUE TRIALS

2 MILLION BIRDS

AMINO ACID RECOMMENDATIONS

META ANALYSIS

EVONIK
Leading Beyond Chemistry

Executive Summary

Dear reader,

Welcome to the 2nd edition of the MetAMINO® ATLAS.

Evonik recommends a bioefficacy of 65% for methionine hydroxy analog free acid and its calcium salt (MHA-FA/Ca) relative to DL-methionine (DL-Met). On the following pages you will find the most comprehensive set of studies challenging and validating the relative bioefficacy (BE) of 65% under various conditions in many countries around the world within the last two years.

The 2024 ATLAS covers:

- *19 trials conducted in 12 countries on 4 continents with*
- *> 2,000,000 broilers, layers, swine and aqua species*

While same performance was achieved in all trials when 100 units MHA-FA/Ca were replaced with 65 units of MetAMINO®, there were significant savings when DL-methionine was used.

Various species

The majority of trials used broilers. However, trials with pigs, laying hens and tilapia were performed with the same conclusion that 100 units MHA-FA/Ca can be replaced by 65 units DL-methionine without compromising performance. In this context, research on methionine sources in turkey nutrition has been compiled and analyzed in a comprehensive review. Accordingly, the 65%-bioefficacy concept is recommended for turkeys, too (article no. 3).

Various farm sizes

Trials were conducted in small-sized pen facilities but also under commercial conditions. The largest trials were carried out with 838,000 and 379,300 ducks in China (trials no. 16, 18), 408,500 broilers in Germany (trial no. 8), 217,000 broilers in Brazil (trial no. 1), 212,000 broilers in China (trial no. 17) and 120,000 laying hens in China (trial no. 19).

Various trial conditions

The trials were conducted not only under commercial feeding conditions but also at different nutritional settings. Various trials (trials no. 3, 4, 6, 7, 9, 10, 12, 13, 14) validated applicability of a 65% relative bioefficacy for MHA-FA, not only at optimal Met+Cys specification, but also at suboptimal Met+Cys specifications. At suboptimal Met+Cys supply, the 100:65-challenge test has higher sensitivity and would thus provide an even stronger confirmation. Also, crude protein levels were reduced for the same intention (trials no. 5, 10). That the recommended relative bioefficacy of 65% for MHA products is applicable at any nutritional setting was also confirmed by a recent meta-analysis (article no. 25).

Various products

The recommended bioefficacy of 65% relative to DL-methionine applies for both liquid MHA-FA and MHA-Ca. The recommended bioefficacy of 65% relative to DL-methionine applies for both liquid MHA-FA and dry MHA-Ca. As liquid MHA-FA is more widely used than dry MHA-Ca, the large majority of the trials were carried-out with liquid MHA-FA. However, the recommendation was also validated for MHA-Ca (trials no. 2, 5, 6, 7). In addition, one trial confirmed that L-methionine has the same bioefficacy as DL-methionine (trial no. 2).

All these results impressively suggest that the 65%-bioefficacy concept is universally applicable!

It is applicable for all MHA products, in all monogastric farm and aqua species, under any nutritional settings, under any climate and production conditions, and at any time!

Acidifying, anti-oxidant and other physiological properties of MHA-FA

While empirical examinations presented in this present compilation and elsewhere are the net outcome of growth response, digestion processes and other physiological processes, there is still an ongoing discussion whether MHA products might have any other added value. The background, why in particular MHA-producers are interested in this, has been summarized in a review (article no. 5).

Trial no. 14 proves that birds do not benefit when MHA-FA is supplemented instead of DL-methionine, neither in regard to acidifying properties for replacing organic acid additives to reduce diet costs nor with showing higher anti-oxidant (microbial) benefits and gut health advantages. Research presented in article no. 13 reported a better absorption of DL-methionine compared to MHA-FA. Another paper (article no. 19) provides evidence that transformation of MHA into L-methionine releases H_2O_2, which is a reactive oxygen species causing oxidative stress to the animals.

Novelties in the 2nd edition of the MetAMINO® Atlas

In addition to the section where all recent animal feeding trials are presented, the MetAMINO® ATLAS also contains a few novelties such as

***NEW Section 2:** Videos covering the pros and cons of supplementing MHA-FA/Ca versus DLM*

***NEW Section 3:** Amino Acid recommendations for broilers, laying hens, ducks, turkeys, swine and aqua species*

*Finally, several abstracts and articles about the most relevant scientific works and papers covering the nutritional value of DL-Met compared to different sources are listed in section 4. Those comprise topics such as "**DL-methionine: The first methionine source,**" and other advantages of MetAMINO®: easy-to-handle dry form, precise dosing, good flowability, convenient storage and high quality. This section is closed with articles on sustainability aspects of MetAMINO®.*

Meta-Analysis

A comprehensive evaluation, including 76 pairs of treatments, providing clear evidence that not only can MHA-FA be replaced by DL-Met in a 100:65 ratio with no risk to animal performance, but also that this conclusion is valid for any general dietary Met-Cys supply status.

If you want to know how much you can save when switching from liquid MHA-FA to DL-Met, please feel free to download the new MetAMINO® Calculator App (page 58) or contact your Evonik representative.

Trust in science. Trust 65

Dr. Dirk Höhler
Head of Product Line Essential Nutrition

Nils Niedner
Director Product Management MetAMINO®

Sustainability is very important to us, which is why there are 2 versions of the MetAMINO® Atlas.

Limited number of printed copies available on request from your local Evonik representative.

Digitally and interactively as a full version with additional content that you can access with a click. Download the online version at **metamino.com** or by scanning below bar code.

Content

BECAUSE IT'S ABOUT

TRIALS

Section 1

Trials

Go to trial

Overview

Performance trials comparing the nutritional value of MetAMINO® (DL-methionine) or PROXYMet™ with MHA-FA/Ca

LATIN AMERICA

1	Brazil / 217,000 mixed-sex Cobb 500 broilers
2	Brazil / 1,334 Hy-line W-80 layers (35 weeks of age)

NORTH AMERICA

3	Mexico / 420 Bovans white layers (37 week of age)
4	USA / 1,350 Male Ross 708 broilers and 1,350 Male Cobb 500 broilers
5	USA / PROXYMet™ / 3,072 Male Ross 708 broilers

EUROPE

6	Portugal / 1,400 Juvenile male Nile tilapia; 22.5 gram
7	Spain / swine
8	Germany / 408,500 as hatched Ross 308 broilers in 10 houses at 1800 m^2
9	Finland / 720 male Ross 308 chicks
10	Finland / 1,440 male Ross 308 chicks
11	Hungary / 576 male Ross 308 broilers

MIDDLE EAST/AFRICA

12	Turkey / 792 day-old male Ross 308 chicks
13	Jordan / 2,500 as hatched Ross 308
14	Iran / 1,300 male Arbor Acers Plus day old chicks
15	Iran / 6,000 as hatched Ross 308 broilers

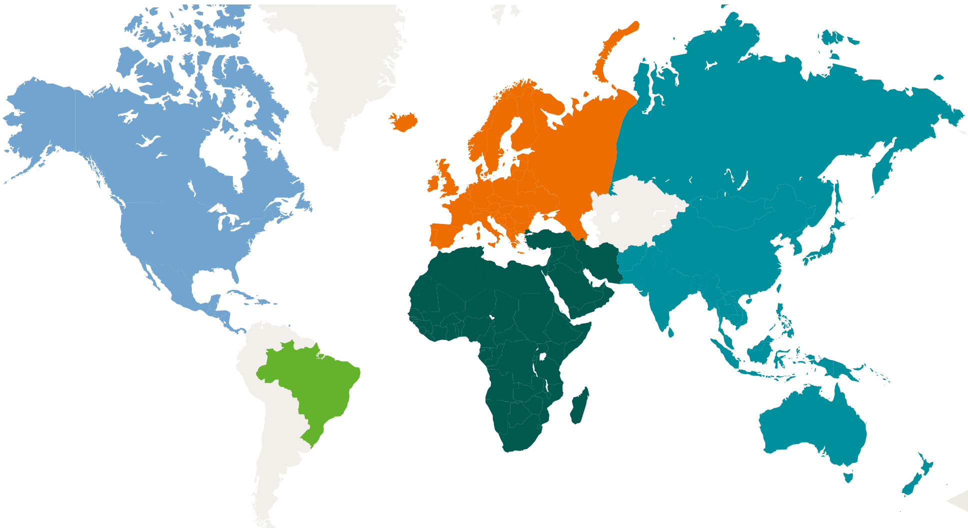
ASIA PACIFIC

16	China / PROXYMet™ / 838,000 Cherry Valley ducks
17	China / PROXYMet™ / 212,000 ROSS 308 broilers
18	China / PROXYMet™ / 379,300 Cherry Valley ducks
19	China / PROXYMet™ / 120,000 Hy-line brown laying hens

Highlights

Methionine and Cysteine are usually the first performance limiting amino acids in broiler feed and typically third limiting in swine diets. Commonly DL-methionine (99% purity), an amino acid, or methionine hydroxy analogue free acid (88% purity), an organic acid, are supplemented to meet those requirements.

The chemical differences between these two compounds influences their nutritional value, expressed as relative bioavailability (RBV), which has been confirmed in previous scientific publications to be at or close to 65% for MHA-FA relative to DL-Met on a product-to-product basis (Lemme et al. 2020; MetAMINO® ATLAS 2022; Li et al. 2023) and validated again with 19 new trials in the MetAMINO® ATLAS 2024.



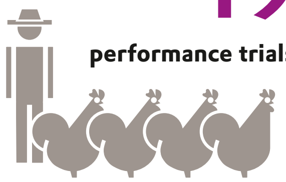
Brazil, Mexico, USA, Portugal, Spain, Germany, Finland, Hungary, Turkey, Jordan, Iran and China

The performance of over
2,000,000
birds was tested

Conducted on
4
continents

12
countries

19
performance trials



12 broiler

3 laying hen

2 duck

1 swine

1 aqua

- **All studies were successful and provided further evidence that 65 units of MetAMINO®** (DL-methionine) **achieves** same animal performance as 100 units of liquid methionine hydroxy analogue free acid or its calcium salt
- For practical application this means **feed and livestock producers can significantly reduce their methionine consumption** when switching from methionine hydroxy analogue products to MetAMINO® (DL-methionine) and consequently apply the **65% relative bioefficacy** concept
- For the specific savings of the 19 trials, **please refer to the economic calculation of each individual trial**
- To quickly calculate your potential savings, please feel free to download the **MetAMINO® Calculator App** (page 58)

PROXYMet™

One small trial but one giant leap for your methionine savings

IMPORTANCE OF MEASURING RELATIVE BIOAVAILABILITY IN METHIONINE SOURCES

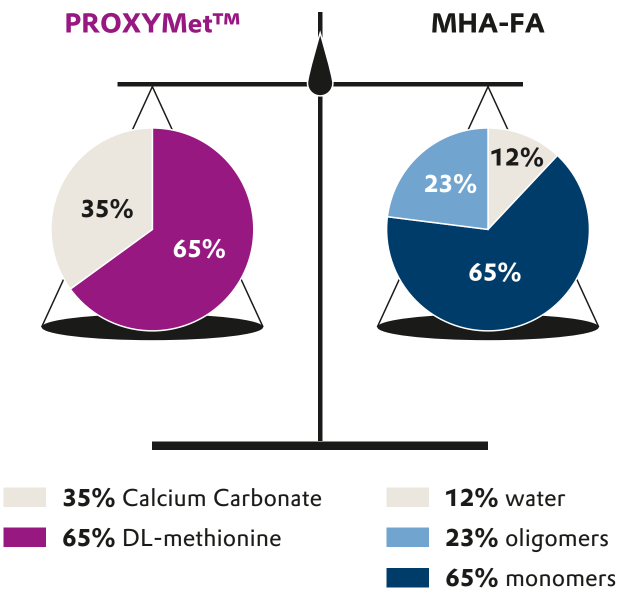
Background

Methionine and Cysteine are usually the first performance limiting amino acids in broiler feed and typically third limiting in swine diets. Commonly DL-methionine (99% purity), an amino acid, or methionine hydroxy analogue free acid (88% purity), an organic acid, are supplemented to meet those requirements.

The chemical differences between the two compounds influences their nutritional value, expressed as relative bioavailability (RBV), which has been confirmed in previous scientific publications to be 65% for MHA-FA relative to DL-Met on a product-to-product basis (e.g. Lemme et al. 2020 Li et al., 2023).

Objective

To allow customers to easily prove to themselves the 65 RBV, Evonik developed PROXYMet™ (Graph 1), a mixture of ~ 65% DL-methionine and ~ 35% carrier (calcium carbonate without any nutritional value), to replace MHA-FA/Ca on a product-to-product basis, one to one, while everything else stays the same: same feed composition, same diet specification, same feeding procedure.



Start your trial

Getting started is as easy as one, two, three: Contact your local Evonik representative, for implementation support, conduct a free trial, and see the savings with PROXYMet™.

Step 1 We'll set up a test run in your commercial operation under real conditions, with PROXYMet™. Application: replace MHA-FA or MHA-Ca 1:1 with PROXYMet™.

Step 2 After completing the production cycle, animal performance of both treatments will be compared. No differences are expected.

Step 3 After demonstrating that the 65 percent bio-efficacy comparison works, Evonik will then assist customers to switch from liquid methionine hydroxy analogue to MetAMINO® to exploit the full savings you'll receive from adopting a few settings in the respective feed formulations.

Benefits

Thanks to its 100% bio-efficacy, your can decrease your methionine consumption, reduce your feed costs and benefit from the additional advantages of using MetAMINO®, including: high and consistent product quality, precise dosing, homogenous mixability, narrower safety margins, easy handling and storage.

Scan the QR code to watch the PROXYMet™ video

Latin America (Brazil)

1	Brazil / 217,000 mixed-sex Cobb 500 broilers
2	Brazil / 1,334 Hy-line W-80 layers (35 weeks of age)

Published in Poult. Sci. 102(E-Supplement 2):107

Large commercial validation of the replacement of DL-methionine-hydroxy analogue (MHA-FA) with DL-methionine (DLM) at 100:65 ratio in broilers produced under Brazilian conditions

Trial conducted at a commercial integration in Brazil

Trial location:
Brazil

Project team leaders:
P. Tomazini, P. Castelo, V. D. Naranjo, A. Lemme, J. Dorigam

TABLE 1: Trial Design, Methods and Materials

Animals	217,000 mixed-sex Cobb 500 broilers	
Diets	1) **MHA-FA:** Customer's commercial diets with MHA-FA (customer's BE of 82%)	
	2) **DLM:** Similar to Diet 1 but with DLM at 65 parts of MHA-FA levels (100:65 replacement)	
Design	**MHA-FA:** 5 tunnel broiler houses	
	(n = 128,000 broilers)	
	DLM: 4 tunnel broiler houses (n = 89,000 broilers)	
	Rearing conditions were similar across houses but capacities ranged from 21,000 to 29,000 broilers per house. Stocking densities varied between 10 to 12 broilers/m²	
Feeding	Commercial 4-phase feeding program	
	Starter	24% CP / 3,020 kcal/kg (1 to 7 d)
	Grower 1	21% CP / 3,100 kcal/kg (8 to 21 d)
	Grower 2	18% CP / 3,130 kcal/kg (22 to 30 d)
	Finisher	18% CP / 3,150 kcal/kg (31 to 45 d)
Parameters	Body weight gain, feed intake and feed conversion ratio	
Duration	1 – 45 days old	
Location	Commercial broilers houses in Brazil	

TABLE 2: Growth performance of mixed-sex broilers reared under commercial conditions from 1 to 45 days of age

Parameters	MHA-FA*	DLM	*P*-value
Average daily gain (g/d)	60.99	61.38	0.35
Final BW (kg)	2.74	2.67	0.90
FCR (kg feed/kg gain)	1.78	1.76	0.68
Adjusted FCR 2.9 kg	1.83	1.83	0.52
Mortality (%)	4.96	5.14	0.36
EPI	325	331	0.33

GRAPH 1: Economic benefits of replacing 100 parts MHA-FA with 65 parts of DL-Met

- Monthly broiler feed production = 23,000 MT
- Monthly MHA-FA demand = 70 MT
- Annual MHA-FA demand = 840 MT

MetAMINO® Value Calculator

Switch from MHA-FA to MetAMINO®	MHA-FA		MetAMINO®
MHA-FA demand in metric tons	840		
MetAMINO® ratio* to replace MHA-FA			65%
Equivalent MetAMINO® demand in metric tons			546
Price in $/€ per kg	1.75		2.20
Price ratio		80%	
Cost in $/€	1,470,000		1,201,200
saving with MetAMINO in $/€			268,800

*Evonik warrants that no significant statistical difference in animal performance, measured as feed conversion ratio (FCR) occurs when 100 parts MHA-FA are replaced with 65 parts MetAMINO® in the animal diet. The position of the "MetAMINO® ratio to replace MHA-FA" is proven by numerous scientific publications and performance trials under research as well as commercial conditions.

Trial **Design**

A large broiler commercial trial was conducted to determine the effect of replacing 100 parts of MHA-FA with 65 parts of DLM on growth performance of mixed sex broilers from 1 to 45 days of age reared under Brazilian production conditions.

A total of 217,000 one-day old Cobb 500 mixed-sex broilers were allocated to 9 tunnel broiler houses with similar rearing conditions according to integrators practice but with capacities ranging from 21,000 to 29,000 broilers per house.

Stocking densities across houses varied between 10 to 12 broilers/m^2. Broilers were fed the integrator´s commercial 4-phase feeding program.

Each feeding phase comprised 2 dietary treatments including 1) MHA-FA: control diet with MHA-FA formulated with the integrator´s RBV of 82% and 2) DLM: similar to diet 1 but with DLM at 65 parts of the MHA-FA levels.

The MHA-FA inclusion levels were: 0.44, 0.34, 0.27 and 0.27% and for DLM were: 0.29, 0.22, 0.18 and 0.18% for each feeding phase, respectively. The MHA-FA diet was offered to 5 broiler houses (total = 128,000 broilers) and the DLM diet to 4 broiler houses (89,000 broilers).

Trial **Objectives**

To validate the commercial application of a relative bioavailabililty (RBV) of 65% of MHA-FA vs. DLM, or in other words, the replacement ratio of 100:65 on growth performance of broilers under Brazilian commercial conditions.

Trial **Results**

Total mortality across houses ranged from 4 to 6% with an average of 5.0% for the MHA-FA and 5.1% for DLM.

Overall, broilers fed the MHA-FA diets and DLM diets had similar ADG (60.99 vs. 61.38 g/d), FCR (1.78 vs. 1.76 g/g) and adjusted FCR to 2.9 kg BW (1.83 vs. 1.83 g/g).

Similarly, the production efficiency factor was not affected by treatments with an average of 325 for MHA-FA and 331 for DLM.

Total savings with DLM account for US Dollar 268,800 (GRAPH 1).

CONCLUSION

Results from this large commercial trial demonstrate that replacing 100 parts of MHA-FA with 65 parts of DLM did not affect the growth performance of broilers but generated important economic savings under Brazilian production conditions.

A more precise and cost-effective Met+Cys nutrition includes: 1) optimal specification of Met+Cys, 2) accurate assessment of AA content in raw materials and 3) appropriate assessment of the nutritional value of supplemental Met sources

FEEDBACK

"With this practical trial, our customer confirmed the 65% RBV of MHA-FA under their production conditions allowing them to precisely meet their Met+Cys specifications and maximize performance and profitability."

Patricia Tomazini,
Technical Service Manager
Evonik Brazil

Performance comparison between DL-methionine, DL-methionine-hydroxy analogue (MHA-Ca), and L-methionine at a quantitative ratio of 65:100 in white layers in conventional cages

Trial conducted by Evonik, Federal University of Paraiba, Agrarian Center of Science - Poultry Science Sector

TRIAL 1 **2** 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

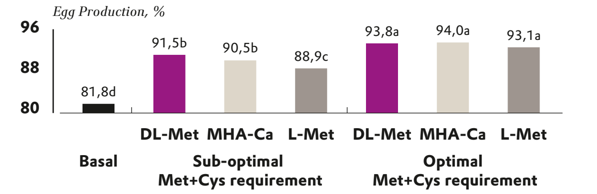
Trial location:
Paraiba/Brazil

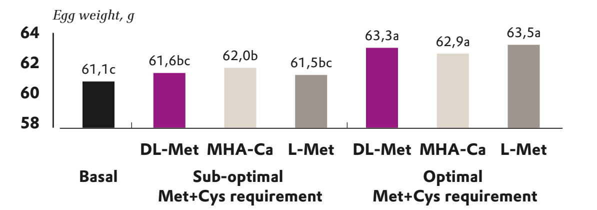
Project team leaders:
Dr. Perazzo; Dr. Dorigam; DVM. de la Cruz

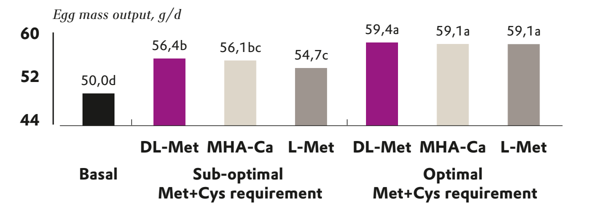
TABLE 1: Trial Design, Methods and Materials

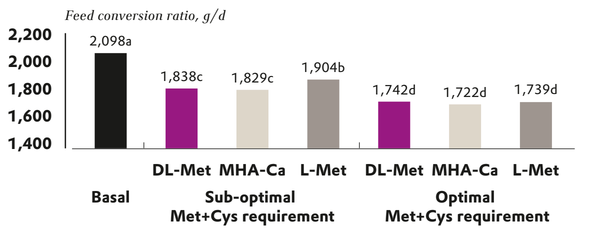
Animals	1,334 Hy-line W-80 layers (35 wk of age)
Diets	Corn-soybean meal based diets
Design	Completely randomized design with 7 trt / 8 reps / 24 hens each
Feeding	**T1)** Control with no supplemented methionine, deficient in in Met+Cys **T2)** Supplemented with 1.46 kg/t MHA-Ca (sub-optimal Met+Cys requirement) **T3)** Supplemented with 2.92 kg/t MHA-Ca (optimal Met+Cys requirement) **T4)** Supplemented with 0.95 kg/t MetAMINO® (sub-optimal Met+Cys requirement) **T5)** Supplemented with 1.90 kg/t MetAMINO® (optimal Met+Cys requirement) **T6)** Supplemented with 0.95 kg/t L-methionine (sub-optimal Met+Cys requirement) **T7)** Supplemented with 1.90 kg/t L-methionine (optimal Met+Cys requirement)
Parameters	Egg production, egg weight, feed intake, egg mass, feed conversion ratio
Duration	32 weeks (35 to 57 wk of age)
Location	Federal University of Paraiba, Agrarian Center of Science - Poultry Science Sector

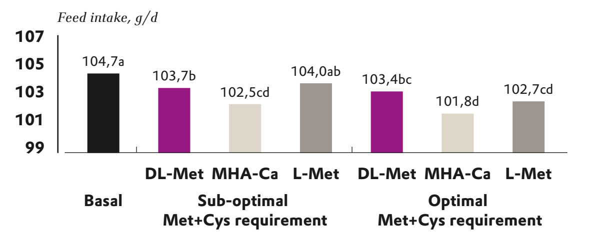
GRAPHS 1, 2, 3, 4, AND 5: Performance parameters when supplementing MHA-Ca (100%), DL-methionine (65%) and L-methionine (65%) at sub-optimal and optimal methionine + cysteine requirement











Means with different superscript differ significantly (P<0.05)

Trial **Design**

The trial was designed (Table 1) in cooperation with Federal University of Paraiba, Agrarian Center of Science - Poultry Science Sector in Brazil.

Trial **Objectives**

The objective of the study is to provide evidence that the replacement of MHA-Ca by MetAMINO® or L-methionine at a 100:65 ratio works at different general Met+Cys levels. As well as offer evidence of the interchangeability of L-methionine with MetAMINO® at 100:100 ratio at different general supplementation levels.

Trial **Results**

Diets deficient in Met+Cys negatively affected layers performance compared to supplemented diets. Moreover, sub-optimal Met+Cys level resulted in lower performance compared to those hens fed adequate Met+Cys levels.

There were no significant differences in productive performance (Graphs 1 – 5) between MHA-Ca, MetAMINO® or L-methionine treatments at adequate Met+Cys levels when the 100:65 ratio was used. Moreover, at sub-optimal levels, there was no difference between MHA-Ca and MetAMINO® at 100:65 ratio but L-Met provided significant worse FCR and egg production.

Overall, replacement of MetAMINO® or L-methionine by MHA-Ca at a quantitative ratio of 65:100 (MetAMINO® or L-methionine : MHA-Ca) had no negative effects on any of the performance parameters in laying hens when supplied at adequate Met+Cys levels and so confirms the outcome of previous regional trials for laying hens in production (de la Cruz, 2018; Santiago, 2017). Additionally, L-Met performed slightly worse under sub-optimal Met+Cys levels.

CONCLUSION

Replacement of MHA-Ca with MetAMINO® or L-methionine in a 100:65 ratio did not compromise any performance parameters of laying hens at adequate Met+Cys levels.

Interchangeability of MetAMINO® with L-methionine in a 100:100 ratio did not have any effect on the performance parameters of laying hens at adequate Met+Cys levels.

Replacement of MHA-Ca with MetAMINO® at 100:65 ratio in sub-optimal Met+Cys levels resulted in similar performance, but L-Met resulted in slightly worse performance.

FEEDBACK

"Trial results show that replacing 100 parts of MHA with 65 parts of DL-Methionine or L-Methionine, as well as replacing DL-Methionine with L-methionine in a 1:1 ratio, yield similar performance parameters of laying hens."

Dr. Fernando Guilherme Perazzo Costa,
Professor at Universidade Federal da Paraíba

North America

Performance comparison between DL-methionine and DL-methionine-hydroxy analogue (MHA-FA) at a quantitative ratio of 65:100 in white layers in conventional cages

Trial conducted by Evonik and the National Autonomous

TRIAL 1 2 **3** 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

Trial location:
Mexico City / Mexico

Project team leaders:
Dr. Avíla; DVM. de la Cruz; DVM. Santiago

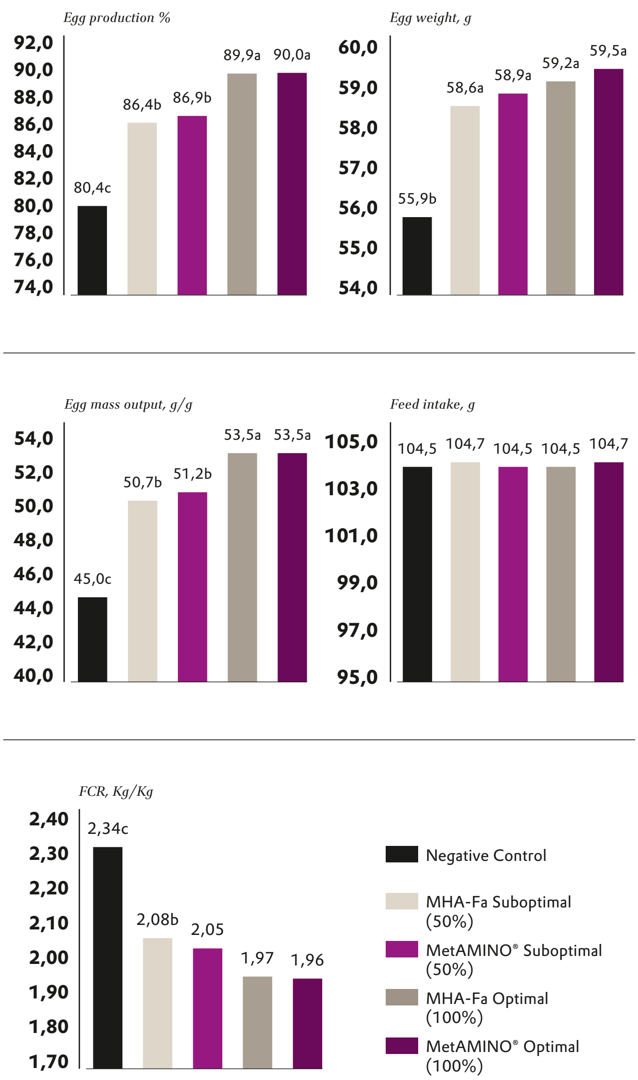
TABLE 1: Trial Design, Methods and Materials

Animals	420 Bovans white layers (37 wk of age)
Housing:	Conventional cages - access 3 hens per cage with a space per bird of 400 cm^2
Diets	Corn-soybean meal based diets
Design	Completely randomized design with 5 trt / 7 reps / 12 hens each
Feeding	**T1)** Control with no supplemented methionine source, deficient in Met+Cys **T2)** Supplemented with 1.12 kg/t MHA-FA (sub-optimal Met+Cys spec) **T3)** Supplemented with 0.73 kg/t MetAMINO® (sub-optimal Met+Cys spec) **T4)** Supplemented with 2.25 kg/t MHA-FA (optimal Met+Cys spec) **T5)** Supplemented with 1.46 kg/t MetAMINO® (optimal Met+Cys spec)
Parameters	Egg production, egg weight, feed intake, egg mass, feed conversion ratio
Duration	12 weeks (37 to 49 wk of age)
Location	Experimental farm in Mexico City

TABLE 2: Economic analysis for optimal Met+Cys req

		Hens fed MHA-FA 100%	Hens fed MetAMINO® 65%
Number of Hens		1,000,000	1.000.000
Period, days	x	365	365
Daily feed consumption, g	x	104.5 g	104.5 g
Total feed consumption, t	=	38,142 t	38,142 t
Dosing of product, kg/t	x	2.25 kg	1.46 kg
Required product, t	=	85.819	55.687
Purchasing price of product, €/kg*	x	1.85	2.30
Product cost, €	=	158,765	128,080
Difference of cost for products	–		**-30,685.00**

GRAPHS 1, 2, 3 4 & 5: Optimal methionine + cysteine requirement performance parameters when supplementing MHA-Fa (100%), DL-methionine (65%)



Means with different letters (a, b, c) differ significantly (P<0.05)

SEE SECTION 4, ARTICLE NO. 14

Trial **Design**

The trial was designed (Table 1) in cooperation with National Autonomous University of Mexico, Faculty of Veterinary Medicine and Husbandry at the Center for Teaching, Research and Extension in Poultry (CEIEPAv).

Trial **Objectives**

The objective of the study is to provide evidence of the interchangeability of MHA-FA with MetAMINO® at a 100:65 ratio at different general supplementation levels.

Trial **Results**

Diets deficient and reduced in Met+Cys negatively affect layers performance. Supplemented methionine is essentially required for optimized performance of laying hens.

There were no significant differences in productive performance (Graphs 1 – 5) between corresponding MHA-FA or MetAMINO® treatments at a quantitative ratio of 100:65.

The study revealed significant financial savings and improved farm profitability for the MetAMINO® treatment (Table 1). In this economic scenario, MHA–FA has to be offered at a lower price than 1.49 €/kg to be competitive.

Overall, a replacement of MHA-FA by MetAMINO® at a quantitative ratio of 100:65 (MHA-FA : MetAMINO®) had no negative effects on any of the performance parameters as well as egg quality criteria (not shown) in laying hens and so confirms the outcome of previous regional trials for laying hens in production.

CONCLUSION

Replacement of MHA-FA with MetAMINO® in a 100:65 ratio did not compromise any performance parameters of laying hens nor egg quality.

Replacement of MHA-FA with MetAMINO® in a 100:65 ratio reduced feed production cost, due to economic savings.

FEEDBACK

"No doubt about the interchangeability of the methionine sources at a ratio of 100:65 (MHA-product to DL-Methionine) and most important: this has significant economic advantages"

DVM. Carlos de la Cruz,
Evonik Operations GmbH,
Nutrition & Care

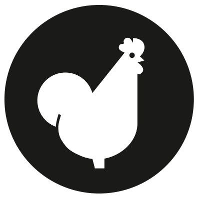
2021 Poult. Sci. 100 (E-Suppl 1), Page 63, Abstract 124

Evaluating the ideal total sulfur amino acid requirements for fast growing and high-yielding broilers utilizing different sources of methionine.

Mississippi State University, Mississippi, USA in collaboration with a commercial poultry integrator

TRIAL 1 2 3 **4** 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

Trial location:
Mississippi State University, MS, USA



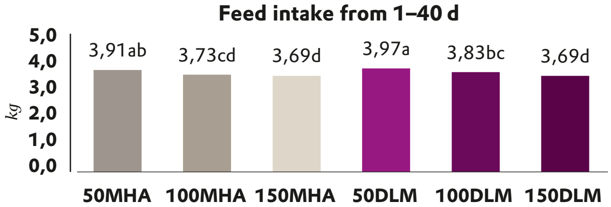
Project team leaders:
Prof. Dr. K. Wamsley, Dr. J. Wen, Dr. K. Smith, Dr. J. Dorigam, Dr. F. L. S. Castro

TABLE 1: Trial Design, Methods and Materials

Animals	1,350 Male Ross 708 broilers 1,350 Male Cobb 500 broilers
Diets	Corn and soybean-meal based diets
Design	Randomized Complete Block Design, in a factorial arrangement 2 by 6, with 12 treatments, 9 replicates of 25 birds each
Feeding	Cobb 500 or Ross 708 receiving: 1) **100MHA: Standard diet with MHA (reference value, 100%)** SID Met+Cys (%)=0.947 (starter), 0.874 (grower), 0.796 (finisher). 2) **100DLM: DLM at 65% of MHA in trt 1** 3) 150MHA: MHA level at 150% of trt 1 SID Met+Cys (%)=1.155 (starter), 1.081 (grower), 1.003 (finisher). 4) **150DLM: DLM at 65% of MHA in trt 3** 5) **50MHA: MHA level at 50% of trt 1** SID Met+Cys (%)=0.740 (starter), 0.667 (grower), 0.588 (finisher). 6) **50DLM: DLM at 65% of MHA in trt 5** *SID Lys (%) = 1.28 (starter), 1.15 (grower), 1.02 (finisher) across all treatment diets.
Traits	Body weight gain, feed intake, feed conversion ratio, carcass and cuts yield
Economic analysis	Feed cost was calculated based on ingredient costs in the USA and the feed intake of birds. The economic return on breast meat was calculated using the total breast weight of the treatment and the USDA report price cent per kg of breast meat. For both analyses, only 100MHA and 100DLM groups were used
Duration	From 1 to 40 days of age
Location	Mississippi State University, MS, USA

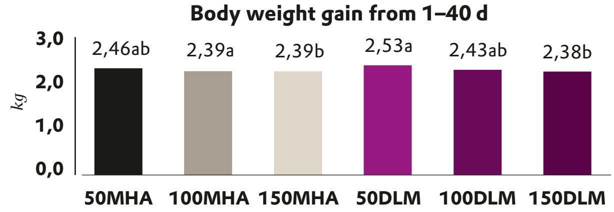
GRAPHS 1 TO 3: Feed intake, body weight gain, and feed conversion ratio from 1-40 days of age

Feed intake from 1–40 d



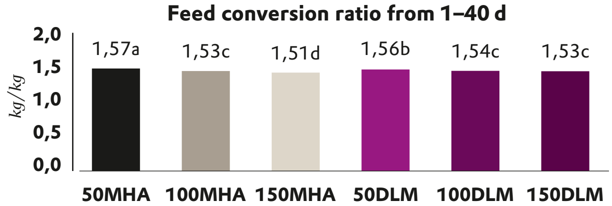
Strain: P<0.0001; Met source: P<0.0001; Interaction: P=0.931; SEM: 0.039

Body weight gain from 1–40 d



Strain: P<0.001; Met source: P=0.003; Interaction: P=0.818; SEM: 0.03

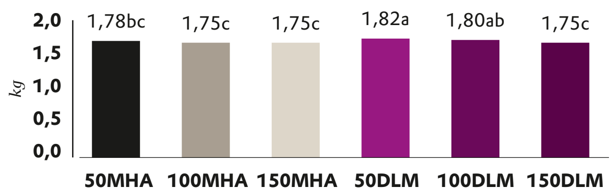
Feed conversion ratio from 1–40 d



Strain: P=0.0002; Met source: P<0.0001; Interaction: P=0.898; SEM: 0.005

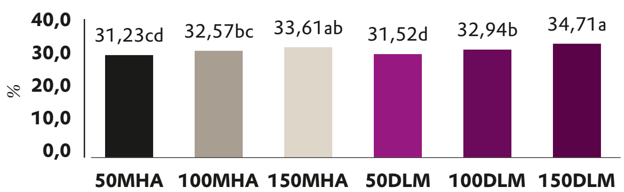
GRAPHS 4 & 5: Carcass weight and breast yield at 41 days

Carcass weight at 41d



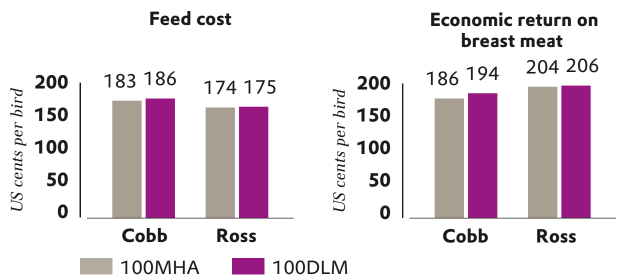
Strain: P<0.0001; Met source: P<0.0001; Interaction: P=0.370; SEM: 0.006

Breast yield at 41d



Strain: P<0.0001; Met source: P<0.0001; Interaction: P=0.081; SEM: 0.436

GRAPH 6: Economic analysis



SEE SECTION 4, ARTICLE NO. 7

Trial **Design**

The trial was designed (Table 1) to compare the use of 65 parts of DL-Methionine replacing 100 parts of liquid MHA at different MHA inclusion levels in two commercially used broiler strains.

Trial **Objective**

To validate that 65 parts of DL-Met can replace 100 parts of MHA, while maintaining performance and processing yields, regardless of the MHA inclusion level in the diet and the broiler genetic line.

Trial **Results**

From 1-40 days, no interaction between Met sources and broiler strain was found for any performance parameter. Therefore, focus was placed on the differences between the Met sources.

The FI from 1-40 days (Graph 1) was similar between DL-Met and MHA for the standard diet (set as 100%) and diet with 150% of the MHA of the standard diet. However, when 50% of the MHA of the standard diet was used, DL-Met birds ate 6 grams more feed. This response could have been led by a marginal Met+Cys deficiency when this low level was used.

The BWG was similar between DL-Met and MHA, regardless of the MHA inclusion level in the diet (Graph 2). Interestingly, as a result from higher feed intake, birds fed 50DL-Met had statistically higher BWG than 100MHA, 100DLM, 150MHA and 150DLM, and grew 7 grams more than its 50MHA counterpart (numerical difference).

The FCR (Graph 3) was similar between MHA and DL-Met in the standard diet, but better for MHA when a higher MHA level was used (150% of the standard), and better for DL-Met when a lower MHA level was used (50% of the standard).

The carcass weight at 41 days (Graph 4) was higher in DL-Met fed birds in 100DLM vs. 100MHA and 50DLM vs. 50MHA, but both sources were similar when 150% of MHA of the standard diet was used.

The breast yield at 41 days (Graph 5) was statistically similar between sources for all the MHA levels used (100, 150, and 50%). However, DL-Met fed birds had, on average, 0.6 percent-point higher breast yield than MHA-fed birds.

On average, the feed cost of 100DLM (cents/bird) was 2 cents higher than 100MHA, due to the numerically higher feed intake of 100DLM vs. 100MHA. However, the economic return based on breast meat (cents/bird) was, on average, 5 cents higher for 100DLM vs. 100MHA (Graph 6).

CONCLUSION

65 parts of MetAMINO® can successfully replace 100 parts of MHA, regardless of the MHA level in the diet or broiler strain, maintaining similar performance.

Modern broilers' performance is dependent on SID Met+Cys levels, as lower levels might lead to a compensatory increase in feed intake, without reflecting at increased breast meat yield.

The economic return based on breast meat (cents/bird) was, on average, 5 cents higher for DL-Met than MHA.

The reduction of MHA level to 50% below the standard inclusion level is not recommended, as it can get the birds close to a marginal Met+Cys deficiency.

FEEDBACK

"Replacing 100 parts of MHA with 65 parts of DL- methionine showed similar performance and better economic return under US commercial broiler production conditions."

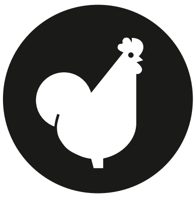
Ph.D. James Wen,
Senior Technical Service Manager and Account Manager

Effects of replacing dietary Methionine Hydroxy Analog Calcium (MHA-Ca) with PROXYMet™ on broiler performance and processing yield in diets with different crude protein levels

Trial conducted at Penn State University, Pennsylvania, USA

TRIAL 1 2 3 4 **5** 6 7 8 9 10 11 12 13 14 15 16 17 18 19

Trial location:
Penn State University, Pennsylvania, USA



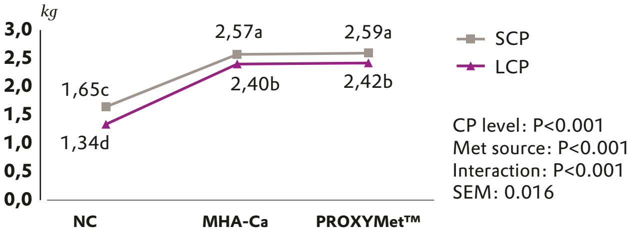
Project team leaders:
Prof. Dr. John Boney, Dr. F. L. S. Castro, Dr. J. Wen, D. Boontarue

TABLE 1: Trial Design, Methods and Materials

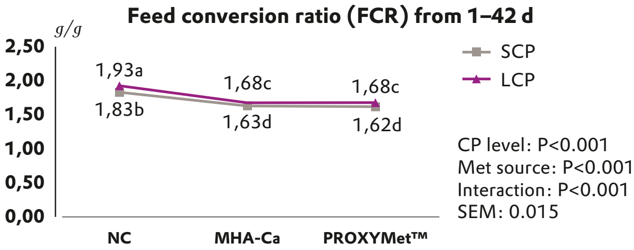
Animals	3,072 Male Ross 708 broilers
Diets	Corn and soybean-meal based diets
Design	Randomized Complete Block Design, in a factorial arrangement 2 by 3, with 6 treatments, 16 replicates of 32 birds each
Feeding	• Standard crude protein (SCP) without Met supplementation (NC), with MHA-Ca or with **PROXYMet™** • Low crude protein (-2% reduction from SCP, LCP) without Met supplementation (NC), with MHA-Ca or with **PROXYMet™**
Parameters	Body weight gain, feed intake, feed conversion ratio, carcass and cuts yield, footpad dermatitis scoring, litter moisture
Duration	From 1 to 42 days of age
Location	Penn State University, Pennsylvania, USA

GRAPHS 1 AND 2: Body weight gain (BWG, kg) and feed conversion ratio (FCR) from 1-42 days

Body weight gain (BWG) from 1–42 d

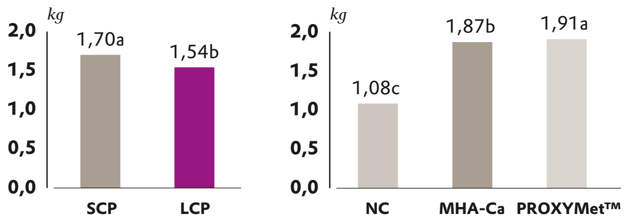


Feed conversion ratio (FCR) from 1–42 d



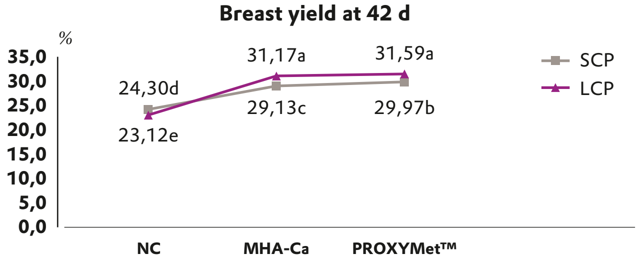
GRAPHS 3 & 4: Chilled carcass weight (kg) and breast yield (%) at 42 days

Chilled Carcass weight at 42 d



CP level: P<0.01; Met source: P<0.01; Interaction: P=0.120; SEM: 0.212

Breast yield at 42 d



CP level: P=0.001; Met source: P<0.001; Interaction: P<0.001; SEM: 0.282

TABLE 2: Thigh yield (%), drumstick yield (%), and wing yield (%) at 42 days

Main effect	Treatment	Thigh (%)	Drumstick (%)	Wing (%)
Crude protein level	**SCP**	16.83 **a**	15.58 **a**	12.08
	LCP	16.15 **b**	14.96 **b**	12.50
	P-value	<0.001	<0.001	0.386
Methionine source	**NC**	17.53 **a**	16.77 **a**	12.99
	MHA-Ca	16.09 **b**	14.68 **b**	11.64
	PROXYMet™	15.86 **b**	14.36 **b**	12.25
	P-value	<0.001	<0.001	0.084

SEE SECTION 2, VIDEO NO. 2

SEE SECTION 2, VIDEO NO. 4

SEE SECTION 4, ARTICLE NO. 8

SEE SECTION 4, ARTICLE NO. 16

Trial **Design**

The trial was designed (Table 1) to allow the direct comparison between 100 parts of MHA-Ca and 65 parts of DL-Met (PROXYMet™, 650 g MetAMINO® + 350 g limestone) supplemented in a Met+Cys deficient basal diet with different crude protein levels.

Trial **Objective**

To validate that 65 parts of DL-Met can replace 100 parts of MHA, while maintaining performance and processing yields in diets containing standard or reduced crude protein levels.

Trial **Results**

The use of 65 parts of DL-Met led to similar body weight gain and feed conversion ratio than 100 parts of MHA-Ca (graphs 1 and 2), regardless of crude protein level in the diet. Diet without Met supplementation showed the worst performance resuts.

Overall, the use of 65 parts of DL-Met resulted in significantly higher chilled carcass weight compared to MHA-Ca and the Met+Cys deficient diet (1.91 kg vs. 1.87 and 1.08 kg, for PROXYMet™, MHA-Ca, and NC, respectively; Graph 3).

The breast yield was significantly higher in PROXYMet™ than MHA-Ca and the NC when birds received SCP diets (31.6% vs. 31.2 and 23.1% for PROXYMet™, MHA-Ca, and NC, respectively; Graph 4). However, in birds receiving LCP, no differences were seen between PROXYMet™ and MHA-Ca.

Both PROXYMet™ and MHA-Ca showed similar thigh, drumstick, and wing yields (Table 2).

The reduction of 2 percent-points in crude protein in all phases resulted in reduced performance and carcass/cuts weight (Graphs 1-4). The low crude protein diet, however, significantly reduced the litter moisture content and footpad dermatitis scoring (data not shown). The crude protein reduction, in this study, was too severe and amino acid imbalances and deficiencies might have occurred.

CONCLUSION

65 parts of MetAMINO® (PROXYMet™) can successfully replace 100 parts of MHA-Ca, regardless of the crude protein level in the diet, maintaining similar performance.

PROXYMet™ use resulted in overall higher chilled carcass weight and higher breast yield in diets with standard crude protein levels, compared to MHA-Ca and the Met+Cys deficient diet.

When reducing crude protein levels, it is important to consider the feeding phase and essential and nonessential amino acid balance to avoid compromised performance.

FEEDBACK

"Trial results clearly show that replacing 100 parts of MHA with 65 parts of DL-Methionine yield similar broiler growth performance and processing parameters."

Dr. John Boney,
Assistant Professor of Poultry Science
Pennsylvanya State University

Europe

6	Portugal / 1,400 Juvenile male Nile tilapia; 22.5 gram
7	Spain / swine
8	Germany / 408,500 as hatched Ross 308 broilers in 10 houses at 1800 m^2
9	Finland / 720 male Ross 308 chicks
10	Finland / 1,440 male Ross 308 chicks
11	Hungary / 576 male Ross 308 broilers

Performance comparison between DL-methionine and DL-2-hydroxy-4-methylthiobutyrate (MHA-Ca) at a quantitative ratio of 65:100 in fish

Trial conducted by SPAROS Lda. and Evonik

TRIAL 1 2 3 4 5 **6** 7 8 9 10 11 12 13 14 15 16 17 18 19

Trial location:
SPAROS Lda. & UTAD, Vila Real, Portugal

Project team leaders:
Dr. Jorge Dias, SPAROS
Dr. Karthik Masagounder, Evonik

TABLE 1: Trial Design, Methods and Materials

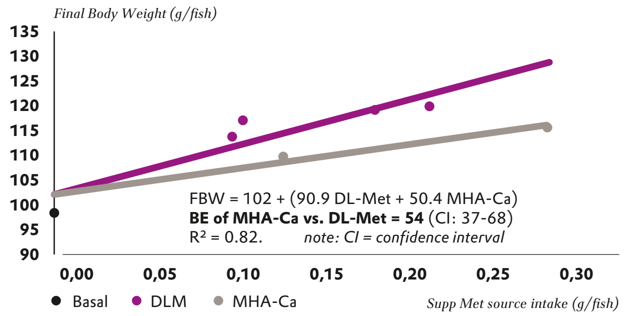
Animals	1,400 Juvenile male Nile tilapia; 22.5g
Diets	Soybean meal (35%), soy protein concentrate (9.8%), pea protein concentrate (6.7%), poultry meal (4.2%), wheat (29.8%) and wheat bran (7.4%) based diets; extruded
Design	Completely randomized design involving 7 dietary treatments with 4 replicate tanks per treatment and 50 fish per tank
Treatments	D1 -> without any supplemental Met source (0.43% Met & 0.91% Met+Cys) D2 and D3 -> with DL-Met at 0.10 and 0.20% (analyzed levels 0.09 & 0.19%) D4 and D5 -> with MHA-Ca at 0.154 and 0.308% (analyzed levels 0.12 & 0.25%) D6 and D7 -> with PROXYMet™ at 0.154 and 0.308% (analyzed levels 0.15 & 0.25%)
Parameters	**Performance:** Final body weight (g/fish), specific growth rate (%/d), feed conversion ratio (FCR), protein retention efficiency (% intake) **Antioxidant status** (liver sample, 3 fish per tank at the end of trial): Catalase, total reduced glutathione (GSH) & oxidized glutathione (GSSG)
Duration	92 days
Location	University of Trás-os-Montes e Alto Douro (UTAD, Vila Real, Portugal) – trial was conducted under the full responsibility of SPAROS

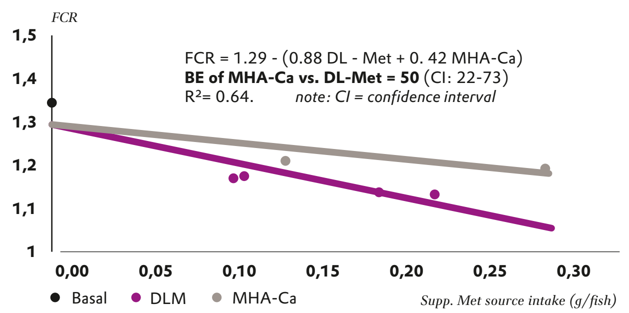
TABLE 2: Growth performance, feed conversion, protein retention and antioxidant capacity of tilapia fed different treatment diets

Diet	FBW g/fish	SGR %/day	FCR	PR % intake	CAT (U/mg protein)	GSH (µmol/g tissue)
D1_Basal	**98 a**	**1.60 a**	**1.34 b**	**31 a**	**26.4 a**	**2.06 a**
D2_0.1 DLM	114 bc	1.76 bc	1.17 a	37 bcd	29.3 ab	2.53 b
D3_0.2 DLM	**120 d**	**1.82 c**	1.13 a	**40 d**	**35.0 b**	**2.66 c**
D4_0.15 MHA	110 b	1.72 b	1.21 a	36 b	30.0 ab	2.52 b
D5_0.31 MHA	116 cd	1.77 bc	1.19 a	36 bc	30.9 ab	2.54 b
D6_0.15 Proxy	117 cd	**1.79 c**	1.17 a	37 bcd	30.1 ab	2.51 b
D7_0.31 Proxy	**119 d**	**1.81 c**	1.14 a	**39 cd**	31.1 ab	2.62 bc
ANOVA p-val.	<0.01	<0.01	<0.01	<0.01	0.02	< 0.01

Note: FBW – final body weight, SGR – specific growth rate, FCR – feed conversion ratio, PR – protein retention, CAT – catalase, GSH – total reduced glutathione

GRAPH 1 & 2: Biological efficiency of Met sources on the final body weight & FCR of tilapia on day 92





SEE SECTION 4, ARTICLE NO. 9

Trial **Design**

The trial was designed (Table 1) to allow the direct comparison between 100 parts of MHA-Ca and 65 parts of DL-Met (provided as MetAMINO® containing 99% DL-Met or PROXYMet™ containing 65% MetAMINO® and 35% limestone) supplemented in a Met deficient basal diet.

Trial **Objective**

The objective of this study was to validate the 65% average biological efficiency of MHA-Ca versus DL-Met, on a product basis, based on the growth performance of Nile tilapia.

Trial **Results**

Basal diet deficient in Met produced significantly lower performance (body weight, growth and FCR), protein retention, and lower antioxidant capacity compared with those of Met supplemented diets.

Supplementing the basal diet with different Met sources (DL-Met; MHA-Ca) significantly improved fish performance, protein retention and their antioxidant capacity (Table 2).

Among the sources, DL-Met (MetAMINO®; PROXYMet™) fed group showed higher performance and nutrient retention than those fed the MHA-Ca although they were supplemented only 65 parts compared with 100 parts of MHA-Ca.

Slope-ratio test analyzed based on the product intake against fish body weight and FCR confirmed a much lower biological efficiency for MHA-Ca versus DL-Met. **Biological efficiency of MHA-Ca versus DL-Met was determined to be 54% for final body weight (Graph 1) and 50% for FCR** (Graph 2). Since the confidence interval of these values overlapped with 65%, they are not significantly different from the hypothesized 65% biological efficiency.

CONCLUSION

Based on the results and in alignment with NRC (2011), **we maintain a recommended biological efficiency of 65% for MHA-Ca** relative to DL-Met, on a product basis, in Nile tilapia.

This means, 65 parts of MetAMINO® (or 100 parts PROXYMet™ containing 65% MetAMINO®) can successfully replace 100 parts of MHA-Ca in tilapia feed.

Such an approach can improve overall profitability by significantly reducing feed costs in tilapia production.

FEEDBACK

“Trial results clearly show that replacing 100 parts of MHA with 65 parts of DL-Methionine yield similar or even better performance of fish”

Dr. Karthik Masagounder,
Head of Aqua Research,
Evonik Operations GmbH,
Germany

Bioavailability of MHA-Ca compared with MetAMINO® to support growth performance of nursery pigs

Collaborative trial by Evonik and Animal Data Analytics, S.L, Segovia, Spain

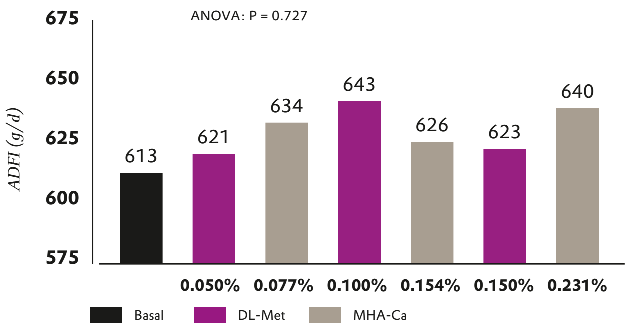
Trial location:
Segovia, Spain

Project team leaders:
Dr. Morales,
Dr. B. Jayaraman,
Dr. J. Htoo

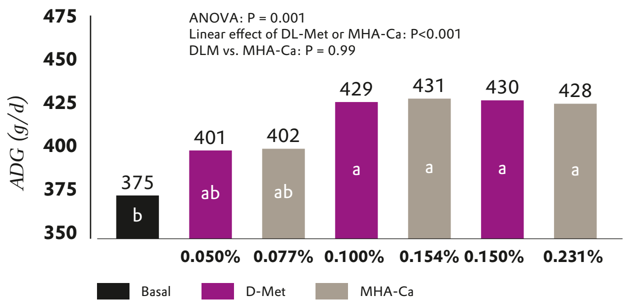
TABLE 1: Animals and dietary treatments

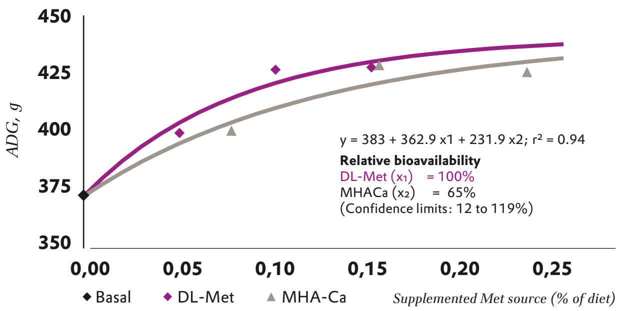
Animals	504 weaned pigs (DNA x Pietrain; initial body weight of 11.0 kg; 42 day of age)
Diets	• A Met-deficient basal diet (0.22% SID Met) was supplemented with 3 graded levels of DL-Met or MHA-Ca at DL-Met to MHA-Ca ratio of 65:100 on product basis to create 7 diets • Mash form
Design	• 6 pigs (3 entire males and 3 gilts) per pen and 12 replicate pens/treatment • Diets and water were offered ad libitum
Parameters	• ADG, ADFI and FCR • Plasma protein, albumin and glucose
Duration	21 days
Location	Commercial research far, Ctra Aguilafuente-Zarzuela del Pinar Aguilafuente, Spain.

GRAPH 1: Average daily feed intake (ADFI) was not affected by dietary treatments

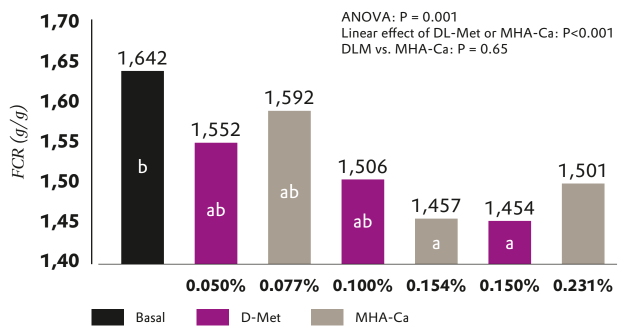


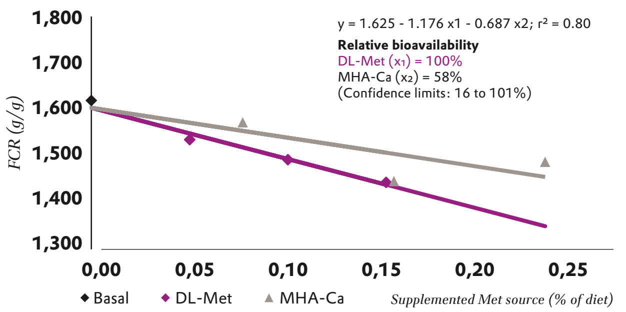
GRAPH 2A AND 2B: Bioavailability of MHA-Ca relative to DL-Met based on ADG (g/day)





GRAPH 3A AND 3B: Bioavailability of MHA-Ca relative to DL-Met based on FCR (g/g)





Trial **Design**

The trial was designed by Evonik (Table 1) and conducted at a Commercial Swine research facility at Aguilafuente, Spain.

Trial **Objective**

The objective was to determine relative bioavailability of MHA-Ca compared with DL-Methionine to support growth performance of 11 to 20 kg pigs.

Trial **Results**

The final BW (day 21) and the overall ADG (375, 401, 429, 430, 402, 431, and 428 g/d for diets 1 to 7) increased linearly ($P < 0.01$) by graded level of supplementation with DL-Met or MHA-Ca (Graph 2a).

The overall FCR (1.64, 1.55, 1.51, 1.45, 1.59, 1.46, and 1.50 for diets 1 to 7) improved linearly ($P < 0.001$) by supplementation with DL-Met or MHA-Ca (Graph 3a).

Average daily feed intake (ADFI) and plasma concentrations of total protein, albumin and glucose on day 21 were not affected ($P > 0.05$) by dietary treatments.

Pig performance responses (ADG, ADFI and FCR) were not different ($P > 0.05$) when Met was supplemented in the Met-deficient diet at a DL-Met to MHA-Ca ratio of 65:100 on a product basis.

Based on ADG and FCR as response of Met supplementation level, the bioavailability of 65% (exponential regression) and 58% (linear regression) was estimated, respectively for MHA-Ca relative to DL-Met (on a product basis) in 11 to 20 kg pigs.

CONCLUSION

Pig performance was not different when the Met-deficient diet was supplemented at a DL-Met to MHA-Ca ratio of 65:100 on a product basis.

Regression analysis estimated the bioavailability of 65% and 58%, based on ADG and FCR, respectively, for MHA-Ca relative to DL-Met on a product basis in 11 to 20 kg pigs.

The current results confirm that the average bioavailability for MHA-Ca is roughly 65% of DL-Met (on a product basis), which should be used in least cost formulation of swine diets to maximize income over feed cost.

FEEDBACK

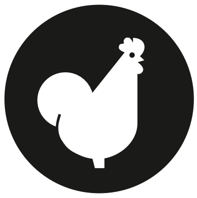
"The current trial results proved that 100 parts of MHA-Ca can be replaced with 65 parts of DL-Met without affecting growth performance of pigs"

Dr. Joaquin Morales,
Head of Digital Transformation and Innovation Department at Animal Data Analytics, S.L, Segovia, Spain

Large Scale Performance Test on a Commercial Farm in Germany

A joint trial of the University of Applied Sciences Osnabrueck, a commercial farm, a feed manufacturer and Evonik

Trial location:
Germany,
Lower Saxonia



Project team leaders:
Prof. Dr. Westendarp,
Kilian Fenske,
Dr. Andreas Lemme

Trial Design, Methods and Materials

Animals	408,500 as hatched Ross 308 broilers in 10 houses at 1,800 m^2
Diets	Wheat (partly unground)-corn-soybean meal-rapeseed meal based diets; pelleted A total of 110 batches were produced ▸ analyses of each batch confirmed expected nutrient levels and, thus, precise manufacturing
Design	**2 treatments x 5 houses** **1)** Standard feed using MHA-FA **2)** Trial feed using DL-Met at 65% ratio
Feeding **3 Crops**	**Starter:** 0-10 d, **Grower 1:** 11-19 d, **Grower 2:** 20-25 d, **Finisher:** 26-42 d at day 29 (16% of overall liveweight) at day 34 (15%) at days 41/42 (69%)
Parameters	**Body weights** ▸ recorded by hopper scales **Final body weights** ▸ as reported by slaughter house Daily weight gain; **Feed conversion ratio** ▸ feed volumes by manufacturer (minus leftovers at end of trial) **Nitrogen balance** ▸ N-analyses of feed; 30N/kg BW
Location	A commercial farm in Lower Saxonia, Germany

TABLE 1: Average final body weights (kg/bird)
GRAPH 1: Growth curves (g/bird)

	Crop 1	Crop 2	Crop 3	Overall
Liquid MHA-FA	**1.601**	**2.003**	**2.874**	**2.434**
CV	2.8%	3.4%	4.5%	4.1%
MetAMINO®	**1.596**	**1.998**	**2.869**	**2.421**
CV	4.4%	3.9%	4.2%	4.1%
p-value	0.88	0.89	0.92	0.76

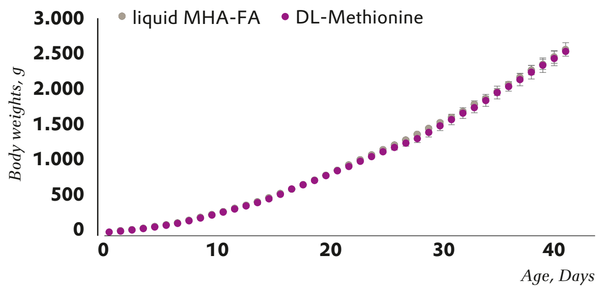


TABLE 2: Average daily body weight gain (g/d/bird)

	Crop 1	Crop 2	Crop 3	Overall
MHA-FA	**53.84**	**57.75**	**68.10**	**63.99**
CV	2.9%	3.4%	3.4%	3.3%
MetAMINO®	**53.65**	**57.58**	**68.00**	**63.79**
CV	4.5%	3.9%	3.3%	3.6%
p-value	0.88	0.89	0.92	0.85

TABLE 3: Average overall feed consumption (kg/bird), feed conversion ratio (kg/kg) and mortality (%)

	Feed consumption	FCR	Mortality
MHA-FA	**3.631**	**1.503**	**2.44**
CV	4.8%	0.8%	25.8%
MetAMINO®	**3.598**	**1.498**	**2.82**
CV	2.5%	1.9%	26.8%
p-value	0.62	0.77	0.47

TABLE 4: Average N-intake, N-retention*, N-excretion (all kg/house) and N-utilization (retained/intake)

	N-intake	N-retention	N-excretion	N-utilization
MHA-FA	**4541**	**2834**	**1707**	**62.4**
CV	3.8%	3.5%	4.5%	0.8%
MetAMINO®	**4525**	**2814**	**1711**	**62.2**
CV	2.8%	4.7%	1.9%	2.1%
p-value	0.82	0.73	0.91	0.73

* Assuming 30g N/kg BW

SECTION 2, VIDEO NO. 6

SECTION 4, ARTICLE NO. 2

SECTION 4, ARTICLE NO. 4

Trial **Objective**

The aim of this study was to challenge Evonik's recommendation that liquid MHA-FA at 65% is as efficient as MetAMINO® and to provide evidence that this recommendation can be applied under commercial broiler production condition without compromising performance.

Trial **Results**

Analysed nutrient and amino acid levels of 110 feed samples were almost exactly matching with expected levels. This also applied for supplemental liquid MHA-FA and MetAMINO® confirming MetAMINO® levels 65% as high as liquid MHA-FA levels.

Final broiler weights achieved in the MetAMINO® treatment were identical to those of the MHA-FA treatment. This was true on average (2 x ~200,000 broilers) but also at each harvest date (Table 1). Moreover, hopper scale recordings showed no statistical difference at any of the 42 days (Graph 1). Consequently, also daily gain did not differ (Table 2). Feed conversion did not differ between treatments (Table 3) and was on average 1.50 kg/kg. The strong growth of broilers and the excellent feed conversion ratio in combination with well balanced, reasonable dietary protein levels resulted in a high N-utilization of 62% which also did not differ between the treatments (Table 4).

Amino acid analyses related to different volumes fed in subsequent phases suggested an average liquid MHA-FA inclusion of 2.95 kg/t. The respective supplementation of MetAMINO® at 65% replacement was 1.92 kg/t. Assuming a MetAMINO® price of 2.50 €/kg and a price ratio to MHA-FA of 80% at purchase results in an MHA-FA price of 2.00 €/kg. Thus, supplementation cost with MetAMINO® would be 4.80 €/t and, thus, 1.10 €/t lower than the MHA-FA supplementation (5.90 €/t). In this trial almost exactly 1455 t of compound feed were fed to the 10 houses which would indicate feed cost savings of 1,600 €/cycle and well above 10,000 €/year when replacing liquid MHA-FA with MetAMINO® at a ratio of 65%.

CONCLUSION

This trial confirms that liquid MHA-FA can be replaced by MetAMINO® at a 100:65 weight ratio without compromising broiler performance or nutrient utilization.

‣ Therefore, this trial **validates Evonik's recommendation** on a relative bioefficacy of 65% for liquid MHA-FA.

Economic assessment indicates that for a ~400,000 broiler farm, anual feed cost savings > €10,000 are realistic.

FEEDBACK

"The trial clearly revealed that replacing 100 parts of MHA with 65 parts of DL-Methionine yields same broiler performance under German large scale production conditions allowing for relevant economic savings"

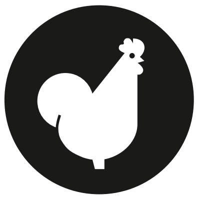
Dr. Kilian Fenske,
University of Applied Sciences Osnabrueck

Supplementation of DL-Methionine at 65% of MHA-FA support similar performance in broilers

Trial conducted by Evonik at Natural Resources Institute Finland (Luke)

TRIAL 1 2 3 4 5 6 7 8 **9** 10 11 12 13 14 15 16 17 18 19

Trial location:
Tavastia, Jokioinen/ Finland

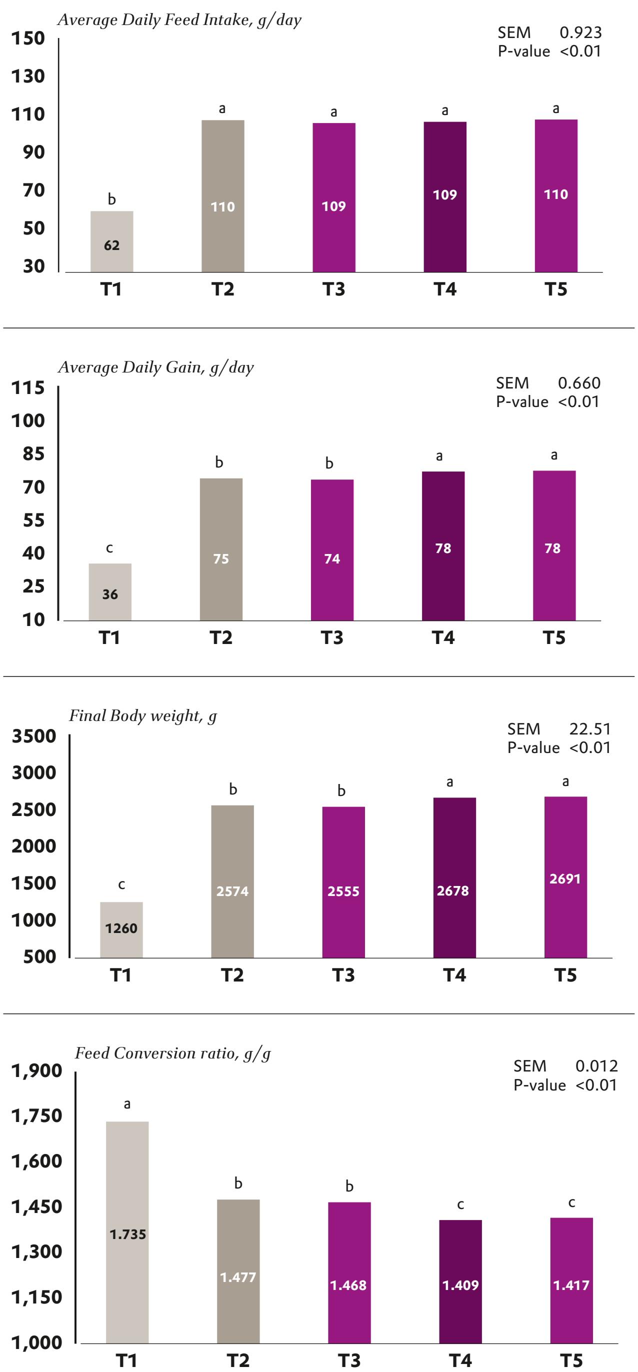


Project team leaders:
Dr. Gabriel da Silva Viana, Dr. Juliano Cesar De Paula Dorigam

TABLE 1: Trial design, Methods and Materials

Animals	720 male Ross 308
Diets	Wheat-soybean based diets, three phases; starter diet with 23.7% CP: 0 – 10 days; grower with 21.8%CP: 11 – 24 days; finisher with 20.6%CP: 25 – 35 days
Design	Completely randomized design of 5 treatments with 9 replicates / treatment, 16 birds each
Feeding	T1 – Basal diet deficient in Met+Cys; T2 – 25% Reduced Met+Cys spec MHA-FA T3 – 25% Reduced Met+Cys spec with DLM replacing MHA-FA at 65%; T4 – Standard Met+Cys spec MHA-FA inclusion; T5 – Standard Met+Cys spec with DLM replacing MHA-FA at 65%;
Parameters	Final body weight, average daily gain, average daily feed intake and feed conversion ratio
Duration	35 days
Location	Natural Resources Institute Finland (Luke)

GRAPH 1: Performance of broilers during 35 days feeding period



SECTION 2, VIDEO NO. 7

SECTION 2, VIDEO NO. 8

SECTION 4, ARTICLE NO. 15

Trial **Design**

The trial was designed (Table 1) to allow the direct comparison between 100 parts of MHA-FA (88%) and 65 parts of DL-Met (99%) supplemented in a Met+Cys deficient basal diet to meet 75% or 100% of Met+Cys requirements.

Trial **Objectives**

The objective of this study was to demonstrate that each 1 kg of MHA-FA in feed for broiler chickens could be replaced by 650 g DL-Methionine with no adverse impact on bird performance and independent of the dietary Met+Cys level.

Trial **Results**

Both Met sources under study supported similar body weight, average daily gain, and feed conversion ratio to birds fed either 75 or 100% Met+Cys recommendations (Graph 1). Regardless of the methionine source assessed, birds fed 100% recommendations exhibited a better performance compared with 75% Met+Cys, confirming that sub-optimal Met+Cys levels limited performance. Thus, marginal reduction of dietary Met+Cys can increase the sensitivity of 65:100 test.

Met+Cys deficiency elicited a depression in average daily feed intake (Graph 1), but no differences were noticed between 75 and 100% Met+Cys groups and between the Met sources assessed ($p > 0.05$). According to NRC (1994), if a diet is deficient in any nutrient, daily feed consumption may decrease in relation to the severity of the deficiency, but a marginal deficiency in amino acid may result in a small increase in feed consumption.

CONCLUSION

1 kg of MHA-products can be replaced with 650 g of DLM to achieve the same level of growth performance at standard Met+Cys levels and at lower Met+Cys levels.

FEEDBACK

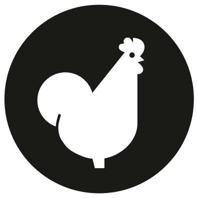
"The outcomes clearly show that both Met sources are suitable Met sources in broiler feeds; and that by replacing 100 parts of MHA with 65 parts of DL-Methionine broiler performance is not compromised"

Dr. Gabriel da Silva Viana,
Senior Scientist
Pig and poultry production, Production Systems
Natural Resources Institute Finland, Luke

Replacement of MHA-FA by 65 parts of DL-methionine in broiler feeds results in same performance even in diets formulated with reduced dietary protein and Met+Cys levels

Trial conducted by Evonik at Natural Resources Institute Finland (Luke)

Trial location:
Kanta Häme, Jokioinen/Finland

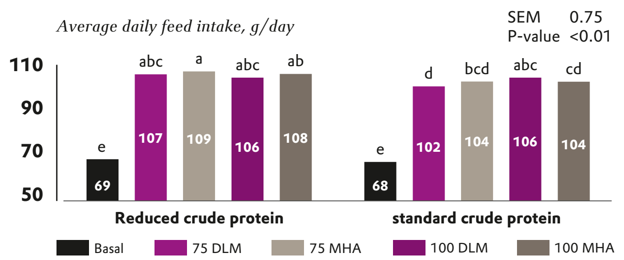


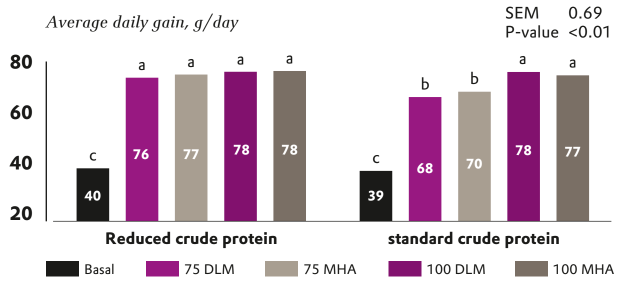
Project team leaders:
Dr. Leticia Soares, Dr. Gabriel Viana, Dr. Juliano Cesar De Paula Dorigam

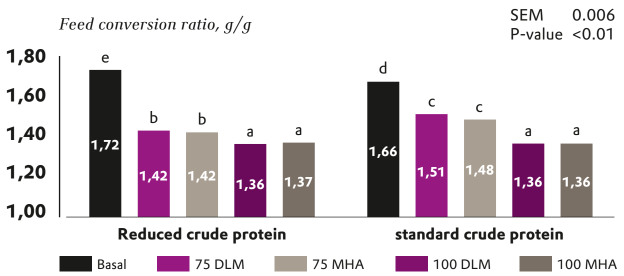
TABLE 1: Trial Design, Methods and Materials

Animals	1,440 male Ross 308 chicks
Diets	Standard and low crude protein (CP) contents in the diets were, respectively, 23.7% and 22.2% (0 – 10 days); 21.8% and 20.3% (11 – 24 days); 20.6% and 19.1% (25 – 35 days). Diets were mainly composed of corn, wheat, soybean and peas (low CP diets only)
Design	Completely randomized design: 10 treatments with 9 replicates/treatment, 16 birds each. Tukey´s multiple comparison test (P < 0.05)
Feeding	**T1)** Basal diet deficient in Met+Cys **T2)** 75% AA Spec MHA-FA **T3)** 75% AA Spec with DLM replacing MHA-FA at 65% **T4)** Standard AA Spec MHA-FA inclusion **T5)** Standard AA Spec with DLM replacing MHA-FA at 65% **T6-T10)** Formulated as diets T1-T5 but with crude protein reduced by 1.5% compared to Aviagen 2018 guidelines
Parameters	Average daily gain (ADG), average daily feed intake (ADFI), feed conversion ratio (FCR) and footpad dermatitis scoring (day 35)
Duration	35 days
Location	Natural Resources Institute Finland (Luke)

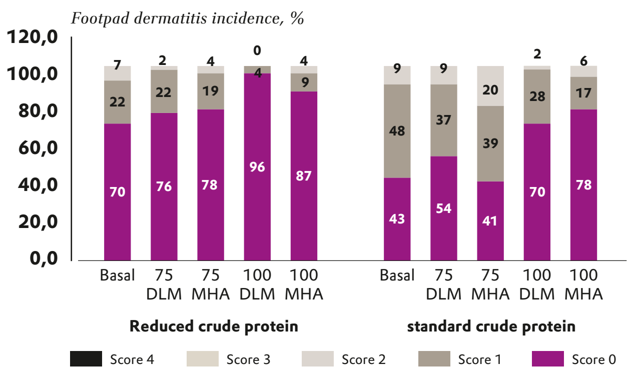
GRAPH 1: Performance of broilers during 35 day feeding period







GRAPH 2: Occurrence of footpad dermatitis in broilers after 35 day feeding period



Trial **Design**

The trial was designed (Table 1) to allow a comparison between 100 parts of MHA-FA and 65 parts of DL-Met (650 g MetAMINO®) supplemented in a Met+Cys-deficient basal diet to meet 75% or 100% of Met+Cys requirements in feeds containing standard or reduced protein levels.

Trial **Objectives**

The objective of this study was to confirm whether 1 kg of MHA-FA in feed for broiler chickens could be replaced by 650 g DL-Methionine and provide the same performance regardless of the dietary protein and/or Met+Cys level.

Trial **Results**

The supplementation of Met improved performance of broilers compared to basal diets, which confirms Met essentiality for growth (Graph 1). ADG was improved in birds fed standard-protein diets as Met+Cys increased from 75 to 100% of recommended levels ($P < 0.05$). The same did not occur in birds fed diets with lower protein levels ($P > 0.05$). The reason underlying such effects might be the ingredients in the feed. Peas were included only in the standard protein feeds.

Because such legume contain tannins and protease inhibitors, it is possible that both antinutritional factors have affected nutrient digestion, which might have impaired, to a greater extent, the performance of birds fed 75% Met+Cys compared with those fed 100%. Birds fed diets supplemented at 100% Met+Cys exhibited a better FCR than birds fed 75% Met+Cys in standard and low-protein levels.

No differences in ADG and FCR were observed in birds fed standard and low-protein level at the level of 100% Met+Cys ($P < 0.05$). Both Met sources under study supported similar performance regardless of the Met+Cys or dietary protein level. The incidence of lesions was higher in standard-protein-fed birds compared with those fed low-protein levels, especially in Met+Cys deficient treatments (Graph 2).

That would be expected since higher dietary protein results in increased uric acid and ammonia production in the litter, and it was aggravated by the deficiency of Met, an essential amino acid for keratin synthesis.

CONCLUSION

650 g of DLM can replace 1 kg of MHA products and support the same broiler growth performance regardless of dietary Met+Cys and protein levels.

The reduction in dietary protein levels by 1.5%, maintaining the ideal protein ratio in feeds, did not compromise broiler performance responses and decreased the incidence of footpad dermatitis.

FEEDBACK

"Trial results clearly show that replacing 100 parts of MHA with 65 parts of DL-Methionine yield similar broiler growth performance independent of the dietary Met+Cys and protein levels."

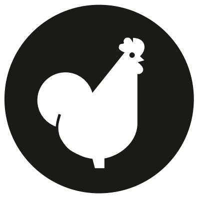
Dr. Letícia Soares,
Pig and Poultry Scientist
Natural Resources Institute
Finland

Performance of PROXYMet™ was the same as MHA-FA in Ross 308 broilers

Trial conducted at Hungarian University of Agriculture and Life Sciences (MATE), Hungary, 2021

TRIAL 1 2 3 4 5 6 7 8 9 10 **11** 12 13 14 15 16 17 18 19

Trial location:
MATE,
Keszthely/Hungary

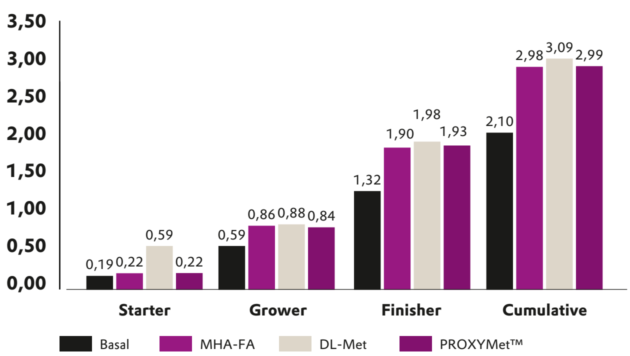


Project team leaders:
Prof. Dr. K. Dublecz,
Dr. M. Mueller

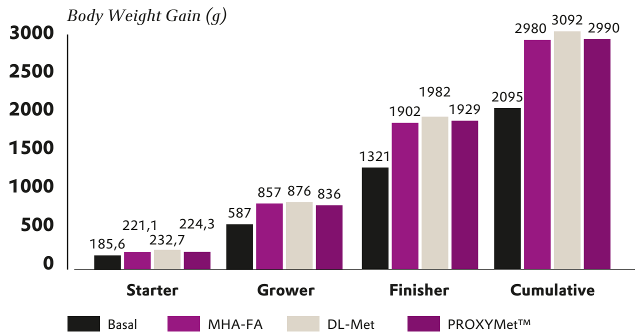
TABLE 1: Trial Design, Methods and Materials

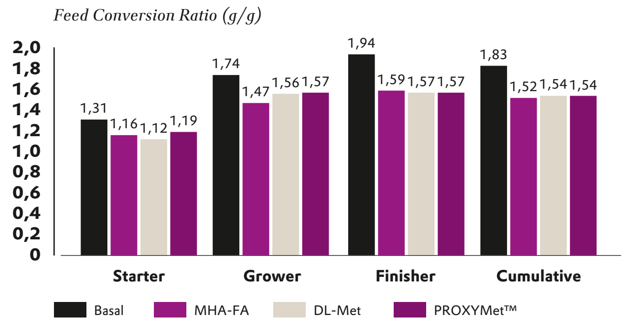
Animals	576 male Ross 308 broilers
Diets	Corn, wheat and soybean meal based diets
Design	24 floor pens, 4 dietary treatments, 6 replicates, 24 birds randomly allocated per pen
Feeding	**T1** – Control (deficient in Met+Cys) **T2** – Control + liquid MHA-FA **T3** – Control + DL-Met at 65% of MHA-FA **T4** – Control + PROXYMet™
Parameters	Body weight gain (BWG), feed intake (FI) and feed conversion ratio (FCR), at d42 carcass characteristics (carcass %, breast meat %, thigh meat %)
Duration	From 0 to 42 days of age Three phases: starter 0-10 days; grower 11-24 days; finisher 25-42 days
Location	Hungarian University of Agriculture and Life Sciences, Keszthely, Hungary

GRAPH 5: Final body weight per phase

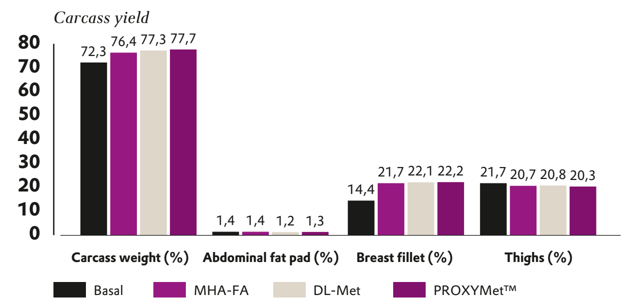


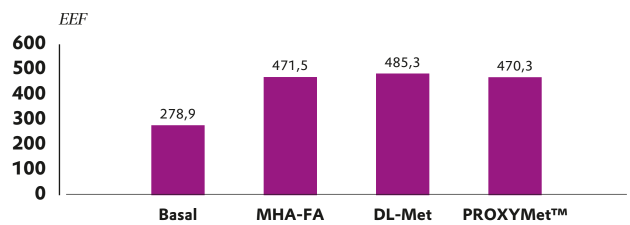
GRAPH 1 & 2: Effect of dietary treatments on growth parameters from 0-42 days of age





GRAPH 3 & 4: Effect of dietary treatments on carcass yield and European Efficiency Factor





Trial **Design**

The trial was designed (Table 1) to show the comparison of bird response to MetAMINO®, PROXYMet™ (DL-methionine diluted to 65% concentration with 35% starch) and MHA-FA when added to a basal diet deficient in methionine.

Trial **Objectives**

The objective of this study was to demonstrate the nutritional value of MHA-FA in comparison to PROXYMet™ and pure DL-Methionine in common Hungarian broiler diets considering growth performance and carcass parameters. The objective was to prove that each 1 kg of MHA-FA in feed for broiler chickens could be replaced with only 650 g DL Methionine with no adverse impact on bird performance.

Trial **Results**

A dietary deficiency in Met+Cys results in significantly reduced growth performance. The final body weight and cumulative weight gain of birds with lower Met+Cys supply was about 30% less. Met+Cys deficiency depressed the feed intake of chickens by about 17% and the relative breast fillet ratio by 35%. The relative thigh weight and abdominal fat was not affected by Met+Cys deficiency.

When comparing MHA-FA, PROXYMet™ and pure DL-Methionine supplementation, there was no significant differences between dietary treatments. However, the results of the DL-methionine supplemented diets tended to be the best. Although the body weight in the DL-Met treatment was only numerically higher than in the MHA-FA group, the difference of +112 g might be a reason, though this could be a topic for further investigation.

Body weight and body weight gain of group T1 was significantly lower than the results of the three other treatments and no significant differences have been found between treatments T2, T3 and T4. This was true for all phases, as well as for the whole production period.

Due to the better weight gain data, FCR was also more favourable in the diets with Met supplements, without significant differences between treatments T2, T3 and T4.

Both relative carcass weight and breast fillet percentages were more favourable in the Met supplemented diets. The thigh ratio was only slightly influenced by the treatments and no differences in the relative abdominal fat ratio were found.

All the Met supplemented diets resulted in higher EEF without significant differences. Met deficiency, however, decreased the efficiency factor by about 200.

Supplementing a control diet deficient in methionine with 100 parts of methionine hydroxy analogue free acid (MHA-FA) or PROXYMet™, or 65 parts of DL-Methionine significantly increased the feed intake and improved the weight gain and feed conversion of broilers from 0 to 41 days of age. The replacement of 100 parts MHA-FA with 65 parts DL-Methionine resulted in a similar live performance as well as carcass quality.

CONCLUSION

The current study confirmed again the importance of methionine supplementation to Met+Cys deficient diets of commercial broilers.

The use of these products with their correct nutritional value provides decisive criteria from a nutritional and financial standpoint.

650g DL-Methionine, or 1kg PROXYMet™, can replace 1kg MHA-FA to provide the same bird performance.

FEEDBACK

"The most surprising result of this trial for me was the sensitivity of the animals to the MET supplementation and the range of growth depression when no additional MET was fed, and that 65 parts of DL-methionine could replace 100 parts of MHA-FA with no difference in animal performance."

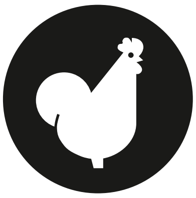
Prof. Dr. Károly Dublecz,
Professor at Hungarian University of Agriculture and Life Sciences

Middle East Africa

The Efficacy of Methionine Hydroxy Analogue (MHA-FA) Compared to DL-Methionine (DLM) on Growth Performance, Carcass Traits, and GHR and IGF-I Expression in Broilers.

Ankara University, Faculty of Agriculture, Animal Science Department, Ankara / Türkiye

Trial location:
Ankara University, Research Facility, Ankara, Türkiye

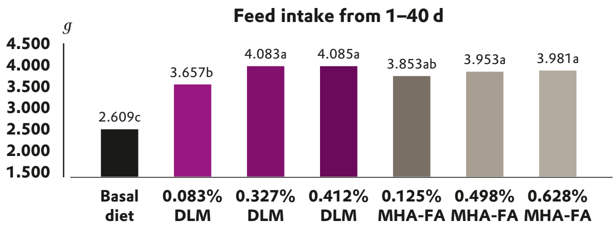


Project team leaders:
Prof. Dr. N. Ceylan, Dr. M. Müller, MSc. O. Kiyak

TABLE 1: Trial Design, Methods and Materials

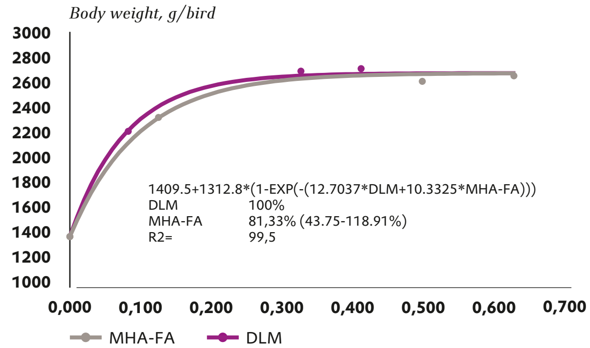
Animals	792 day-old male Ross 308 chicks
Diets	Corn and soybean-meal based diets
Design	Two sources of Methionine (DL-Methionine (DLM) and liquid methionine hydroxy analogue (MHA-FA)) and three levels of supplementation (25%, 100% and 125%; levels of addition relative to required amount of additional Met to meet SID Met+Cys requirements) with a common basal diet in a randomized complete block design
Feeding	**1)** Negative Control (Common commercial diet, corn-soybean based without Methionine) **2)** 0.083% DLM (25% of required methionine suppl.) **3)** 0.327% DLM (100% of required methionine suppl.) **4)** 0.412% DLM (125% of required methionine suppl.) **5)** 0.125% MHA-FA (25% of required methionine suppl.) **6)** 0.498% MHA-FA (100% of required methionine suppl.) **7)** 0.628% MHA-FA (125% of required methionine suppl.)
Traits	Body weight gain, feed intake, feed conversion ratio, carcass, cuts yield and gene expression in the liver
Duration	From 1 to 40 days of age
Location	Ankara University, Faculty of Agriculture, Animal Science Department, Ankara / Türkiye

GRAPH 1: Feed intake 1-40 days of age

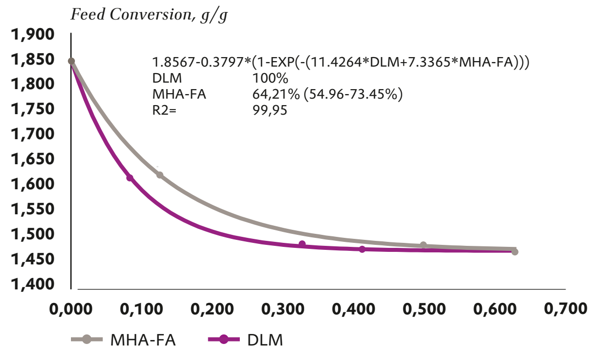


Met source: P<0.05; Interaction: P=0.050; SEM:70.725

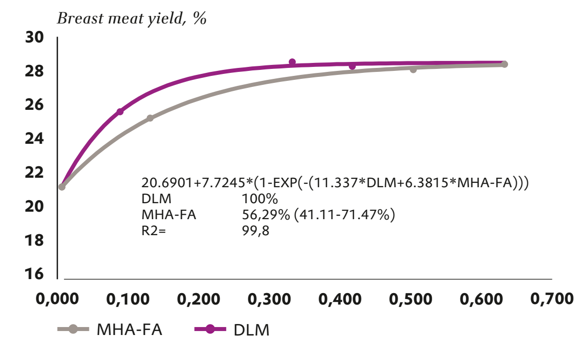
GRAPHS 3 TO 5: Relative bioavailability of MHA-FA compared to DL-Met based on final body weight, FCR and breast meat yield at 40 days



Relative bioavailability of MHA-FA compared to DL-Met based on final body weight as the response criteria of broiler chickens on d 40. Values in brackets indicate 95% confidence intervals.



Relative bioavailability of MHA-FA compared to DL-Met based on FCR as the response criteria of broiler chickens for 0-40 d. Values in brackets indicate 95% confidence intervals.



Relative bioavailability of OH-Met compared to DL-Met based on breast meat yield as the response criteria of broiler chickens. Values in brackets indicate 95% confidence intervals.

SEE SECTION 4, ARTICLE NO. 17

Trial **Design**

One-day-old birds were weighed and then randomly allotted to 7 treatments with 7 replicates (except common basal diet which had 6 replicates) using a 2 × 3 + 1 factorial arrangement, two sources of Met (DL-Met and OH-Met) and three levels of supplementation (25%, 100% and 125%; levels of addition relative to required amount of additional Met to meet SID Met+Cys requirements) with a common basal diet in a randomized complete block design.

Trial **Objective**

To investigate bioefficacy of DL-methionine and methionine hydroxy analogue-free acids in corn-soybean meal-based broiler diets by considering growth and slaughter performance.

Trial **Results**

Effects of levels and sources of supplemental Met on feed intake is given in Table 1. There were interactions between the level and source of supplemental Met for feed intake in finisher and overall ($P < 0.05$).

In the starter and grower period, incremental Met supplementation gradually increased feed intake ($P < 0.05$) as no significant effect of Met source was observed ($P > 0.05$).

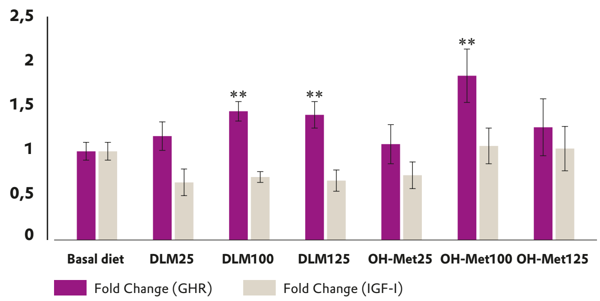
Met addition to the basal diet improved feed intake, BWG, and FCR in all growth periods ($P < 0.05$).

The corresponding relative bioavailability of MHA-FA compared to DL-Met was 79.8% for BW (Graph 3), 62.8% for FCR (Graph 4), and 55.3% for breast meat yield (Graph 5) on a product basis.

The RBV values of MHA-FA for FCR and breast meat yield were significantly lower than that of DL-Met ($P < 0.05$), whereas the difference in BW was not significant ($P > 0.05$).

The FCR was similar between MHA-FA and DL-Met in the standard diet, but better for MHA-FA when a higher MHA-FA level was used (150% of the standard), and better for DL-Met when a lower MHA-FA level was used (50% of the standard).

The relative fold expressions of GHR and IGF-I mRNA in broiler liver are given in Graph 2. A significant interaction between the level and source of supplemental Met was observed for GHR expression($P < 0.05$), while any of the factors studied had no effect on IGF-I expression ($P > 0.05$).



GRAPH 2. Relative fold expression of GHR and IGF-I mRNA in broiler liver. Changes in GHR and IGF-I gene expression in the liver are normalized to ß-actin reference genes and expressed relative to the basal diet group as the mean fold difference (2-ΔΔCT). Values are means of 7 biological replicates and 3 technical replicates. ** P<0.01 Means differed from the basal diet group.

CONCLUSION

The supplementation of Met to a corn-soybean meal-based diet improved growth performance and carcass and cut yields without any significant difference in breast meat traits in the current study.

DL-Met and MHA-FA showed similar growth performance, carcass and cuts yields and breast meat traits when about 1.5 times higher amount of MHA-FA was added due to assumed 65% of bioefficacy compared to DL-Met on a product basis.

Overall, the results from the current study demonstrate that about 1.5 times higher amount of MHA-FA can replace DL-Met in corn-soybean meal-based broiler diets without compromising growth performance, carcass and cuts yields and breast meat traits.

FEEDBACK

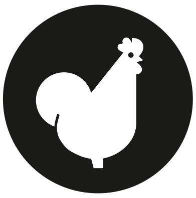
"Although there were no differences between either Met sources for growth performance and carcass quality of broiler chickens, relative bioefficacy of liquid MHA-FA was found 79.80% (BW), 62.80% (FCR), and 55.30% (breast meat yield) as efficacious as pure DL-Met on an as fed basis."

Prof. Dr. Necmettin Ceylan,
Department of Animal Science, Faculty of Agriculture, Ankara University, Ankara, Türkiye

Bioefficacy of MHA-FA Compared to DL Methionine is Confirmed at 65%; Trial in Jordan

Trial conducted by Evonik at the Al-Estesharia Trial Facility, Jordan

Trial location:
Amman Jordan

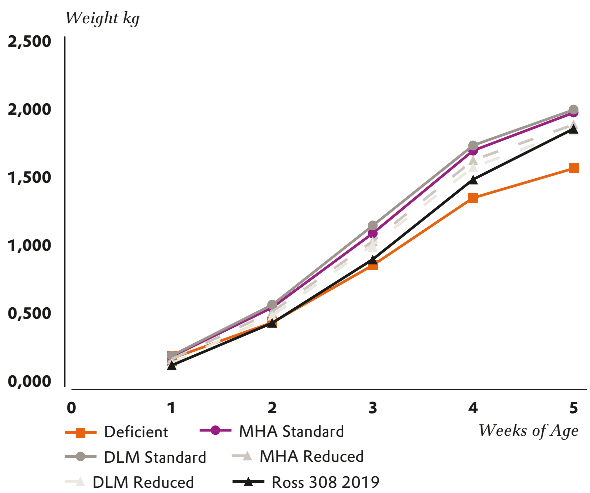


Project team leaders:
Dr. Nasim Al Mefleh, Dr. Ali Afsar, Ing. Esham Mubarash

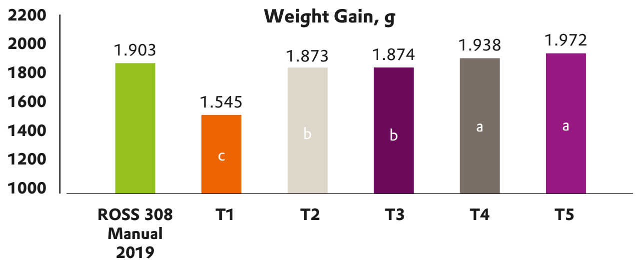
TABLE 1: Trial Design, Methods and Materials

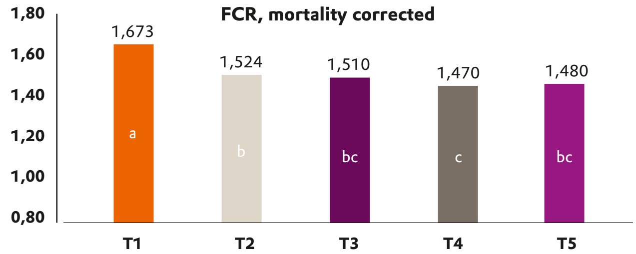
Animals	2,500 as hatched Ross 308 broilers
Diets	Corn-soybean based diets, three phases; starter: 0 – 12 days; grower: 13 – 24 days; finisher: 25 – 32 days
Design	Completely randomized design of 5 teatments with 10 replicates / treatment, 50 birds each
Treatments	T1 – Negative control deficient in Met+Cys T2 – 25% Reduced Met+Cys Spec MHA-FA T3 – 25% Reduced Met+Cys Spec with DLM replacing MHA @ 65% T4 – Standard Met+Cys Spec MHA-FA T5 – Standard Met+Cys Spec with DLM replacing MHA @ 65%
Parameters	Body weight gain (BWG), feed intake (FI) and feed conversion ratio (FCR). At 32d, carcass characteristics

GRAPH 1: Bodyweight development

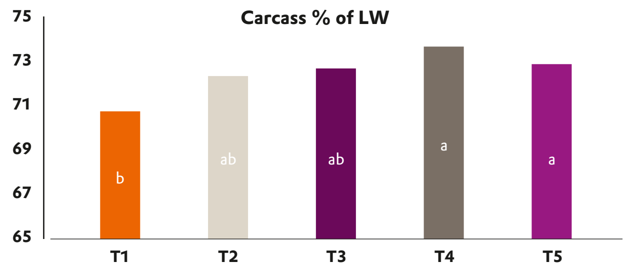


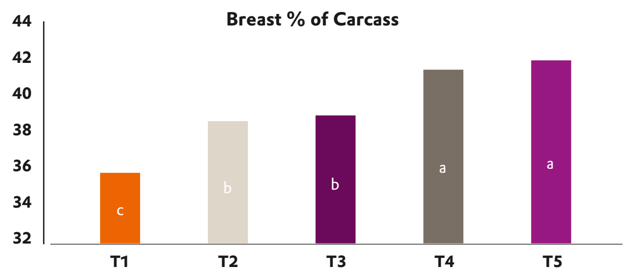
GRAPHS 2 & 3: Broiler performance to 32 days





GRAPHS 3 & 4: Carcass and breast yield





SECTION 2, VIDEO NO. 7

SECTION 2, VIDEO NO. 8

SECTION 4, ARTICLE NO. 15

Trial **Design**

The trial was designed by Evonik (Table 1) and carried out at the Research Facility of Al-Estesharia for Poultry and Feed, Amman, Jordan.

Trial **Objectives**

The objective of the present study was to demonstrate that each 1 kg of MHA-FA in feed for broiler chickens could be replaced with only 650 g DL Methionine with no adverse impact on bird performance; and that both supplemented diets would produce better bird performance than a deficient diet.

Trial **Results**

Diets deficient in Met+Cys negatively affect growth performance and carcass yields of broilers.

Replacing 100 parts of MHA-Ca with 65 parts of DLM did not affect growth performance (Graphs 2 and 3) and carcass parameters (Graphs 4 and 5) of broilers at both supplementation levels (dietary Met+Cys level).

Reducing amino acid specification by 25% had a minor impact on growth and FCR, but significantly reduced breast meat yield. Even at these reduced amino acid levels, replacement of 100 parts of MHA-Ca with 65 parts of DLM still gave equivalent performance.

The replacement of 65 parts of DLM by MHA showed similar performance for all treatments (performance and carcass yield) and so confirms the outcome of previous trials in the regions: Rostagno & Barbosa (1995), Hoehler et al. (2005), Sangali (2012), Bertechini et al. (2016), and Sakomura et al. (2016).

Economic calculations showed a reduction in feed cost per bird of abut 0.5%; equivalent to approximately USD $7,000 per 1 million birds processed (correct for location and time of trial).

CONCLUSION

1 kg of MHA-products can be replaced with 650 g of DLM to achieve the same level of growth performance at standard SID amino acid levels and at lower SID amino acid levels.

Such an approach improves overall profitability by reducing feed costs whilst maintaining poultry meat income.

In the reported situation, this is equivalent to USD 7000 per 1 million birds processed.

FEEDBACK

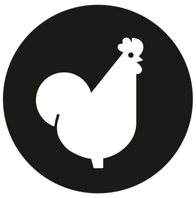
"This trial confirmed our belief in the superiority of MetAMINO® over other sources of Methionine."

Eng. Ehsan Musharbash,
CEO of Al-Estesharia for poultry and feed

Effects of dietary methionine source and levels on gut health and oxidative markers of broiler chickens

Trial conducted at Animal Science Research Institute of Iran (ASRI), Iran

Trial location:
Karaj – Iran

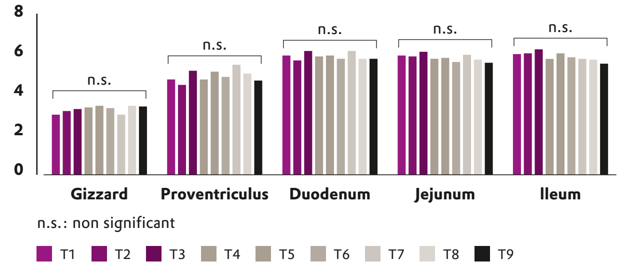


Project team leaders:
Dr. Naser Mousavi (ASRI)
Ali Afsar

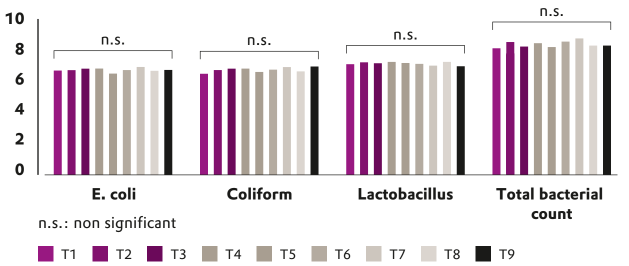
TABLE 1: Trial Design, Methods and Materials

Animals	1,300 male Arbor Acers Plus day old chicks (49.6 ± 0.63)
Feed	Corn-soybean based diets, three phases; starter: 0 – 10 days; grower: 11 – 24 days; finisher: 25 – 42 days
Design	Completely randomized design of 9 treatments with 6 replicates/treatment, 25 birds each (treatments 5 & 8 with 5 replicates)
Treatments	**T1 –** Negative control deficient in Met+Cys (av. 34.5% below the recommendation) **T2-T3-T4-T5** supplemented with 0.04, 0.08, 0.16 and 0.24% DL-Met respectively **T6-T7-T8-T9** supplemented with 0.04, 0.08, 0.16 and 0.24% liquid MHA-FA respectively
Parameters	pH of proventriculus, gizzard, duodenum, jejunum and ileum, three birds/pen Microbial analysis- cecal contents of the three birds/pen (pooled) Liver concentrations (two birds/pen) of GPX, SOD, GSH & GSSH, total glutathione For evaluation of feed preservative effect of Met sources (mold growth and total bacterial count in the feed) 1 sample/pen - stored in room temperature for 6 weeks and then sent to lab for analysis
Duration	1 – 42 days old
Location	Animal Science Research Institute of Iran (ASRI), Iran

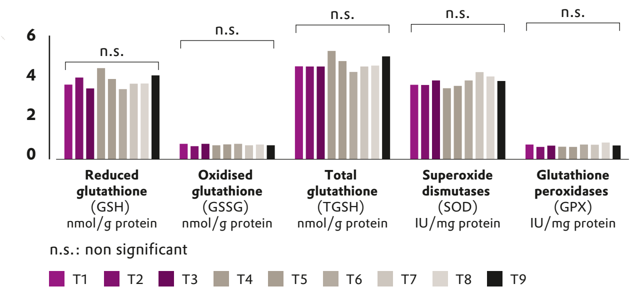
GRAPH 1: Effect of different Met sources on pH of different part of GIT Day 42



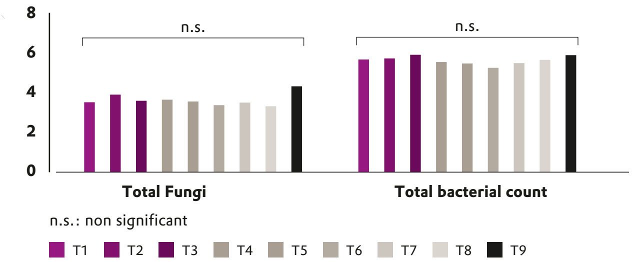
GRAPH 2: Effect of different Met sources on cecal bacterial count (log10 cfu /gr) of broilers on day 42



GRAPH 3: Effect of different Met sources on Oxidative biomarkers/ liver day 42



GRAPH 4: Effect of different Met sources on feed total bacterial and fungal count (log10 cfu /gr)



Trial **Design**

The effect of Methionine sources in terms of their functional effectiveness as organic acid and anti-oxidative properties was investigated in male Arbor Acres broilers.

Birds were fed a corn-soybean meal-based diet over 3 feeding phases from 0 to 42 days of age.

The study comprised nine treatments consisting of a negative control and four graded supplementations of either liquid MHA-FA or DL-Methionine (Table 1).

pH in the GIT and concentrations of various molecules indicative of oxidative status (Table 1) in the liver as well as mold growth and bacterial count in the experimental feeds were analyzed.

Trial **Objectives**

Few information is available in relation to the effect of Methionine sources on gut health and antioxidant status. The current experiment was conducted to address two areas of interest:

Gain further insights into the effects which MHA-FA and DL-Met may have on gut health and antioxidant status of broilers.

Investigate organic acid properties of MHA-FA and check potential paths of action for organic acids in animal diets as 1) to protect compound feed from microbial deterioration during storage, 2) to create an unfavorable environment for microbes in the gut and 3) to decrease the pH of the gut, which can result in an increase in enzyme activity to aid in digestion.

Trial **Results**

No significant differences were found between the two methionine sources and levels regarding the oxidative status, cecal microbial population, GIT sections pH and feed bacterial and fungal count.

CONCLUSION

Our data indicates that the antioxidant defense system of healthy birds does not benefit when MHA-FA is supplemented instead of DLM.

In addition, there are no significant improvements in gut bacterial counts and pH, feed fungi and total count when MHA-FA is supplemented instead of DL-Met.

FEEDBACK

"We have conducted series of university and farm trials in Iran. Results of all investigations confirmed 65% RBV Liquid MHA-FA compared to DL-Met (data not shown here).
With our data, none of the claimed organic acid properties of liquid MHA-FA are confirmed."

Ali Afsar,
Technical Account Manager
Evonik Iran AG

Section 1 — Middle East | Africa
Section 2
Section 3
Section 4

Farm comparison of DL Methionine and MHA-FA confirms 65% Bioefficacy

Trial conducted at Saba Morgh Noavaran Farm facility, 2022

Trial location:
Zanjan – Iran

Project team leaders:
Dr. Alireza Rostamkhani
Ali Afsar

TABLE 1: Trial Design, Methods and Materials

Animals	6,000 as hatched Ross 308 broilers
Diets	Corn-soy bean meal based diets: Starter (0-10 crumble), Grower (11-24 pellet 3mm) and Finisher (25-slaughter pellet 4 mm)
Design	Single farm, divided logitudinally, separate feeding and drinking system
Treatmets	Standard diets based on customer common practice; Diet 1: Liquid MHA-FA Diet 2: Liquid MHA-FA replaced with DL-Met using 65% RBA
Parameters	Feed intake, weight gain, body weight, mortality date and weight, average daily gain ADG g/b/d, average daily feed intake ADFI g/b/d, FCR and European efficiency factor
Duration	49 days
Location	Zanjan –Iran

GRAPH 2: Saving with DL-Methionine vs. MHA-FA

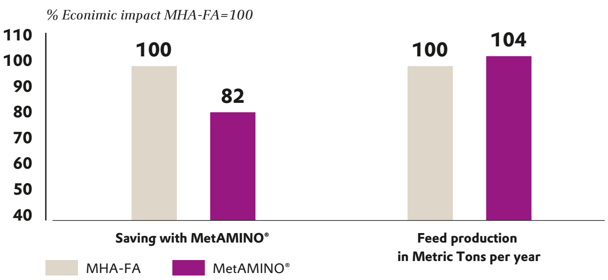
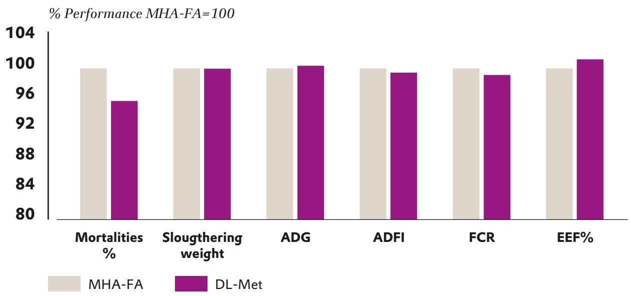


IMAGE 1: Broiler house divided into two equal parts (Left MHA-FA - Right DL-Met, day 36)

IMAGE 2: Feed supplied to each part by different hoppers

GRAPH 1: Performance compared to MHA-FA



European Efficiency Factor, EEF = (Livability (%) x live weight (kg)) / (age (days) x FCR) x 100

Trial **Design**

Farm trial was carried out in a controlled environment broiler house that was divided into two equal parts with total of 6,000 (3,000 in each) hatched day-old Ross 308 broilers 40 g.

Similar corn-soybean based diets supplemented with both liquid MHA-FA or DL-Met were used. Supplementation rate of DL-Met diet was set as 65% of supplantation rate of Liquid MHA-FA diets in all phases; Starter (MHA-FA 0.368%, DL-Met 0.239%), Grower (MHA-FA 0.313, DL-Met 0.203%) and (MHA-FA 0.237, DL-Met 0.154%).

Feeds were supplied in each part of the poultry house by separate feeding systems.

Feed intake was measured at the end of each phase (feed in – feed out).

Mortality dates and weights were recorded daily.

Body weight and weight gain were recorded at the end of each phase and after harvesting the flock at the end of the experiment (Day 49).

Average daily gain (ADG), average feed intake (ADFI), feed conversion ratio (FCR) and European efficiency factor were calculated at the end of the experiment.

Trial **Objectives**

The main objective of the trial was to validate that in commercial farm levels, every kg of Liquid MHA-FA could be replaced with 0.65 kg of DL-Met and achieve the same performance.

Trial **Results**

Replacing 100 parts of Liquid MHA-FA with 65 parts of DL-Met in broiler feed resulted in the same performance.

Some numerical improvements were seen in FCR and EEF.

CONCLUSION

Results of the current trial confirmed previous reports that 1 kg of MHA-FA can be replaced with 650 g of MetAMINO® to achieve the same level of performance.

There are some significant economic improvements and feed cost savings that can be expected from changing Methionine source and increasing feed mill production capacity.

FEEDBACK

"Results of the current trial indicates we can replace 100 parts of MHA-FA with 65 parts of DL-Met and achieve the same performance."

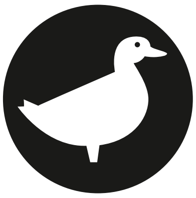
Dr. Alireza Rostamkhani,
R&D Manager
Saba Morgh Noavaran

Asia Pacific

Effect of PROXYMet™ and equal MHA-FA on performance in meat duck

Commercial trial conducted by customer in Henan province, 2021

Trial location:
Henan, China

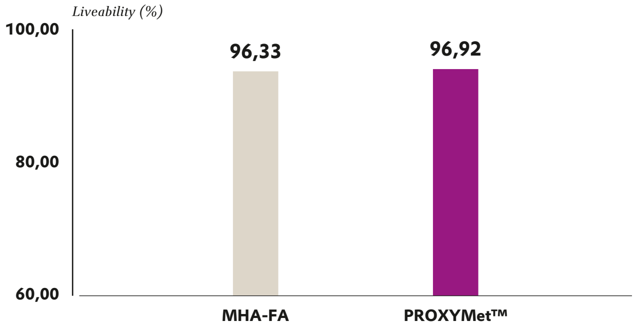


Project team leaders:
Mr. Daniel Gao
Dr. Brian Wang

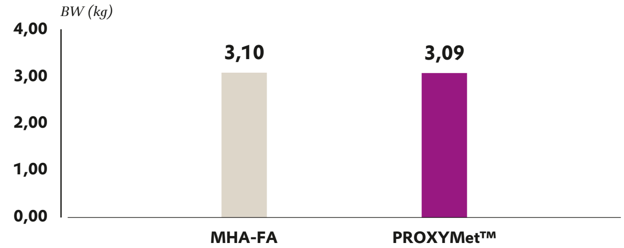
TABLE 1: Trial Design, Methods and Materials

Animals	Total 838,000 Cherry Valley ducks
Diets	Commerical duck feed included starter (1-14d) and grower (15- 39d)
Design	Total 83 houses of ducks were used in two treatments: MHA-FA treatment: Ducks were fed feed added with MHA-FA (2.5kg/T in starter, 2.2kg/T in grower); PROXYMet™ treatment: Ducks were fed feed with equal weight PROXYMet™ (MetAMINO® diluted to 65% with limestone)
Feeding	49 houses of ducks were fed with MHA-FA treatment feed, while 34 houses of ducks were fed with PROXYMet™ feed
Parameters	Liveability, final body weight, FCR
Duration	Around 38-39 days
Location	Commercial farms in Henan

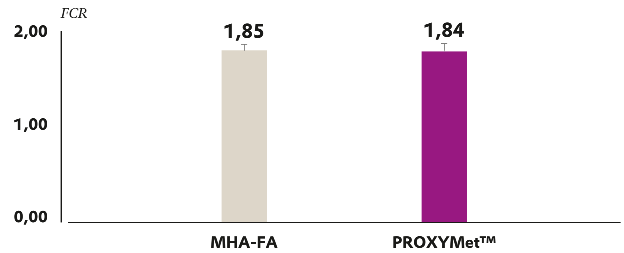
GRAPH 1: Effect of PROXYMet™ and equal MHA-FA on liveability of duck



GRAPH 2: Effect of PROXYMet™ and equal MHA-FA on body weight of duck



GRAPH 3: Effect of PROXYMet™ and equal MHA-FA on FCR of duck



Trial **Design**

Total 83 houses of Cherry Valley ducks (total 838,000 ducks) were used in this commercial trial. The ducks in the control group (MHA-FA treatment) were fed feed added with MHA-FA (MHA-FA treatment), while those in the treatment group (PROXYMet™ treatment) were fed feed added with PROXYMet™ (MetAMINO® diluted to 65% content with limestone). The dosage of MHA-FA or PROXYMet™ in the diets was equal (2.5kg/t in starter, 2.2kg/t in grower). 49 houses of ducks were fed with MHA-FA treatment feed, while 34 houses of ducks were fed with PROXYMet™ treatment feed. The dosage of MHA-FA or PROXYMet™ was equal in the diets, while the basal diet was the same except for the methionine source. The commerical duck feed included starter (1-14d) and grower (15-39d).

Trial **Objectives**

The objective of this test was to determine the effect of replacing equal MHA-FA by PROXYMet™ (65% DL-Methionine) on performance of duck under commercial conditions.

Trial **Results**

- Ducks in MHA-FA or PROXYMet™ treatments had similar liveability (96.33% vs 96.92%).
- Ducks in MHA-FA or PROXYMet™ treatments had similar final body weight (3.10 vs 3.09 kg).
- Ducks in MHA-FA or PROXYMet™ treatments had similar FCR (1.85 vs 1.84).
- No difference in duck performance was observed in either treatment, however, adding PROXYMet™ to replace equal parts MHA-FA in duck feed can save on the cost of adding a met source in feed.

TABLE 2: Cost saving of different Methionine source per ton feed

	Price, RMB/kg	Dosage, kg/MT	Met cost, RMB/MT	Cost saving
MHA-FA	13.6	2.35	32.0	
PROXYMet™	11.05	2.35	26.0	6.0 RMB/MT feed

CONCLUSION

PROXYMet™ (65% DL-Methionine) can replace equal quantity MHA-FA in duck diets with no difference on performance parameters according to this large scale commercial trial.

This commercial trial confirmed the nutritional value of MHA-FA was 65% compared to DLM.

FEEDBACK

"PROXYMet™ (65% DL-Methionine) can replace equal parts MHA-FA, which means the nutritional value of MHA-FA is 65% compared to DLM and can save you money for using DLM compared with MHA-FA."

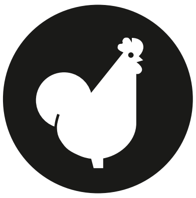
Mr. Daniel Gao,
Sales Manager
Evonik China

Performance test in commercial farm confirmed that 65 parts of DL-Methionine can replace 100 parts of MHA-FA in broiler diets

Trial conducted by customer in Shandong province, 2021

TRIAL 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 **17** 18 19

Trial location:
Shandong, China

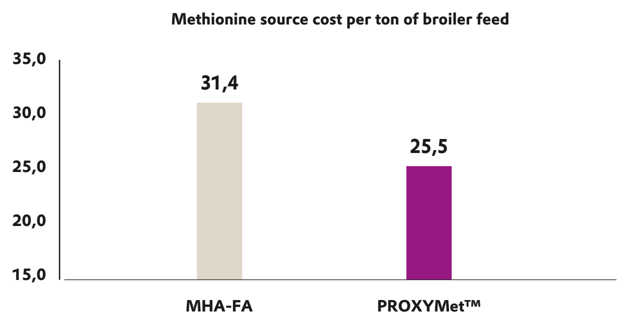


Project team leaders:
Dr. Mandy Yan, Joe Wang

TABLE 1: Trial Design, Methods and Materials

Animals	212,000 ROSS 308 broilers
Diets	Wheat-rice-soybean meal-based commerical broiler diets containg 4 phases (1-10, 11-20, 21-30, 31-40 d)
Design	Control group, MHA-FA, with 4 replicates; Trial group, PROXYMet™ (MetAMINO® diluted to 65% with limestone), with 4 replicates
Feeding	Broilers were fed in cage system under the customer's commercial conditions
Parameters	Final body weight (kg), feed intake (kg), FCR, liveability (%), EFF
Duration	40 days
Location	Shandong

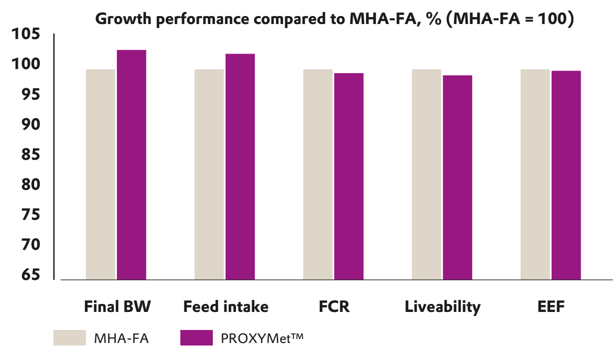
GRAPH 1: Saving with DL-methionine vs. MHA-FA



Price of MHA-FA at RMB 13.60/kg vs. DLM at RMB 17.00/kg x 65% = RMB 11.05/kg PROXYMet™

Price of MHA-FA at RMB 13.60/kg vs. DLM at RMB 17.00/kg x 65% = RMB 11.05/kg PROXYMet™

GRAPH 2: Growth performance compared to MHA-FA



Trial **Design**

Total of 212,000 ROSS 308 broilers were raised in a farm in 8 houses. In 4 houses broilers were fed MHA-FA diets, as a control group, and in the other 4 houses broilers were fed **PROXYMet™ (MetAMINO® diluted to 65% content with limestone)** diets, as a trial group. The numbers of broilers in each house was 28,000 or 25,000 depending on the house size. All of the broilers were raised following the customer's SOP under commercial conditions.

Trial **Objectives**

The objective of this study was to determine the effects of replacing 100-parts of MHA-FA with 65-parts of DL-Methionine on broiler performance under a customer's commercial conditions.

Trial **Results**

Birds fed PROXYMet™ showed no differences in final body weight, feed intake, FCR, liveability and EEF (European efficacy factor), compared to those fed MHA-FA (Graph 2).

It can save about 6 RMB/MT broiler feed when using PROXYMet™ instead of MHA-FA (Graph 1 and Table 2).

TABLE 2: Cost saving of different Methionine source per ton feed

	Price, RMB/kg	Dosage, kg/MT	Met cost, RMB/MT	Cost saving
MHA-FA	13.6	2.31	31.4	
PROXYMet™	11.05	2.31	25.5	5.9 RMB/MT feed

CONCLUSION

1 kg of MHA-FA can be directly replaced by the same product weight of PROXYMet™ without compromising growth performance in ROSS 308 broilers.

The large-scale trial results indicate that a customer can use 650 g of MetAMINO® to replace 1 kg of MHA-FA in broiler feeds to save money under commercial situations.

This commercial trial confirms that the nutritional value of MHA-FA is 65%, which is recommended by Evonik.

FEEDBACK

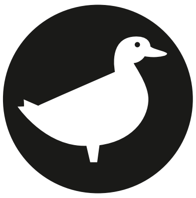
"Customer was convinced by the results and began to use DLM instead of MHA-FA."

Dr. Mandy Yan,
Technical Manager
Evonik China

The comparation between PROXYMet™ and MHA-FA in meat ducks

Trial conducted by customer in Shandong province, 2021

Trial location:
Shandong, China

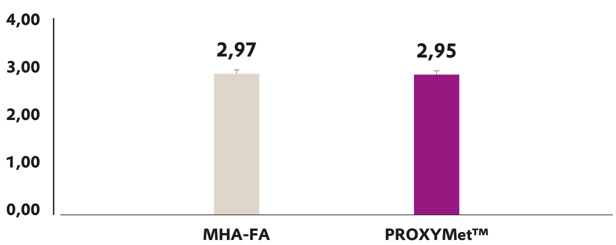


Project team leaders:
Dr. Lorin Zhang

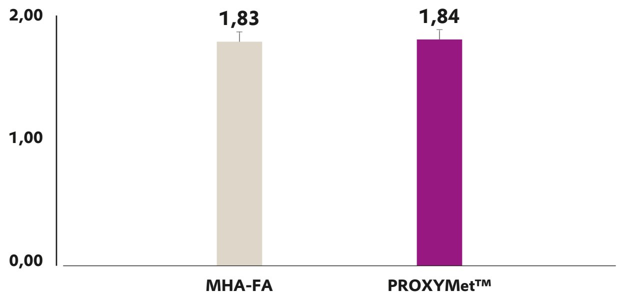
TABLE 1: Trial Design, Methods and Materials

Animals	379,300 Cherry Valley ducks
Diets	Corn-mix-meal-based commerical duckling, grower and finisher duck feed
Design	Ducks in control group were fed MHA-FA, and ducks in treatment groups were fed **PROXYMet™** (MetAMINO® diluted to 65% with limestone)
Feeding	10 customers used MHA-FA formulated feed for ducks, and 13 customers used **PROXYMet™** formulated feed for ducks. Diets are same except for the methionine source
Parameters	Final body weight (kg), feed intake (kg), FCR, liveability (%)
Duration	39 days
Location	Shandong

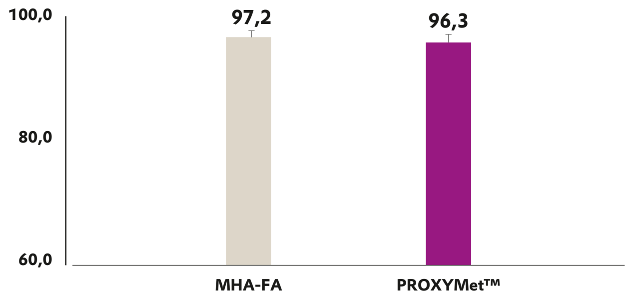
GRAPH 1: Body weight (kg)



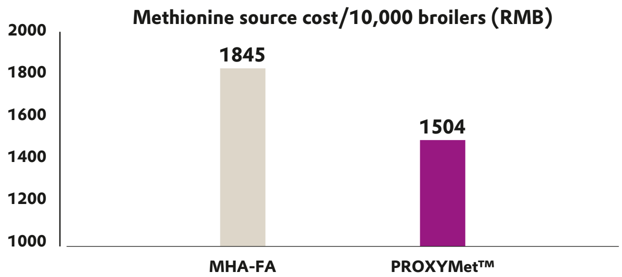
GRAPH 2: FCR



GRAPH 3: Liveability



GRAPH 4: Saving with DL-methionine vs. MHA-FA



- Price of MHA-FA at RMB 13.60/kg vs. DLM at RMB 17.00/kg x 65% = RMB 11.05/kg PROXYMet™
- Cost = Feed intake x MHA or PROXYMet™ dosage x Price x 10,000 ducks
- Average total feed intake per duck in MHA group and PROXYMet™ group, 5.43 vs 5.45 kg

Trial **Design**

Total 379,300 ducks were used in this commercial trial. The ducks in the control group were fed MHA-FA formulated diets, while those in the treatment group were fed PROXYMet™ (MetAMINO® diluted to 65% content with limestone) formulated diets. The control group consisted of 10 customers with 168,000 ducks, while the treatment group consisted of 13 customers with 211,300 ducks.

The dosage of MHA-FA or PROXYMet™ was equal in the corresponding diets.

Trial **Objectives**

To validate that PROXYMet™ can replace MHA-FA in commercial meat duck feeds without compromising animal performance.

To provide evidence to customers to switch from MHA-FA to DL-methionine.

Trial Results

Ducks in both MHA-FA and PROXYMet™ groups had a similar final body weight (2.97 vs 2.95 kg / Graph 1).

No differences were found in feed intake, FCR (Graph 2) and liveability (Graph 3) for the two groups during the whole period.

Savings of 341 RMB are possible when rearing 10,000 ducks using PROXYMet™ instead of MHA-FA. (Graph 4 and Table 2).

TABLE 2: Cost saving of different Methionine source per 10,000 ducks

	Price, RMB/kg	Dosage, kg/MT	Average total feed intake, kg/duck	Calculated Met consumption, kg/10,000 ducks	Met cost, RMB/10,000 ducks	Cost saving/ 10,000 ducks
MHA-FA	13.6	2.5	5.43	135.65	1845	
PROXYMet™	11.05	2.5	5.45	136.13	1504	341 RMB

1) Price of MHA-FA at RMB 13.60/kg vs. DLM at RMB 17.00/kg x 65% = RMB 11.05/kg PROXYMet™;
2) Cost =Feed intake x MHA or PROXYMet™ dosage x Price x 10,000 ducks,
3) Average total feed intake per duck in MHA group and PROXYMet™ group, 5.43 vs 5.45 kg

CONCLUSION

1 kg of MHA-FA can be directly replaced by the same weight of PROXYMet™ without negative influences on growth performance in meat ducks.

This large-scale trial's results indicate that feed mills can use 650 g of MetAMINO® to replace 1 kg of MHA-FA in duck feed under commercial situations.

This commercial trial confirmed the nutritional value of MHA-FA was 65% compared to DL-methionine.

FEEDBACK

"Customer was very satisfied with the trial use results and switched from MHA-FA to DLM"

Dr. Lorin Zhang,
Senior Sales Manager
Evonik China

Effect of PROXYMet™ and equal MHA-FA on performance in laying hens

Trial conducted by customer in Jiangsu province, 2022

TRIAL 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 **19**

Trial location:

Jiangsu, China

Project team leaders:

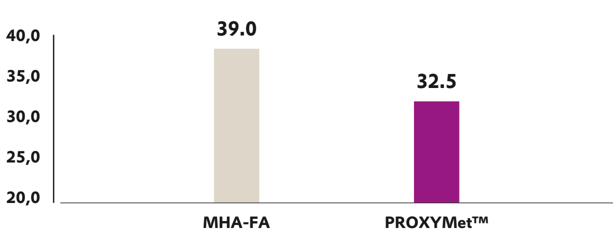
Ms. Sara Yang

Dr. Brian Wang

TABLE 1: Trial Design, Methods and Materials

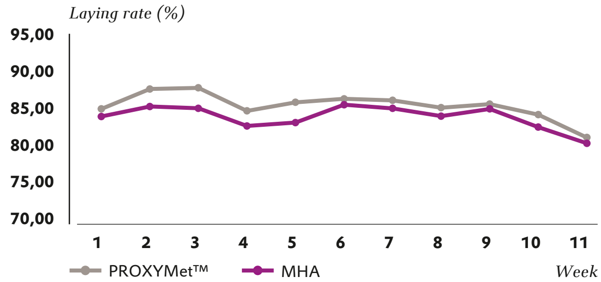
Animals	120,000 Hy-line brown laying hens
Diets	Corn-soybean meal basal commerical layer diets
Design	Two houses of 60 wk layers were conducted into two treatments: One house for MHA-FA treatment: layers were fed feed added with MHA-FA (2.5kg/T); Another house for PROXYMet™ treatment: layers were fed feed with equal weight PROXYMet™ (MetAMINO® diluted to 65% with limestone)
Feeding	Layers were fed in stacked cage system under commercial production conditions
Parameters	Laying rate, egg mass, FCR
Duration	60-70 weeks
Location	Conmercial layer farm in Jiangsu

GRAPH 1: Cost saving with MHA-FA vs PROXYMet™

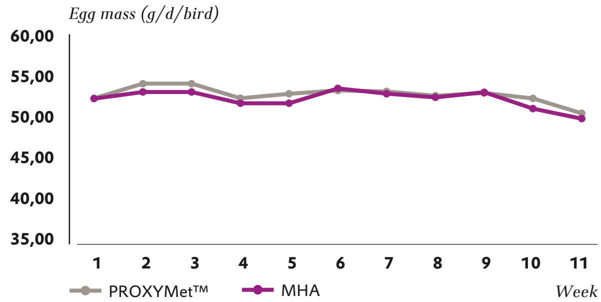


*Price of met source was referenced by the average price in 2022 (DLM 20, MHA-FA 15.6 RMB/kg)

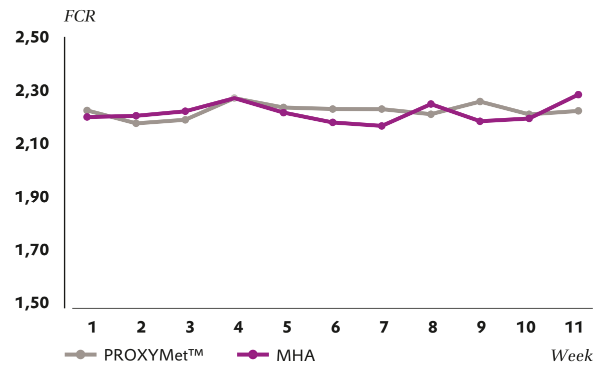
GRAPH 2: Effect of PROXYMet™ and equal MxHA-FA on laying rate of laying hens



GRAPH 3: Effect of PROXYMet™ and equal MHA-FA on egg mass of laying hens



GRAPH 4: Effect of PROXYMet™ and equal MHA-FA on FCR of laying hens



Trial **Design**

Two houses of total 120,000 Hy-line brown laying hens were used in this commercial trial. Layers in one house were fed feed with MHA-FA (2.5kg/T), while layers in another house were fed feed with an equal amount of PROXYMet™ (MetAMINO® diluted to 65% with limestone). The corn-soybean meal basal commercial layer diet was the same except for the methionine source. Layers were fed in a stacked cage system under commercial production conditions. The duration of the commerical trial was 60-70 weeks for laying hens. Performance parameters including the laying rate, egg mass, and FCR were observed.

Trial **Objectives**

The objective of this trial was to determine the effect of replacing equal parts MHA-FA with PROXYMet™ (65% DL-Methionine) on the performance of laying hens under commercial conditions.

Trial **Results**

60-70 weeks of laying hens fed feed with PROXYMet™ showed no difference in laying rate, egg mass, and FCR compared to layers fed feed added with equal parts MHA-FA.

Adding PROXYMet™ to replace equal parts MHA-FA in layer feed can save about 6.5 RMB/T cost of adding a met source in feed (32.5 vs 39.0 RMB/T).

TABLE 2: Cost saving of different Methionine source per ton feed

	Price, RMB/kg	Dosage, kg/MT	Met cost, RMB/MT	Cost saving
MHA-FA	15.6	2.5	39.0	
PROXYMet™	13.0	2.5	32.5	6.5 RMB/MT feed

CONCLUSION

PROXYMet™ (65% DL-Methionine) can replace an equal quantity of MHA-FA in laying hen diets with no difference on performance parameters, according to this large scale commercial trial.

This commercial trial confirmed the nutritional value of MHA-FA was 65% compared to DLM.

Using PROXYMet™ to replace equal MHA-FA in layer feed can reduce the cost of adding a met source in feed.

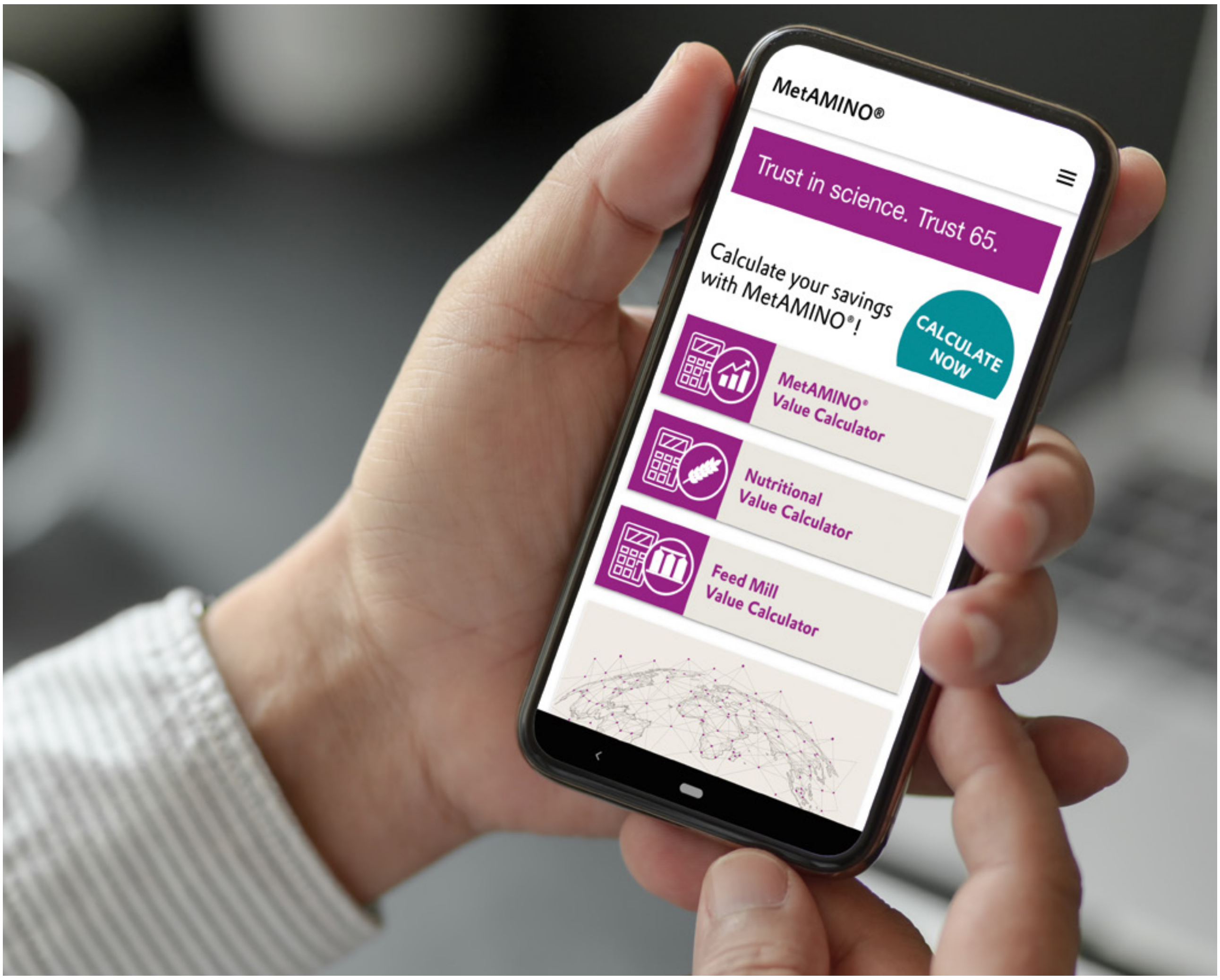
FEEDBACK

"Customer accepted that the nutritional value of MHA-FA is 65% compared to DLM according to this trial. Replacing equal parts MHA-FA with PROXYMet™ (65% DL-Methionine) can reduce feed costs."

Dr. Brian Wang,
Technical Service Manager
Evonik China

MetAMINO® Calculator App

Do you want to calculate your potential savings with MetAMINO®?
We have three different calculators that can be used depending on your needs.



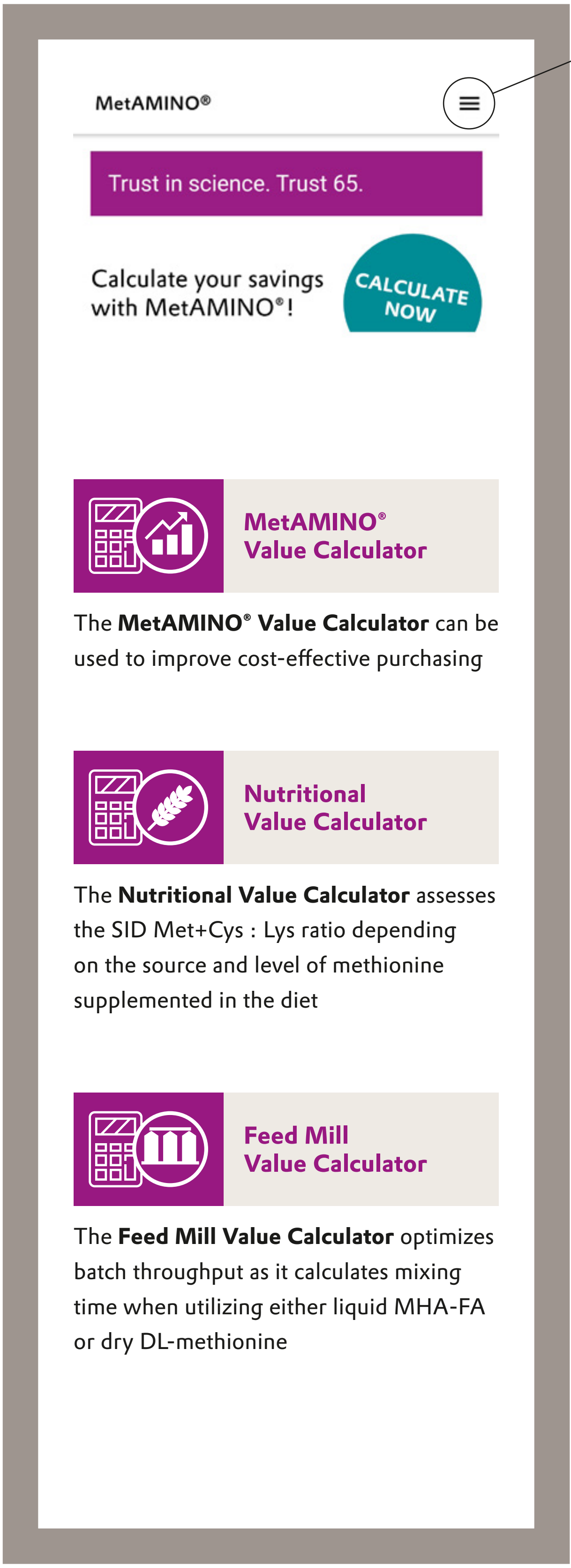
YOU CAN DOWNLOAD THE APP FOR FREE HERE:

GET IT ON Google Play

Download on the App Store

MetAMINO® Calculator page, **Chinese**

metamino.com



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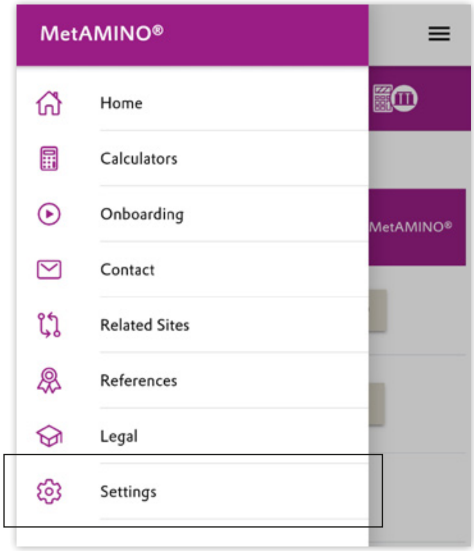
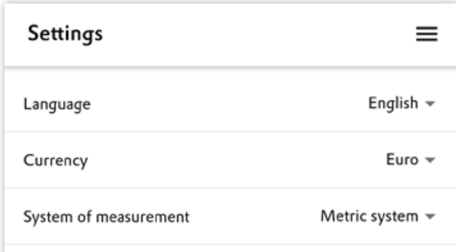




System of measurement
Metric system
Imperial system

Language
Chinese | English | French
German | Portuguese | Spanish

Currency
Argentine peso, Australian dollar, Brazilian real, Canadian dollar, Chinese yuan, Indian rupee, Japanese yen, Mexican peso, Pound sterling, Russian ruble, South African rand, South Korean won, Swiss franc, Turkish lira, Thai baht, Vietnamese dong

BECAUSE IT'S ABOUT

EXPERTISE

Section 2

Videos

Go to video

Overview

1	"BAM! Biological availability of methionine and its analogues"
2	"Benefits beyond growth: How methionine levels, sources boost poultry health" in cooperation with Feed Strategy (see section 1, trial no. 5)
3	"PROXYMet™: a mixture of 65% DL-methionine and 35% calcium carbonate to replace MHA-FA/Ca one-to-one"
4	"Effects of methionine supplement sources and crude protein on Ross 708 male broiler performance" in cooperation with the Department of Animal Science, Pennsylvania State University, University Park, PA 16802, USA (see section 1, trial no. 5)
5	"Sustainable low protein feeding strategies help to enable increased sustainability performance while decreasing nitrogen pollution"
6	"Importance of Methionine as a feed additive and its economic relevance" in cooperation with WATT POULTRY (see section 1, trial no. 8)
7	"Evaluation of methionine sources on performance and carcass traits of broilers at different dietary sulfur amino acid levels under northern European and middle Eastern conditions" (see section 1, trials no. 9 and 13)
8	"Supplementation of DL-methionine at 65% of MHA-FA support similar performance in broilers" (see section 1, trial no. 13)
9	"Be precise with 'Precise bio-efficacy' in swine nutrition"
10	"Methionine: A Functional Nutrient for a Greener Blue Revolution"
11	How important are mixing homogeneity and dosing accuracy
12	How Mepron® can benefit your farm
13	Profitable dairy production with Evonik's solutions
14	inoSust®
15	Sustainability Podcast

1. BAM!
Biological availability of methionine and its analogues

In this video Dr. Andreas Lemme

- explains why consideration of the biological effectiveness of methionine and its analogues is important
- explains that classical methods such as digestibility assays are not sufficient to answer the question on biological availability of methionine hydroxy analogues.
- explains how relative biological bioavailability it is determined.
- provides information on the validation of the method of determination of the relative bioavailability
- suggests how everybody can challenge and validate Evonik's recommendation of 65% bioavailability for methionine hydroxy analogues relative to MetAMINO®.

2. Benefits beyond growth: How methionine levels, sources boost poultry health

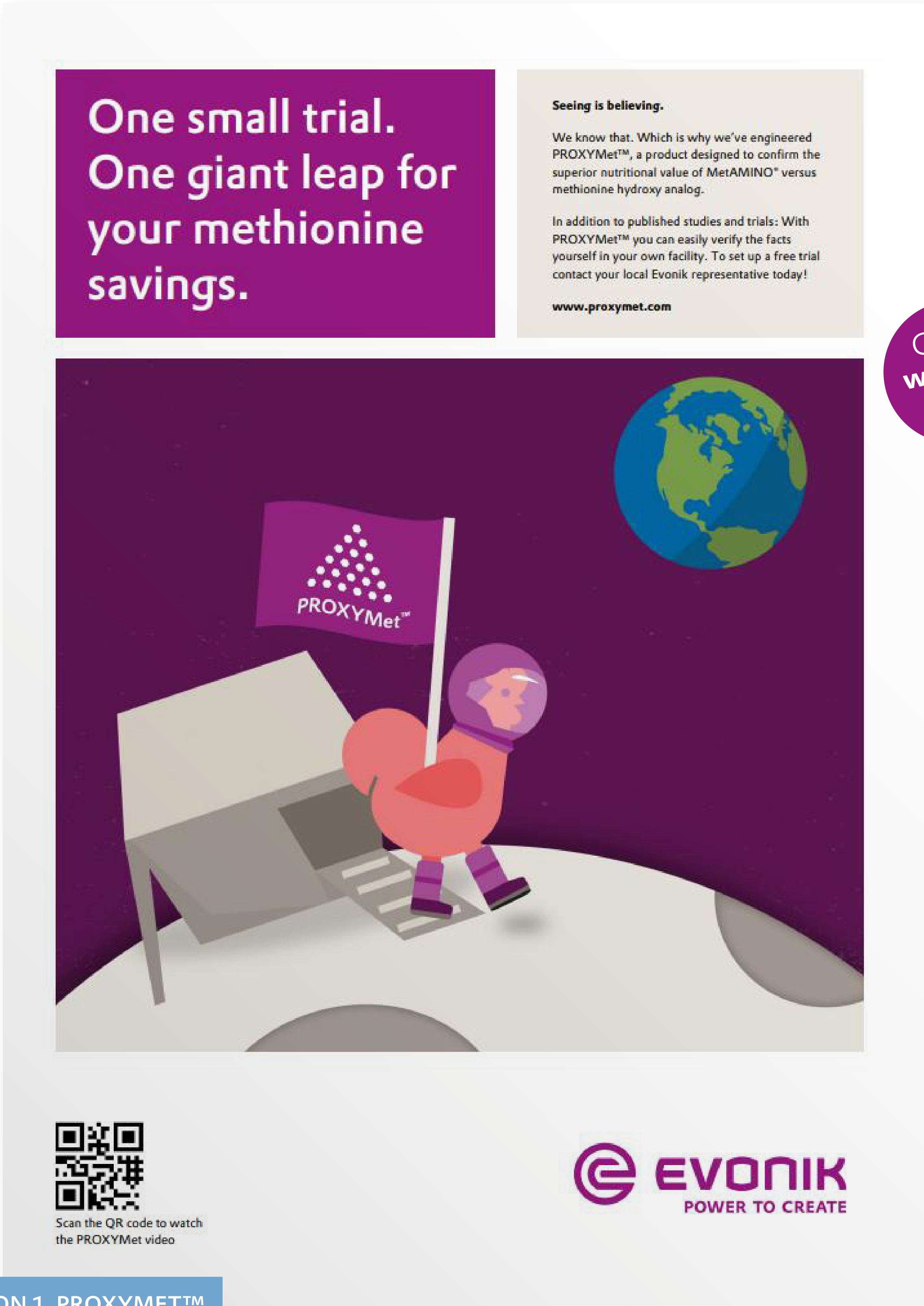
Our Technical Services Director for the Americas region,@Victor Naranjo,was interviewed by Feed Strategy on "Benefits beyond growth: How methionine levels, sources boost poultry health."

In the interview, he touches on the differences between DL-Met and MHA and which of the two exhibitbetter antioxidant function.He also highlights the other benefits of DL-met:

- Bioavailability
- Handling properties
- Better feathering
- Health performance
- As well as some of our ongoing research on this topic.

SECTION 1. TRIAL NO. 5

3. PROXYMet™: a mixture of 65% DL-methionine and 35% calcium carbonate to replace MHA-FA/Ca one-to-one



Go to website

SECTION 1, PROXYMET™

4. Effects of methionine supplement sources and crude protein on Ross 708 male broiler performance

SECTION 1, TRIAL NO. 5

SECTION 4, ARTICLE NO. 8

5. Sustainable low protein feeding strategies help to enable increased sustainability performance while decreasing nitrogen pollution

Implementing animal diets with lower protein levels and balanced amino acids can mitigate the negative impact of animal husbandry on the biogeochemical nitrogen cycle, thereby contributing to the maintenance of the natural processes of the Earth.According to a rule of thumb in the animal feed industry, a one-percent reduction of protein level in the feed while balancing its amino acid profile leads to a ten-percent reduction of nitrogen excretion with the associated negative environmental impact. Such strategies promote sustainable livestock production and ensure a safe and stable operating space for future generations.

SEE SECTION 4, ARTICLE NO. 27

6. Importance of Methionine as a feed additive and its economic relevance

In this webinar we will have two contributions on methionine's importance as a feed additive. Methionine is an essential amino acid, and limiting in most common poultry diets, which makes balancing the dietary amino acid profile with supplemental methionine necessary. This importance increases the more that dietary protein reduction and precise nutrition are considered. Finally, cost effectiveness is key in times of high feed material prices and the correct application of supplemental methionine can help to reduce costs while ensuring optimal animal performance.

SECTION 1. TRIAL NO. 8

SECTION 4. ARTICLES & ABSTRACTS NO. 4

SECTION 4. ARTICLES & ABSTRACTS NO. 6

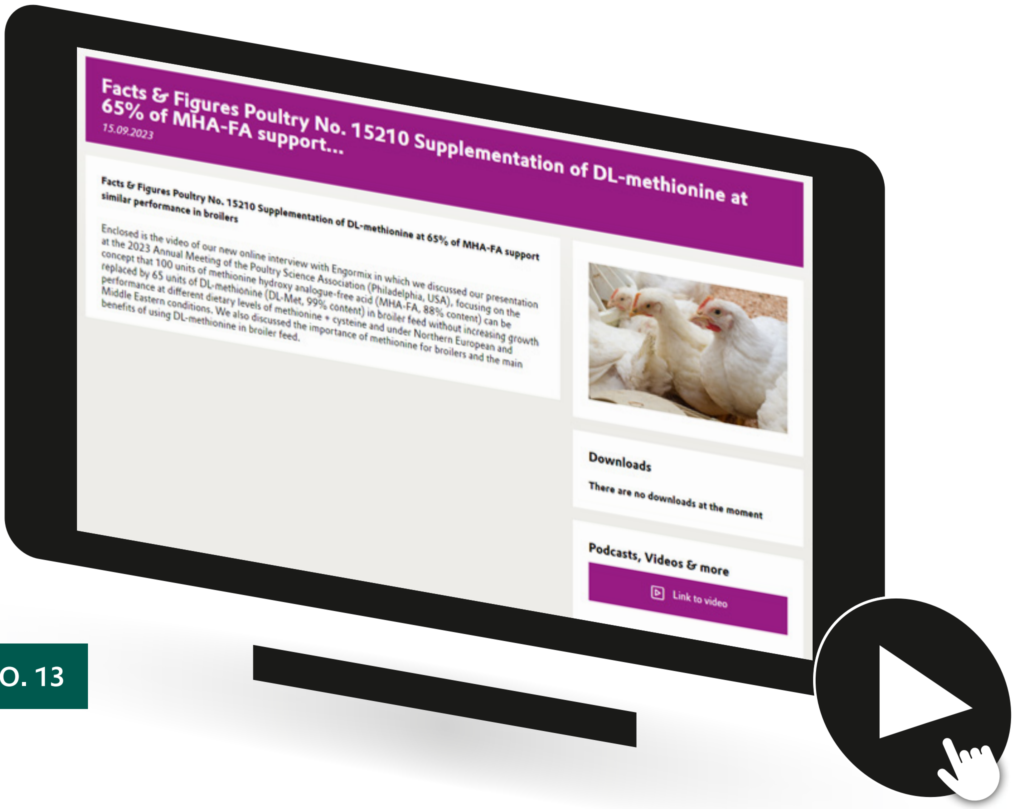
Section 1
Section 2
Section 3
Section 4

7. Evaluation of methionine sources on performance and carcass traits of broilers at different dietary sulfur amino acid levels under northern European and middle Eastern conditions

SECTION 1, TRIAL NO. 9

SECTION 1, TRIAL NO. 13

8. Supplementation of DL-methionine at 65% of MHA-FA support similar performance in broilers



SECTION 1, TRIAL NO. 13

9. Be precise with 'Precise bio-efficacy' in swine nutrition

10. Methionine: A Functional Nutrient for a Greener Blue Revolution

11. How important are mixing homogeneity and dosing accuracy

12. How Mepron® can benefit your farm

13. Profitable dairy production with Evonik’s solutions

14. inoSust®

Evonik's service offer that helps clients to calculate and improve the environmental footprint of feed and animal protein production.

SEE SECTION 4, ARTICLE NO. 27

15. Sustainability Podcast

Hear from key opinion leaders about their insight and uptakes on sustainability in animal nutrition and farming. The task of feeding an ever-growing world population while keeping the environment healthy is in everyone's agenda because it's all about life.

HOW CAN WE FEED AN EVER-GROWING POPULATION HEALTHILY IN A WAY THAT ISN'T HARMFUL TO THE PLANET?

That's the burning question facing the animal nutrition and animal farming industries and we'll be looking at the answers in our podcast.

Each month we'll be speaking to leading industry voices and opinion leaders to get their cutting-edge insights on the challenges and solutions to making animal nutrition and farming more sustainable.

Because the task of feeding future generations in a sustainable way is an issue that affects us all. It's a global challenge needing global solutions. Let's science it.

Wish for more? Then, keep following us!

BECAUSE IT'S ABOUT
FACTS

Section 3

Amino Acid Recommendations

Go to document

Overview

Recommendations for Broilers

Amino acids and more.

Male Broilers

Recommendations for Standardized Ileal Digestible Amino Acids (% of diet)

Days	Metabol. Energy (MJ/kg)	(kcal/kg)	Lys	Met	Met + Cys	Thr	Trp	Arg	Ile	Leu	Val	His	Phe + Tyr
1 – 12*	12.70	3030	1.27	0.50	0.92	0.80	0.20	1.30	0.86	1.36	1.00	0.42	1.47
13 – 22	12.90	3080	1.09	0.44	0.81	0.70	0.18	1.13	0.75	1.17	0.87	0.36	1.26
23 – 35	13.00	3100	1.00	0.42	0.76	0.65	0.16	1.05	0.71	1.07	0.80	0.33	1.16
36 – 48	13.20	3150	0.95	0.40	0.74	0.63	0.16	1.01	0.68	1.02	0.77	0.31	1.10
> 49	13.40	3200	0.89	0.39	0.70	0.60	0.15	0.96	0.65	0.96	0.73	0.29	1.04

Female Broilers

Recommendations for Standardized Ileal Digestible Amino Acids (% of diet)

Days	Metabol. Energy (MJ/kg)	(kcal/kg)	Lys	Met	Met + Cys	Thr	Trp	Arg	Ile	Leu	Val	His	Phe + Tyr
1–12*	12.70	3030	1.25	0.50	0.91	0.79	0.20	1.28	0.85	1.34	0.99	0.41	1.45
13–22	12.90	3080	1.04	0.42	0.77	0.67	0.17	1.08	0.72	1.11	0.83	0.34	1.21
23–35	13.00	3100	0.93	0.39	0.70	0.61	0.15	0.98	0.66	1.00	0.75	0.31	1.08
36–48	13.20	3150	0.83	0.35	0.64	0.55	0.14	0.88	0.59	0.88	0.67	0.27	0.96
>49	13.40	3200	0.73	0.31	0.57	0.49	0.12	0.78	0.53	0.78	0.59	0.24	0.84

* equals a cumulated feed intake about 350 – 400 g/broiler.

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Recommendations for Laying Hens

Amino acids and more.

Laying Hens

Recommendations for Standardized Ileal Digestible Amino Acids (daily amino acid intake/mg)

	Lys	Met	Met+Cys	Thr	Trp	Arg	Ile	Leu	Val	His	Phe+Tyr
Amino acid intake (mg/day)	831	415	756	582	174	864	665	997	731	249	997

Laying Hens

Recommendations for Standardized Ileal Digestible Amino Acids (% of diet)

Feed intake (g/day)	Metabol. Energy (MJ/kg)	Metabol. Energy (kcal/kg)	Lys	Met	Met + Cys	Thr	Trp	Arg	Ile	Leu	Val	His	Phe + Tyr
80	11.82	2820	1.04	0.52	0.95	0.73	0.22	1.08	0.83	1.25	0.91	0.31	1.25
85	11.82	2820	0.98	0.49	0.89	0.68	0.21	1.02	0.78	1.17	0.86	0.29	1.17
90	11.82	2820	0.92	0.46	0.84	0.65	0.19	0.96	0.74	1.11	0.81	0.28	1.11
95	11.82	2820	0.87	0.44	0.80	0.61	0.18	0.91	0.70	1.05	0.77	0.26	1.05
100	11.82	2820	0.83	0.42	0.76	0.58	0.17	0.86	0.66	1.00	0.73	0.25	1.00
105	11.82	2820	0.79	0.40	0.72	0.55	0.17	0.82	0.63	0.95	0.70	0.24	0.95
110	11.82	2820	0.76	0.38	0.69	0.53	0.16	0.79	0.60	0.91	0.66	0.23	0.91
115	11.82	2820	0.72	0.36	0.66	0.51	0.15	0.75	0.58	0.87	0.64	0.22	0.87
120	11.82	2820	0.69	0.35	0.63	0.48	0.15	0.72	0.55	0.83	0.61	0.21	0.83

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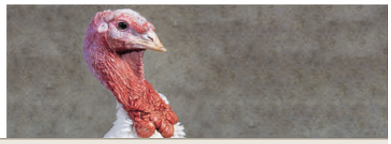
Recommendations for Turkeys

Amino acids and more.



Heavy Turkeys

Recommendations for Standardized Ileal Digestible Amino Acids (% of diet)

Sex	Weeks	Metabol. Energy (MJ/kg)	Metabol. Energy (kcal/kg)	Lys	Met	Met + Cys	Thr	Trp	Arg	Ile	Leu	Val	His
male female	1–2 1–2	11.50	2740	1.55	0.58	0.98	0.87	0.25	1.63	0.95	1.70	1.05	0.54
male female	3–5 3–5	11.70	2790	1.41	0.53	0.90	0.79	0.23	1.48	0.86	1.55	0.95	0.49
male female	6–9 6–9	12.10	2890	1.31	0.50	0.84	0.74	0.21	1.37	0.80	1.44	0.88	0.46
male female	10–13 10–13	12.50	2980	1.14	0.44	0.74	0.65	0.19	1.20	0.70	1.25	0.77	0.40
male female	14–17 14–15	12.80	3050	1.01	0.40	0.67	0.58	0.17	1.06	0.62	1.11	0.68	0.35
male female	18–22 16–20	13.20	3150	0.91	0.36	0.61	0.53	0.15	0.96	0.56	1.00	0.61	0.32

Medium Heavy Turkeys

Recommendations for Standardized Ileal Digestible Amino Acids (% of diet)

Sex	Weeks	Metabol. Energy (MJ/kg)	Metabol. Energy (kcal/kg)	Lys	Met	Met+Cys	Thr	Trp	Arg	Ile	Leu	Val	His
male female	1–2 1–2	11.50	2740	1.63	0.61	1.03	0.91	0.27	1.72	1.00	1.79	1.10	0.57
male female	3–5 3–5	11.70	2790	1.49	0.56	0.95	0.83	0.24	1.56	0.91	1.63	1.00	0.52
male female	6–9 6–9	12.10	2890	1.31	0.50	0.84	0.74	0.21	1.37	0.80	1.44	0.88	0.46
male female	10–13 10–13	12.50	2980	1.14	0.44	0.74	0.65	0.19	1.20	0.70	1.25	0.77	0.40
male female	14–17 14–15	12.80	3050	1.01	0.40	0.67	0.58	0.17	1.06	0.62	1.11	0.68	0.35

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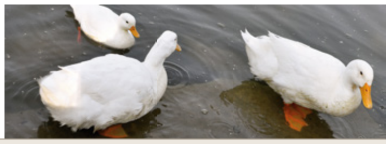
Recommendations for Peking Ducks

Amino acids and more.



Peking Ducks
Recommendations for Total Amino Acids (% of diet)

Days	Metabol. Energy (MJ/kg)	Metabol. Energy (kcal/kg)	Lys	Met	Met + Cys	Thr	Trp	Arg	His	Val
1–21	12.20	2940	1.16	0.42	0.76	0.84	0.21	0.94	0.42	0.77
22–49	12.60	3000	0.90	0.42	0.77	0.66	0.20	0.76	0.32	0.59

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Recommendations for Swine

Amino acids and more.


Growing Swine

Recommendations for Standardized Ileal Digestible Amino Acids (% of diet)*

Body weight (kg)	Net Energy** (MJ/kg)	Net Energy** (Mcal/kg)	Lys	Met	Met+Cys	Thr	Trp	Arg	Ile	Leu	Val	His	Phe+Tyr	Lys (g/MJ NE)	Lys (g/Mcal NE)
<10	10.7	2.56	1.42	0.47	0.85	0.89	0.31	0.60	0.78	1.42	0.97	0.45	1.35	1.33	5.55
10–20	10.4	2.49	1.32	0.43	0.79	0.83	0.29	0.55	0.72	1.32	0.89	0.42	1.25	1.26	5.29
20–40	10.2	2.44	1.08	0.37	0.67	0.70	0.22	0.43	0.60	1.08	0.74	0.35	1.03	1.06	4.44
40–60	10.2	2.44	0.94	0.32	0.58	0.61	0.19	0.38	0.52	0.94	0.64	0.30	0.89	0.92	3.86
60–80	10.0	2.39	0.84	0.29	0.53	0.56	0.17	0.30	0.46	0.84	0.57	0.27	0.80	0.84	3.50
80–100	10.0	2.39	0.75	0.27	0.49	0.53	0.14	0.24	0.41	0.75	0.51	0.24	0.71	0.75	3.15
100–120	10.0	2.39	0.65	0.23	0.42	0.45	0.12	0.21	0.36	0.65	0.44	0.21	0.61	0.65	2.70

Reproductive Swine

Recommendations for Standardized Ileal Digestible Amino Acids (% of diet)

	Net Energy** (MJ/kg)	Net Energy** (Mcal/kg)	Lys	Met	Met+Cys	Thr	Trp	Arg	Ile	Leu	Val	His	Phe+Tyr	Lys (g/MJ NE)	Lys (g/Mcal NE)
Sows Gestating	8.9	2.13	0.59	0.21	0.39	0.41	0.13	0.53	0.35	0.57	0.40	0.21	0.59	0.66	2.80
Sows Lactating	9.8	2.34	0.85	0.28	0.51	0.58	0.19	0.48	0.50	0.97	0.72	0.34	0.96	0.87	3.60

* High lean growth potential (> 875 g ADG or >140 g body protein deposition per day from 20 to 120 kg)
** For conversion to NE: ME x 0.74
DE x 0.71

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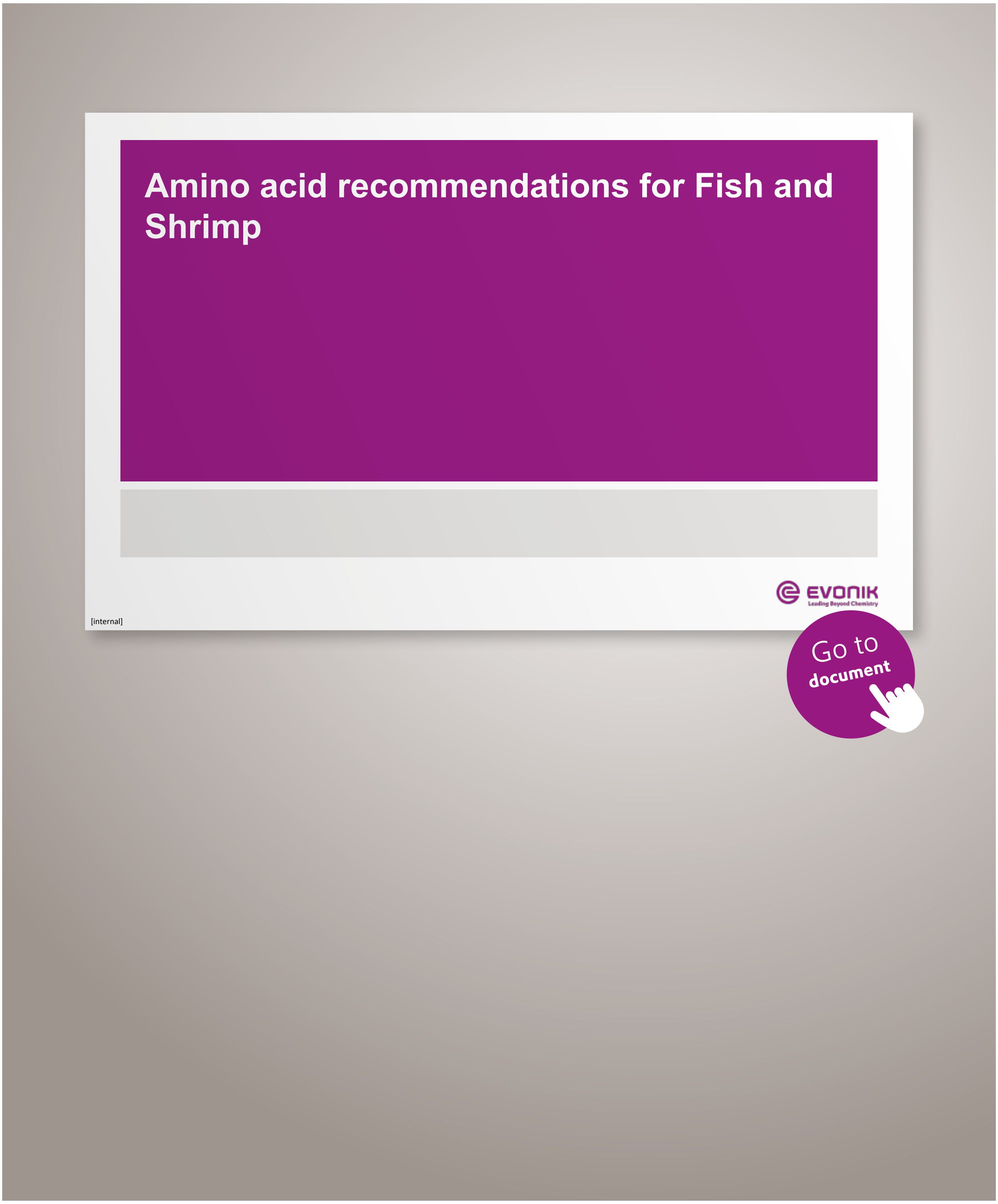
6. Aqua



Section 1
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Section 4

BECAUSE IT'S ABOUT

LEARNING

Section 4

Articles & Abstracts

Go to document

Overview

FEED TECHNOLOGY SERVICES @ EVONIK ANIMAL NUTRITION

Handle micro-ingredients with ease and precision

Tiny proportions have huge effects. Whether medical additives, vitamins, enzymes or amino acids, micro-ingredients can make all the difference in feed. No wonder micro-ingredient dosing and handling are such critical factors in profitable feed production.

The globally leading animal nutrition specialists at Evonik have developed handling solutions **(AMINOSys® DOSING SYSTEMS)** and services to bring feed production up to the next level of efficiency. Based on the requirements for product dosing and handling – whether tiny proportions or full bulk deliveries – you can count on our local feed technology experts for the support you need to optimize your processes.

Adding a high number of different micro-ingredients directly to your feed composition allows fine-tuning of least-cost formulations that optimize animal performance according to the needs of the individual species and age groups. No wonder the number of micro-ingredients continues to increase in step with scientific advances in animal nutrition. Manual handling of bagged micro-ingredients is labor-intensive. Dosing may become a bottleneck and significant cost-driver for your process.

Evonik Animal Nutrition has the answer, with a dosing and handling portfolio that includes solutions and services for full bulk, big bag and – new – small bag deliveries to improve feed mill productivity and feed quality.

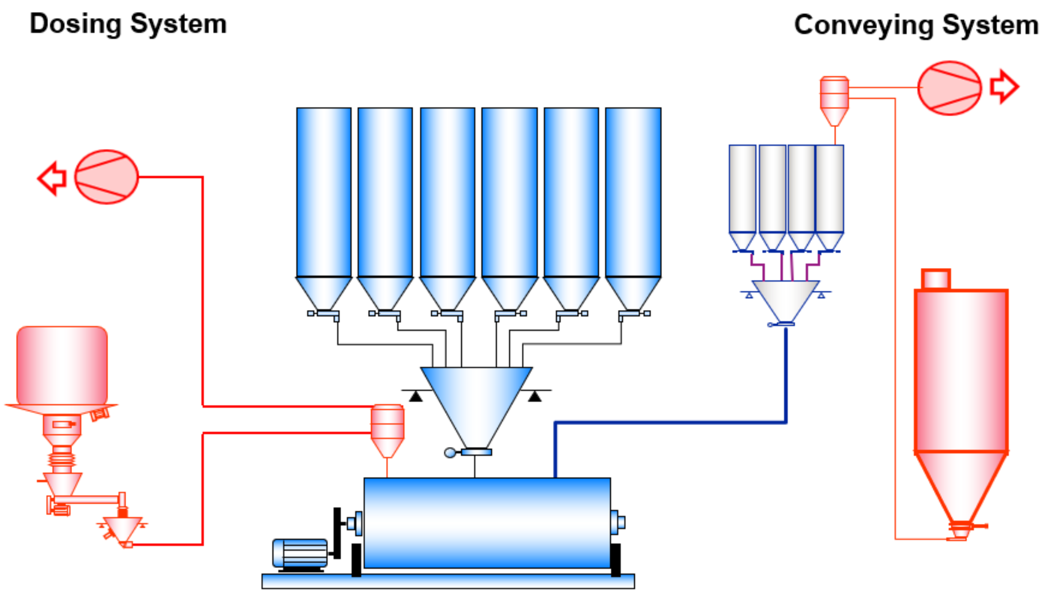
AMINOSys® DOSING SYSTEMS HELP OUR CUSTOMERS TO MANAGE THEIR DOSING PROCESSES

Evonik AMINOSys® dosing system provides our customers with several benefits. These include

- accurate and reliable amino acid dosage going into the mixer (+/- 50g per batch)
- storage, dosing and conveying of up to six micro ingredients
- fully automated dosing process (integrated into the feed mill process control system).
- long-term customer relationships for more than 30 years on six continents.
- Today over 700 systems are installed, running and linked with approximately 65 million tons of feed production per year.

AMINOSys® IS TAILORED TO YOUR NEEDS

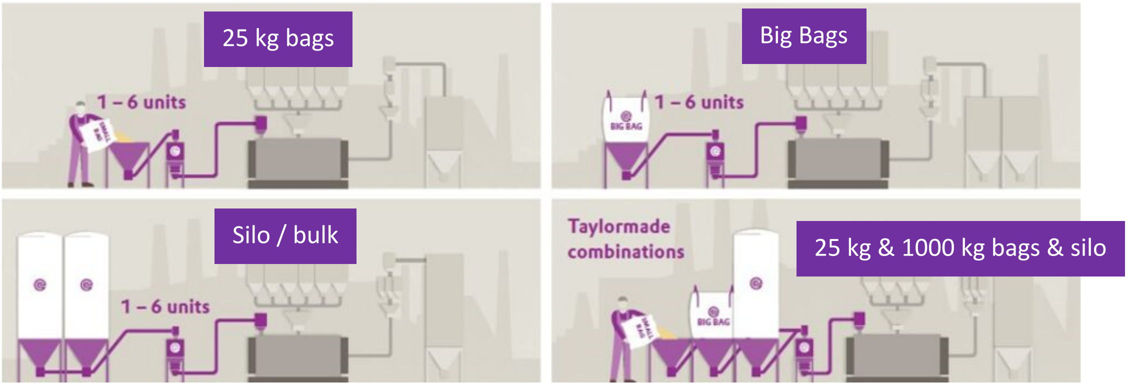
- **Evonik AMINOSys®** provides solution for dosing and pure conveying systems



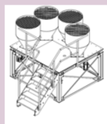
- **Evonik AMINOSys®** provides solutions for all packaging forms

Full Bulk	Small Silo	Big Bag	25kg Bag
			

- **Evonik AMINOSys®** is a flexible turnkey solution



- **Evonik AMINOSys®** is adjustable for every batch size

Dosing range of 1 – 150 kg			Dosing range of 0.1 – 10 kg		
Full Bulk	Big Bag	25kg Bag	Loss-In-Weight (25kg Bag)	1 Product (25kg Bag)	4 Product (25kg Bag)
					

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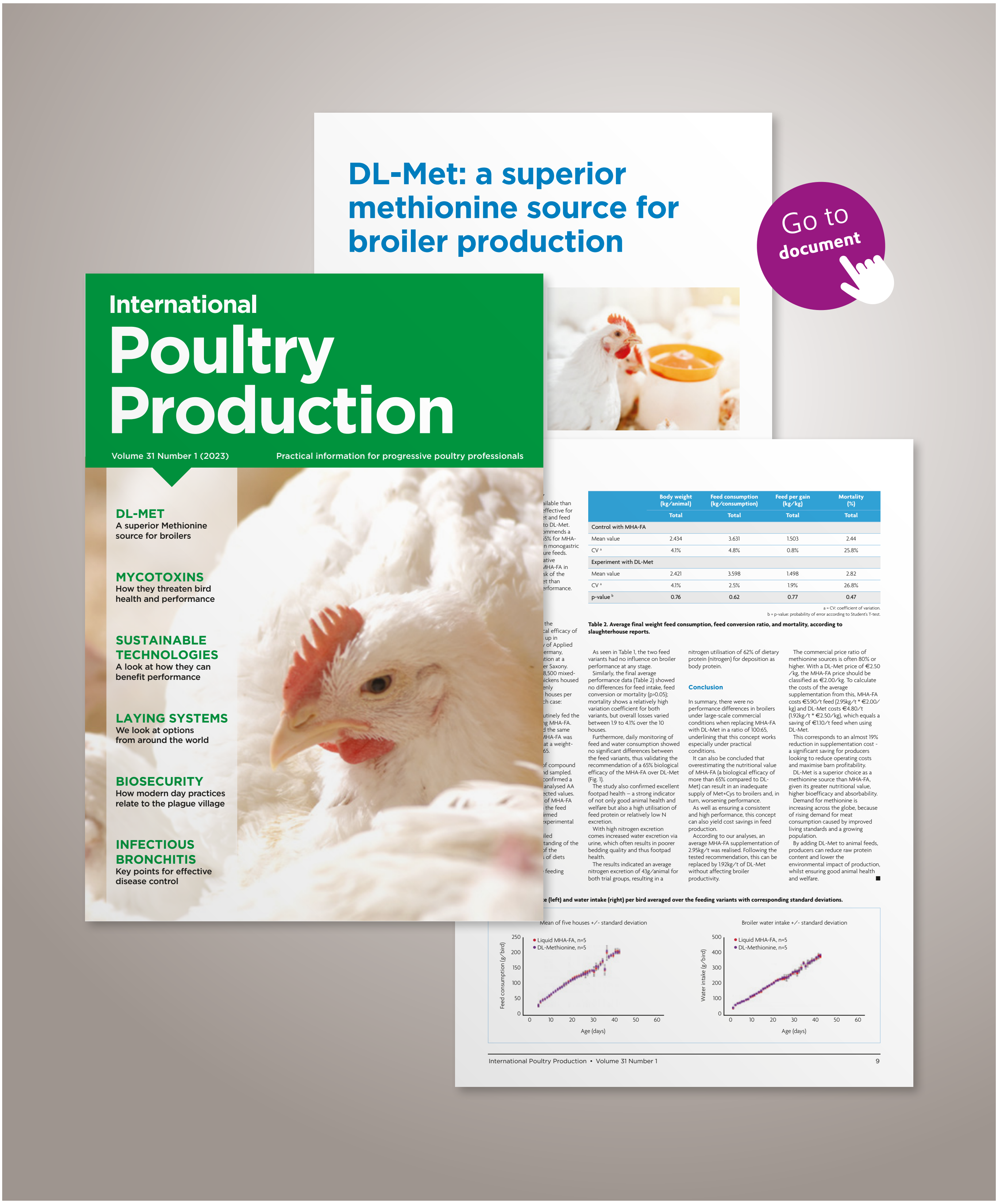
2. DL-Met: a superior methionine source for broiler production



3.

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METHIONINE SOURCES IN TURKEYS – AN UPDATE*

KEY INFORMATION

- A compilation of scientific information was done based on 15 available data sets from studies conducted since 1981 resulting in average relative efficacy value (RBV) of 76 % (weight gain), and 68 % (feed conversion) for liquid MHA-FA compared to DL-Met in turkeys.

- Despite the compilation indicate slightly higher values, a RBV of 65 % on a weight-to-weight basis is recommended for liquid MHA-FA in turkey nutrition. The recommendation was validated in several feeding trials where DL-Met and liquid MHA-FA were supplemented at 65:100 ratio without significant change in performance.

- At marginal dietary Met+Cys levels, which represent more sensitive test conditions, liquid MHA-FA could be replaced by DL-Met in turkey diets without compromising performance and DL-Met even provided extra benefits regarding improved breast meat yield, antioxidant capacity of liver and foot pad health.

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INTRODUCTION

Commercial poultry diets are routinely supplemented with methionine or its precursors to precisely meet their sulphur amino acid (SAA) specifications. Methionine (Met) is an essential amino acid for poultry and serves as a building block for protein synthesis, being also a precursor for cysteine (Cys) and important methyl donor (Selle *et al.*, 2020). Most of the supplemental Met commercially available is supplied as crystalline DL-methionine (DL-Met, 99 % content) or as liquid DL-2-hydroxy-4-methylthio butanoic acid (methionine hydroxy analogue-free acid, MHA-FA; 88 % content) (Willke, 2014). Both products provide Met activity to poultry, but chemically MHA-FA is not an amino acid due to the replacement of the characteristic amino group by a hydroxy group (Yang *et al.*, 2020). In addition to the chemical differences, there are studies indicating slower and less efficient absorption of liquid MHA-FA due to differences in transport systems in intestinal brush border membrane and potential catabolism by enteric bacteria (Maenz and Engele-Schaan 1996, Drew *et al.*, 2003). Therefore, understanding the nutritional value indicated by the relative bioefficacy value (RBV) of liquid MHA-FA compared to DL-Met is an important precondition to cost-effective purchasing, feed formulation, and optimum animal production (Sauer *et al.*, 2008).

A RELATIVE BIOEFFICACY OF 65 % FOR LIQUID MHA-FA IS RECOMMENDED FOR TURKEYS

A proper evaluation of potential differences in the bioefficacy of two products is strongly dependent on an adequate trial design. In such experiments, the treatments comprise a basal diet deficient in Met+Cys and a set of diets with incremental Met+Cys levels. The effect of the incremental Met supplementation on performance criteria describes the dose-response relationship which is not linear but follows the law of diminishing returns. The first unit of supplemental Met results in a relatively strong effect, i. e. significantly increases the performance. This effect diminishes progressively with each additional amount of Met supplementation. Eventually an optimum supply status is reached where no further increase in performance can be achieved. This curve can accurately be described by an exponential regression equation (Rodehutscord and Pack, 1999). The more data points describe the non-linear first section of the response curve, the more robust is the conclusion. The methodology of simultaneous exponential regression as proposed by Littell *et al.* (1997) assumes that both nutrient sources under test allow for the same asymptote of the response curves. Although the experimental setup to determine the RBV has been a matter of discussion and different asymptotes have been proposed by Gonzales-Esquerra *et al.* (2007), the meta-analysis performed by Sauer *et al.* (2008) including 46 dose-response experiments with broilers, as well as a more recent broiler trial (Lemme *et al.*, 2020), provided evidence that the asymptotes are the same for liquid MHA-FA and DL-Met.

Table 1: Relative bioefficacy of liquid MHA-FA compared to DL-met (%) in turkeys from fifteen available data sets[1]

Author	Institute	published	Relative Bioefficacy	
			Weight gain	Feed conversion ratio
Schmidt	Virginia Polytech. Ins. & Univ., USA	Master Thesis, 1981	75	63
Schmidt	Virginia Polytech. Ins. & Univ. , USA	Master Thesis, 1981	64	67
Blair	Virginia Polytech. Ins. & Univ. , USA	Master Thesis, 1983	80	72
Blair	Virginia Polytech. Ins. & Univ. , USA	Master Thesis, 1983	105	84
Noll *et al.*	Univ. Minnesota, USA	Poultry Science 63:2458-2470, 1984	98	84
Noll *et al.*	Univ. Minnesota, USA	Poultry Science 63:2458-2470, 1984	76	48
Noll *et al.*	Univ. Minnesota, USA	Poultry Science 63:2458-2470, 1984	89	81
Harms	Univ. Florida, USA	Carolina Nutr. Conference, 1987	63	64
Potter *et al.*	Virginia Polytech. Ins. & Univ. , USA	Trial report, 1987	59	80
Potter *et al.*	Virginia Polytech. Ins. & Univ. , USA	Trial report, 1987	56	55
Hoehler *et al.*	Akey Inc., Lewisburg, USA	Journal of Appl. Poultr. Res 14:296-305, 2005	66	44
Hoehler *et al.*	Michigan State Univ. , USA	Journal of Appl. Poultr. Res 14:296-305, 2005	68	56
Gonzales-Esquerra *et al.*	Grupo Techn. Agroindustrial, Mex	Poultry Science 86:517-527, 2007	81	66
Gonzales-Esquerra *et al.*	Grupo Techn. Agroindustrial, Mex	Poultry Science 86:517-527, 2007	87	95
Batonon-Alavo *et. al.*	Missouri Contract Poultry Research, USA	26th World's Poultry Congress, ID:2191, 2022	76	66
		Average	**76**	**68**
		n	**15**	**15**

[1] updated table from Lemme *et al.* (2012)

The European Food Safety Authority (EFSA), which examines and assesses dossiers for product registration in the European Union, released a scientific opinion on liquid MHA-FA and its calcium salt in 2018 (Rychen *et al.*, 2018). This opinion concludes a lower RBV for MHA-products for non-ruminant animals and fish and suggests an

RBV of 75 % for MHA-products compared to DL-Met on equimolar basis which is equivalent to 66 % on product-to-product basis. This is in line with a recent meta-analysis by Lemme *et al.* (2020) concluding that RBV of MHA-FA was 62 %. In contrast to broilers, less scientific dose-response data on turkeys is available. While a couple of studies were published back in the 1980's, Hoehler *et al.* (2005), Gonzales-Esquerra *et al.* (2007) and Batonon-Alavo *et al.* (2022) conducted trials to determine the RBV of MHA-FA relative to DL-Met in turkeys using the simultaneous dose response approach more recently (**Table 1**). If only these studies would be considered, average RBV for liquid MHA-FA would be 75 % and 66 % for body weight gain and feed conversion ratio, respectively, and are therefore slightly lower than the overall average. Indeed, particularly the RBV for feed conversion ratio would be in line with the conclusion by EFSA (2018) indicating a RBV of 66 % for monogastric animals on product basis. Therefore, like recommendations for broilers, laying hens, swine, and aqua species (Lemme *et al*., 2012; Htoo and Rademacher, 2012; Lemme, 2010) an RBV of 65 % for liquid MHA-FA compared to DL-Met is recommended for turkey nutrition.

The following example is given to demonstrate an appropriate experimental design, as well as the proper mathematical model which should be used for data analysis and proper interpretation. In a feeding trial from day 7 to 50 with female Hybrid Converter turkeys, the effects of DL-met (99 % pure), a diluted DL-Met (65 %) which was made by blending DL-Met (99 %) with glucose, and liquid MHA-FA (88 %) on performance were compared (Hoehler *et al*., 2005). Corn-soy diets were supplemented with graded levels of the products (0.07, 0.14, 0.21, 0.28 %). In this trial, a RBV of 65 % was assumed a priori for diluted DL-Met (65 %) relative to pure DL-Met (99 %). Thus, these treatments could be regarded as an internal standard to check the validity of simultaneous regression analysis as suggested and validated by Lemme *et al.* (2020). With 3 out of 4 inclusion levels within the curve-linear part of the curve, the weight gain response of turkeys to graded levels of DL-Met, diluted DL-Met (65 %), and liquid MHA-FA described a nonlinear trend and, therefore, data were suitable for simultaneous exponential regression according to procedure proposed by Littell *et al.* (1997) (Figure 1). The determined RBV for diluted DL-Met (65 %) confirmed expectations although it was slightly lower than expected 65 % which is due to biological variation of data. RBV of both diluted DL-Met (65 %) and liquid MHA-FA were significantly lower than 88 %.

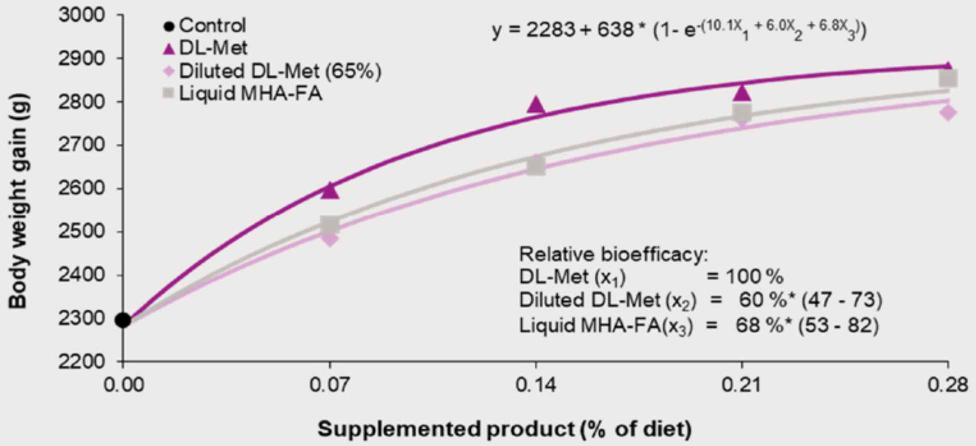

Figure 1: Weight gain of female Hybrid turkeys 7 to 50 days of age fed incremental levels of DL-Met, diluted DL-Met (65 %), or the liquid hydroxy analogue of Met (MHA-FA; 88 %). Values in brackets indicate the 95 % confidence interval.

*Significantly less than 88 % ($P < 0.05$).

Section 1
Section 2
Section 3
Section 4

A recent publication by Batonon-Alavo *et al.* (2022) proposed Single and Two Slope broken line regression to determine Met+Cys requirements of turkeys with DL-Met and liquid MHA-FA from 0 to 28 days. The authors concluded there is no difference in requirement regarding Met sources. While data confirm that both products can be used to meet the Met+Cys requirement of turkeys, the required supplementation to achieve the maximum response is different between the sources. The data by Batonon-Alavo *et al.* (2022) were re-analyzed by simultaneous exponential regression. The supplemental levels of DL-Met were calculated as the difference between the dietary SAA in the supplemented feeds and the SAA in the basal diet (0.700 % Met+Cys). For liquid MHA-FA, equimolar inclusion levels were assumed as suggested by the authors (88 %). The results of the re-evaluation can be obtained from **Figure 2**.

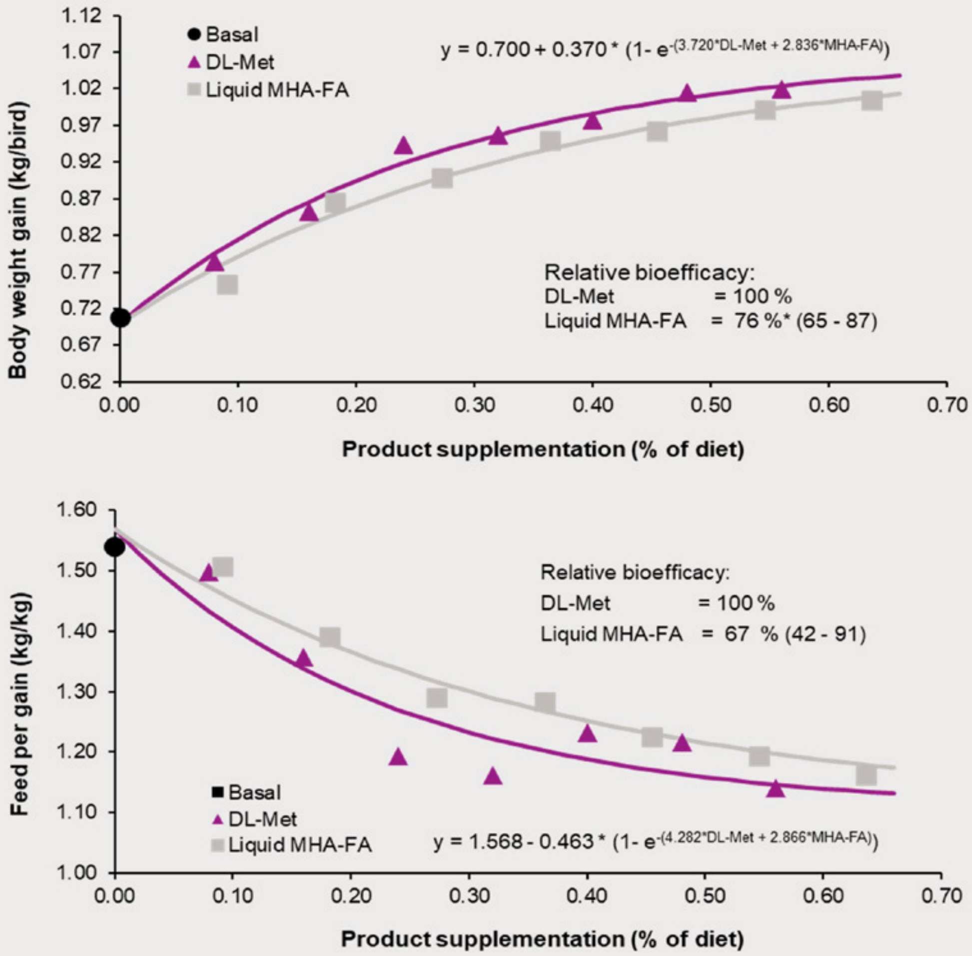

Figure 2: Re-evaluation of data reported by Batonon-Alavo *et al.* (2022) using simultaneous exponential regression on weight gain and feed conversion of Hybrid Converter poults fed increasing doses of either DL-Met (99 %) or MHA-FA (88 %) from 0 to 28 days of age. Values in brackets indicate the 95 % confidence interval.

*Significantly less than 88 % ($P < 0.05$).

THE VALIDATION OF THE RECOMMENDATION ON RELATIVE BIOEFFICACY

The recommended RBV of 65 % for liquid MHA-FA as compared with DL-Met (on product basis) was challenged and validated in feeding trials. Male 1-d-old B.U.T. Big 6 turkeys were evaluated in a 21 day feeding trial where dietary treatments comprised a basal diet, which was deficient in Met+Cys, and six diets with three graded levels of liquid MHA-FA (0.154, 0.308, and 0.462 %) or DL-Met (0.100, 0.200, and 0.300 %; Hoehler *et al.*, 2005). The ratio between both products at each of the three corresponding inclusion levels was 65 %, assuming that 100 units of liquid MHA-FA can be replaced by 65 units DL-Met without compromising performance. The summary of the results is presented in **Table 2**.

Table 2: Effect of graded levels of DL-Met and the liquid hydroxy analogue of Met (MHA-FA; 88 %) on weight gain and feed conversion in male B.U.T. Big 6 turkey poults from 1 to 21 d of age, trial 2 (Hoehler *et al.*, 2005)

Treatment	Met Source	Addition of Met source (% of product)	Weight gain ± SD	Feed per gain ± SD
1	Basal	---	481 ± 33[c]	1.547 ± 0.042[a]
2	DL-Met	0.100	520 ± 21[bc]	1.490 ± 0.057[ab]
3	DL-Met	0.200	550 ± 32[ab]	1.458 ± 0.033[b]
4	DL-Met	0.300	567 ± 29[a]	1.462 ± 0.075[ab]
5	Liquid MHA-FA	0.154	525 ± 31[abc]	1.496 ± 0.071[ab]
6	Liquid MHA-FA	0.308	550 ± 12[ab]	1.476 ± 0.034[ab]
7	Liquid MHA-FA	0.462	564 ± 21[ab]	1.469 ± 0.035[ab]

[a–c]Means with no common superscript within a column indicate significant differences ($P < 0.05$).

Accordingly, performance in corresponding treatments (2 vs 5, 3 vs 6, and 4 vs 7) did not differ, thus, confirming and validating the recommendation.

Lemme and Meyer (2009) conducted a trial with B.U.T. Big 6 turkey toms in a 6-phase feeding program. Also in this study, DL- Met or MHA-FA were supplied in a 65:100 ratio to either meet adequate Met+Cys levels in turkey diets or to be below requirement by supplementing half of the dose of both products. Dietary Met +Cys levels (normal vs half) resulted in a significant final body weight difference indicating that at half dosage Met+Cys supply was limiting performance (**Table 3**) making the 65:100 test more sensitive at lower supply.

Table 3: Growth and slaughter performance of male B.U.T. Big 6 turkeys toms fed with adequate and low Met+Cys levels and supplemented with either DL-Methionine (DL-Met) or liquid methionine hydroxy analogue free acid (MHA-FA) at a ratio of 65:100 after 21 weeks of life (Lemme and Meyer, 2009)

Met+Cys level	Normal[1]		Half (50%)		Statistics		
Met source	DL-Met	MHA-FA	DL-Met	MHA-FA	P-value	P-value	P-value
Treatment	1	2	3	4	(level)	(source)	L x S
Final body weight (kg)	21.42	21.68	20.86	20.94	**0.01**	0.430	0.679
FCR (g/g)	2.613	2.635	2.598	2.618	0.13	*0.054*	0.925
Mortality (%)	7.13	9.74	7.3	8.12	0.61	0.264	0.568
Carcass yield (% LW)	71.56	72.27	69.05	69.5	0.022	0.424	0.915
Breast meat (% CW)	42.85	42.56	41.2	42.43	0.334	0.381	0.184

LW = Live weight, CW = carcass weight, FCR = feed conversion ratio.

[1]Met+Cys levels were 10.8, 9.9, 9.0, 8.0, 7.3, and 6.7 g/kg feed in phases 1 to 6.

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Supplementation of the products in a 65 (DL-Met) : 100 (MHA-FA) ratio revealed similar body weight, mortality and carcass traits. However, there was a trend for better feed conversion ratio which may confirm a basically lower RBV observed in the literature review (**Table 1**).

Agostini *et al.* (2017) conducted a study with similar design. Male B.U.T. Big 6 turkeys were used. Four dietary treatments comprised two products (DL-Met, liquid MHA-FA) and two dietary Met+Cys levels. Sub-optimal digestible Met+Cys levels were around 87 % of the optimal levels which were set at 9.9, 9.0, 8.5, 7.4, 6.6, and 5.8 g/kg feed in phases 1 to 6. The amount of DL-Met added in both Met dose groups was 65 % of that of added MHA-FA (on product basis). Again, growth rate of turkeys fed the sub-optimal Met+Cys diets was significantly lower confirming that sub-optimal Met+Cys levels limited performance although no difference in feed conversion was observed (Table 4). In corresponding treatments neither a difference in body weight nor in feed conversion ratio was observed. In contrast, especially at low Met+Cys supply, breast meat yield was higher with DL-Met than with liquid MHA-FA.

Table 4: Growth and slaughter performance of male B.U.T., Big 6 turkeys fed diets with adequate and marginal Met+Cys levels and supplemented with either DL-Methionine (DL-Met) or liquid methionine hydroxy analogue free acid (MHA-FA) at a ratio of 65:100 after 21 weeks of life (Agostini *et al.*, 2017)

Met+Cys level	Normal[1]		Low			statistics	
Met source	DL-Met	MHA-FA	DL-Met	MHA-FA	P-value	P-value	P-value
Treatment	1	2	3	4	(level)	(source)	L x S
Body weight (kg)	20.025	19.956	19.259	19.609	**0.03**	0.55	0.37
Feed intake(kg)	53.136	52.853	51.675	52.499	0.12	0.63	0.33
FCR (g/g)	2.665	2.659	2.658	2.69	0.63	0.68	0.52
Mortality (%)	5.9	8.9	7.1	8.5	0.84	0.26	0.67
Slaughter yield (% LW)	77.8	75	77.2	78.1	0.51	0.69	0.40
Breast meat (% CW)	37.2	37.1	36.5	35.7	**<0.001**	**0.02**	0.12
Litter score (wk8)	5.6	5.8	5.1	5.1	0.19	0.72	0.83

LW = live weight, CW = carcass weight, FCR = feed conversion ratio.

[1]Met+Cys levels were 9.9, 9.0, 8.5, 7.4, 6.6, and 5.8 g/kg feed in phases 1 to 6.

More recently, Lingens *et al.* (2021) evaluated the effects of DL-Met and liquid MHA-FA in adequate and low protein diets on performance parameters, footpad health, liver health and oxidative stress. 63 day-old female turkeys (B.U.T. Big 6) were randomly assigned to four groups fed with diets differing in methionine source (DL-Met (65 %) vs. liquid MHA-FA (100 %) and crude protein content (15 % vs. 18 %) for 35 days. The results showed no interactions between the dietary crude protein and Met sources. Strong protein reduction significantly impaired water intake, feed intake, weight gain and feed conversion ratio, but improved footpad health. There was a trend for higher final body weight and weight gain, respectively with DL-Met, which was due to significantly higher feed consumption. However, feed conversion ratio was not affected by products at either dietary protein level. DL-Met resulted in a significant increase in the liver's antioxidative capacity compared to liquid MHA-FA. Although the protein reduction resulted in impaired performance, the study showed that MHA-FA can be replaced by DL-Met in a 100:65 weight ratio without compromising performance and additional benefit of DL-met to improve the antioxidative capacity of the liver.

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Table 5: Performance of female turkeys fed experimental diets with different dietary protein content and using either DL-Methionine (DL-Met) or liquid methionine hydroxyl analogue-free acid (MHA-FA) from day 63 to 98 days (Lingens *et al.*, 2021)

Crude Protein (CP) level	18%CP		15%CP		Statistics		
Met source	DL-Met	MHA-FA	DL-Met	MHA-FA	P-value	P-value	P-value
Treatment	1	2	3	4	(protein)	(source)	P x S
Final body weight (kg)	9.06	8.85	8.56	8.27	**<0.05**	*0.09*	0.80
Body weight gain	4.991	4.857	4.505	4.255	**<0.05**	*0.08*	0.59
Feed intake(kg)	13.006	12.589	12.532	11.868	**<0.05**	**<0.05**	0.53
Water intake (kg)	26.464	25.428	23.862	22.623	**<0.05**	**<0.05**	0.83
Water : Feed intake	2.04	2.02	1.9	1.91	**<0.05**	0.81	0.71
FCR (g/g)	2.61	2.6	2.78	2.79	**<0.05**	0.97	0.72
TAC (umol UAE/g protein)	1.080	1.000	1.020	0.930	0.11	**<0.05**	0.86

TAC = total antioxidant capacity of liver, FCR = feed conversion ratio

Additionally, Lingens *et al.* (2021) observed a trend for lower footpad dermatitis (FPD) scores for DL-Met compared to MHA-FA fed turkeys at d 98. This result confirms earlier findings by Abd El-Wahab *et al.* (2014), who found that young turkeys fed higher levels of methionine (2 or 3g/kg diet) supplemented with DL-Met led to significantly lower FPD scores compared to those same levels in MHA-FA supplemented diets (4.54 vs. 5.04 and 4.12 vs. 5.19, $P < 0.05$). The level of dietary Met plays an important role for health of skin of foot pad. Already in 1974 Chavez and Kratzer (cited in Kamphues *et al.*, 2011) reported higher frequency and score of FPD in turkeys fed liquid MHA-FA compared to turkeys fed DL-Met. Thus, it seems that Met has a structural function regarding foot pad health via protein synthesis and continuous production of keratin. Consequently, low availability of Met could affect protein synthesis negatively and affect skin of foot pad.

Table 6: Comparison of responses to liquid MHA-FA and DL-Met1 on body weight gain or feed conversion ratio at adequate or marginal dietary Met+Cys

Parameter	Body weight gain				Feed conversion ratio			
Met+Cys supply	adequate		marginal		adequate		marginal	
Met source	MHA-FA	DL-Met	MHA-FA	DL-Met	MHA-FA	DL-Met	MHA-FA	DL-Met
	%	%	%	%	%	%	%	%
Hoehler *et al.*, 2005 (1)[2]	100.0	99.8	100.0	98.7	100.0	103.2	100.0	99.2
Hoehler *et al.*, 2005 (2)[3]	100.0	100.5	100.0	99.0	100.0	99.5	100.0	99.6
Hoehler and Hooge, 2003 (1)[4]	100.0	98.5	100.0	100.0				
Hoehler and Hooge, 2003 (2)[4]	100.0	100.6	100.0	102.2				
Lemme and Meyer, 2009	100.0	98.8	100.0	99.6	100.0	99.2	100.0	99.2
Agostini *et al.*, 2017	100.0	100.3	100.0	98.2	100.0	100.2	100.0	98.8
Lingens *et al.*, 2021[5]	100.0	102.4	100.0	103.5	100.0	100.4	100.0	99.6
Average	**100.0**	**99.8**	**100.0**	**100.2**	**100.0**	**100.5**	**100.0**	**99.3**

[1]DL-Met responses relative to MHA-FA responses, MHA-FA = 100 %. [2] adequate and marginal represented by highest and lowest supplementation of liquid MHA-FA or diluted DL-Met. [3] adequate and marginal are represented by highest and lowest supplementation level. [4] FCR was not reported. [5] no Met+Cys reduction but crude protein reduction.

Table 6 summarizes the results of seven turkey feeding trials where DL-Met and liquid MHA-FA were supplemented at a 65:100 ratio at either adequate or marginal Met+Cys supply. These trials comprise experiments conducted in well controlled pen facilities as well as under commercial production conditions (Hoehler and Hooge, 2003). These commercial trials used a total of 54,906 turkeys and it should be noted that MHA-FA fed birds at adequate Met+Cys supply were slaughtered one day later which would explain the differences in final body weight. This compilation in Table 6 serves as strong validation for the recommended RBV of 65 % for liquid MHA-FA relative to DL-Met. Accordingly, it is applicable at any dietary Met+Cys level. This appears to be in contrast with Jankowski *et al.* (2017) who supplemented equimolar levels of liquid MHA-FA or DL-Met at Met+Cys at NRC (1994) recommendations, which were considered low, and at about 40 % higher dietary Met+Cys level. At both dietary Met+Cys levels, there were no performance differences between both products. There were indeed small but significant differences (10.8 vs 11.0 kg final body weight; 2.40 vs 2.37 kg/kg FCR) between dietary Met+Cys levels; however, respective recommendations by the breeder (Hendrix Genetic Company, 2014) suggested final body weights of 10.8 kg which indicates that Met+Cys supply was not strongly limiting performance. Indeed, such pairwise comparison is particularly sensitive at marginal Met+Cys supply and results in Table 6 are therefore strong evidence.

CONCLUSIONS

A relative effectiveness of 65 % of liquid MHA-FA relative to DL-Methionine on a weight basis (1 kg liquid MHA-FA to 0.65 kg DL-Met) is recommended. A number of recently published validation studies not only provide the evidence that 100 units of MHA-FA can be substituted by 65 units of DL-Met at any dietary Met+Cys supply level or at different protein levels without affecting bird's performance, but that DL-Met also provides additional benefits regarding improved breast meat yield and foot pad health.

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Methionine Sources in Turkeys – an Update

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Abstract

In this review, scientific data on the relative bioefficacy value (RBV) of methionine sources in turkeys will be presented and discussed. A compilation of scientific information on RBV of methionine sources in turkeys was done and based on 15 available data sets from studies conducted since 1981. An average RBV of 76 % (weight gain), and 68 % (feed conversion) for liquid methionine hydroxy analogue (MHA-FA) compared to DL-methionine (DL-Met) in turkey was found. Despite these values being slightly higher, a RBV of 65% on a weight-to-weight basis is recommended for liquid MHA-FA in turkey nutrition which is confirmed by a recent opinion of the European Food Safety Authority for monogastric animals. Applicability of this recommendation is justified and validated by several challenge-feeding trials with turkeys where DL-Met and liquid MHA-FA were supplemented in a respective 65:100 ratio in corresponding treatments. While this recommendation was always confirmed, it is evident that especially at marginal dietary Met+Cys levels, which represent more sensitive test conditions, liquid MHA-FA could be replaced by DL-Met in turkey diets without compromising performance. Even the contrary, results indicated extra benefits regarding improved breast meat yield, antioxidant capacity of liver and foot pad health with DL-Met.

Introduction

Commercial poultry diets are routinely supplemented with methionine or its precursors to precisely meet their sulphur amino acid (**SAA**) specifications. Methionine (**Met**) is an essential amino acid for poultry and serves as a building block for protein synthesis, being also a precursor for cysteine (**Cys**) and important methyl donor (Selle *et al*., 2020). Most of the supplemental Met commercially available is supplied as crystalline DL-methionine (**DL-Met**, 99% content) or as liquid DL-2-hydroxy-4-methylthio butanoic acid (methionine hydroxy analogue-free acid, **MHA-FA**; 88% content) (Willke, 2014). Both products provide Met activity to poultry, but chemically MHA-FA is not an amino acid due to the replacement of the characteristic amino group by a hydroxy group (Yang *et al.*, 2020). In addition to the chemical differences, there are studies indicating slower and less efficient absorption of liquid MHA-FA due to differences in transport systems in intestinal brush border membrane and potential catabolism by enteric bacteria (Maenz and Engele-Schaan 1996, Drew *et al.*, 2003). Therefore, understanding the nutritional value indicated by the relative bioefficacy value (**RBV**) of liquid MHA-FA compared to DL-Met is an important precondition to cost-effective purchasing, feed formulation, and optimum animal production (Sauer *et al*., 2008).

A relative bioefficacy of 65% for liquid MHA-FA is recommended for turkeys

A proper evaluation of potential differences in the bioefficacy of two products is strongly dependent on an adequate trial design. In such experiments, the treatments comprise a basal diet deficient in Met+Cys and a set of diets with incremental Met+Cys levels. The effect of the incremental Met supplementation on performance criteria describes the dose-response relationship which is not linear but follows the law of diminishing returns. The first unit of supplemental Met results in a relatively strong effect, i. e. significantly increases the performance. This effect diminishes progressively with each additional amount of Met supplementation. Eventually an optimum supply status is reached where no further increase in performance can be achieved. This curve can accurately be described by an exponential regression equation (Rodehutscord and Pack, 1999). The more data points describe the non-linear first section of the response curve, the more robust is the conclusion. The methodology of simultaneous exponential regression as proposed by Littell *et al.* (1997) assumes that both nutrient sources under test allow for the same asymptote of the response curves. Although the experimental setup to determine the RBV has been a matter of discussion and different asymptotes have been proposed by Gonzales-Esquerra *et al.* (2007), the meta-analysis performed by Sauer *et al.*

4. DL-methionine proves more beneficial for broilers

SECTION 1, TRIAL NO. 8

SECTION 2, VIDEO NO. 6

5.

"MHA: All arguments speak for a bioefficacy of 65%"

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Executive summary

- The perception of the nutritional value of methionine hydroxy analog (MHA) products is of high economic importance, not only for the feed industry but also for the producers of MHA.
- Evonik and organizations including the European Food Safety Authority (EFSA), Centraal Veevoeder Bureau (CVB) in the Netherlands and the National Research Council (NRC) in the USA, recommend a bioefficacy of around 65% for MHA relative to DL-Methionine.
- While slope-ratio or multi-exponential regression are established and validated methods to determine the bioefficacy of nutrient sources relative to a reference, producers of MHA try to introduce alternative statistical approaches for evaluating their product. With those, they aim to show the nutritional equivalence of their product to DL-Methionine and discredit the nutritional superiority of DL-Methionine.
- The lower bioefficacy of MHA can be well explained by various physiological research findings. MHA producers recently published reviews which excluded unfavorable publications and discredited established methods in physiological research indicating MHA shortcomings.
- The producers of MHA made several attempts to assign additional value to their products and how they can support cost savings in feed formulation. Among those are a high energy value, acidifying properties for replacing organic acid additives, and high anti-oxidative capacity. All these aspects are scientifically doubtful.
- All the above listed activities do not negate the fact that DL-Methionine is the superior Methionine source and applying a relative bioefficacy of 65% for MHA is recommended. This recommendation is based on validated and scientifically established methodologies and has repeatedly been proven under various scientific and practical conditions.

Introduction

In a review on the relative bioefficacy of amino acids published in 1995 by Lewis and Baker, a bioavailabilty of 66% for liquid methionine hydroxy analog-free acid (**MHA-FA**) relative to DL-methionine (**DL-Met**) on weight basis in practical-type diets was reported [1]. This means 100 parts MHA-FA can be replaced by 66 parts DL-Met in feed without impacting performance. Since then, the debate about the relative bioefficacy of methionine sources has continued; in the early 1980s there were bioefficacies between 63% and 70% for liquid MHA-FA relative to DL-Met reported [2–4].

In 2003 main producers of DL-Met and liquid MHA free acid (MHAFA) were invited by the Centraal Veevoederbureau (**CVB**) in the Netherlands to agree on the methodological approach to determine the biological efficacy of MHA-FA in pigs and poultry, and to contribute publications and data to this study. Accordingly, Aventis Animal Nutrition (now known as Adisseo), Novus International Inc, Degussa AG (known today as Evonik

Industries GmbH) and CVB agreed on a protocol to determine the bioefficacy of MHA-FA relative to DL-Met by simultaneous linear or exponential regression. The outcome of this project suggested that MHA-FA is on average 68% as efficient as DL-Met in broilers, the species with by far the highest number of suitable data sets [5]. The analysis revealed this outcome statistically significant. For laying hens, turkeys and swine, results were less clear because of a very limited number of studies, and it was recommended to generate further data. More recently, the European Food Safety Authority (**EFSA**) concluded that "there is convincing evidence" that MHA-FA (and its calcium salt) has a significantly lower bioefficacy than DL-Met in all non-ruminant species [6]. Accordingly, MHA-FA was reported to be 67% as efficient as DL-Met. Moreover, organizations including the National Research Council (NRC) in the USA concluded that "it is reasonable to assume" that the bioefficacy of MHA-FA in fish is about 67% to 71% that of DL-Met [7].

Based on own comprehensive meta-analyses, Evonik recommends a bioefficacy of 65% for all MHA products (MHA-FA; MHA-Ca) for all farmed monogastric terrestrial and aqua species under any production condition [8–13]. In addition, there is a lot of research providing evidence on physiological mechanisms behind the lower bioefficacy of MHA-FA [6]. Additionally, the 65% recommendation can be challenged under any production and nutritional condition without compromising animal performance [14–20,11,21–26,13]. Finally, applying our recommendation will save money for the feed mill and avoid animal performance losses. Consequently, it will have impact on the price MHA-FA producers would achieve, which is most likely the major reason for them doing the utmost to discredit our recommendation and the established methodologies behind it. MHA-FA producers are particularly (mis)using the scientific platform to confuse and misinform nutritionists.

Methodology for bioefficacy determination

The methodology to determine the relative bioefficacy has been described by Littell et al. [27]. In summary, it involves two (multiple) dose response data sets being analyzed by either linear (slope-ratio) or exponential regression simultaneously. The steepness within the regression equations are related to each other taking – in this case – DL-Met as reference. The resulting coefficient suggests how much DL-Met is needed to replace MHA-FA to achieve the same animal performance, independent of general supplementation level and performance level. This approach assumes that the maximal achievable performance (asymptote) is similar for both products. Several attempts have been made to provide evidence that this method would not be applicable for MHA-FA; Vazquez-Anon et al. (Novus International) reported four simultaneous dose response studies and concluded that the nature of dose-response curve would differ between MHA-FA and DL-Met fed broilers [28]. Interestingly, when data were analyzed separately for each trial, linear, exponential and quadratic regressions fit best to DL-Met and MHA-FA responses but were different between trials and products. Whereas, a meta-analysis of combined data of these four trials suggested a linear response to MHA-FA with no asymptote and a quadratic response for DL-Met [28]. In the same year, Vazquez-Anon et al. (Novus International) identified quadratic responses for both products [29] and a further broiler trial suggested linear responses to both products [30]. Thus, the team around Vazquez-Anon and Knight from Novus International demonstrated biologically fallacious and inconsistent conclusions but stated no difference between product efficacies. The linear responses were used for comparing slopes [30], evidentially accepting the slope-ratio approach. However, there were no significant responses of broilers to either product which would be prerequisite for reliable slope-ratio assay. After an unconventional processing of data, a meta-analysis sponsored by Adisseo accepted and applied the slope-ratio approach as well, concluding that efficiency of MHA-FA would not differ from that of DL-Met [31]. Concerns were addressed particularly with respect to data treatment and selection of publications considered [32], but authors only partly could justify their conclusions [33] apart from the fact that it is impossible for the reader to reproduce this analysis. Kratzer (who co-authored [29]) and Littell (who originally described the slope-ratio and multi-exponential approach for methionine sources [27]) referred to the above mentioned study by CVB [5] (which was accepted by all companies involved) and concluded that MHA-FA and DL-Met would not result in the same asymptote and, therefore, the conclusion of lower bioefficacy of MHA-FA by Jansman et al. [5] would not be valid [34]. An

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immediate response to this article announced doubts [35] and a deep-dive meta-analysis then provided clear evidence that asymptotes for both products are similar, while the dose needed to get to this maximum differs between products [36]. Since then, the methodological approach has not been questioned any more in the scientific forum, although the International Methionine Analogue Association (IMAA; founded in 2012) used the above publications to "promote the reputation" of MHA-FA [37].

However, the ultimate evidence for validity of multiple-exponential regression is provided by using diluted DL-Met as an internal standard. With a known concentration of only 65% DL-Met in a premix (DL-Met65), the simultaneous dose-response trial should reveal a bioefficacy of about 65% relative to pure DL-Met. Broiler trials using DL-Met65 suggested an average bioefficacy of 63% which, in addition, was identical to the bioefficacy determined for MHA-FA [38,18,20]. Interestingly, these studies were published before 2006 and were, therefore, known already before the above publications suggesting different regression models, pre-treating data for slope-ratio, etc. became available. Meanwhile, further DL-Met65 trials have validated both method and bioefficacy of products [11,16], and thus disproving the concept of the two having the same bioefficacy, different asymptotes or different nature of responses. An amusing sidenote is that actually Rhône-Poulenc (now known as Adisseo) once introduced the inclusion of diluted DL-Met as an internal standard into the experimental design to determine the bioefficacy of MHA, resulting in similar conclusions as recent research [39].

More recently it was argued that a fair comparison should be done at "commercial" supplementation levels at requirement [40–42]. This is a ridiculous suggestion as the maximum performance is achieved even with DL-Met65 at such "commercial" levels [16,18,38,11,20]. Nobody would conclude on same bioefficacy of DL-Met65 compared to pure DL-Met. Also, Batonon-Alavo et al. supplemented DL-Met and MHA-FA at equimolar levels to achieve broiler breeder recommendations [43]. They introduced the non-inferiority test as a "new statistical approach" to show that MHA-FA is not inferior to DL-Met. However, the application of this test included major errors [44], which the authors of course did not accept [45]. First, the non-inferiority test pre-assumes a lower efficacy of the product under test – in this case MHA-FA – and the question to be solved is just whether this lower efficacy is in an acceptable range. Doing the stats on the data reported correctly reveals that non-inferiority cannot be confirmed for MHA-FA compared to DL-Met [44].

In summary, publications initiated by MHA-FA producers aim to create doubt on the correctness and validity of a significantly lower bioefficacy of MHA-FA relative to DL-Met. In order to achieve this aim, they have suggested various regression models, conducted meta-analyses in which data were prepared in a way that a fair comparison would disregard, and suggest test conditions where comparisons are not meaningful. At the same time, slope-ratio and multi-exponential regression is an established method to compare a nutrient source with a reference. This model has been proven effective by testing it with DL-Met65. While the recommended bioefficacy of 65% for MHA-FA relative to DL-Met can be challenged under any production condition, any climate, with any non-ruminant farm species and with any MHA product (MHA-FA, MHA-Ca) without compromising animal performance, it indeed allows for considerable cost savings and other benefits.

Physiological background

There is extensive research published regarding the metabolic and physiological fate of DL-Met and MHA-FA. The EFSA has previously concluded that the major reasons for a lower bioefficacy of MHA-FA can be related mainly to larger degradation by intestinal microbes, and a particularly lower digestion and utilization of the di- and trimers of MHA-FA [6]. Becquet, who is currently president of the above mentioned IMAA, and co-workers at Adisseo and Novus International recently published two detailed reviews on the metabolism of methionine sources [46,47]. The first review focuses on the digestion and absorption of the molecules from digesta and the second review looks at the transformation of D-MHA, L-MHA, and D-Met into L-Met. While not obvious for a reader with only little insight on these topics, authors were selective with their chosen references, which by definition avoided a comprehensive and scientifically reliable review [48]. The review not only ignored publications in favor of MHA-FA, but discredited methodological approaches used in studies revealing disadvantages for MHA-FA compared to DL-Met. This is remarkable as all the research on the physiological background of these products would not allow to quantify the effects and, thus, to revise the determined relative bioefficacy – it only allows to explain the empirical observation. The topics addressed in the reviews [46,47] cover those which were listed in the EFSA report [6] and it appears that with scientific publications like this, new “evidence” shall be established which would allow for revising the respective assessment by the authority. Our response letter passed the review process of the journal quickly and accepted that the “chain of argumentation is aimed at discrediting studies reporting lower absorption of MHA-FA. The impression of a biased review is strengthened due to the omission of a number of easily accessible publications.” [48].

Approaches to increase the nutritional value of MHA-FA

With respect to pricing of DL-Met and MHA-FA, matrix values for least cost feed formulation (LCF) are central when assessing the relative attractiveness of an ingredient in the final recipe. For example, if the only nutritional information in the matrix was the available Met (Met+Cys) content, the value of MHA-FA would be 65% as high for DL-Met according to Evonik’s recommendation. If the price ratio between products is > 65%, LCF would favor DL-Met and suggest a competitive shadow price for MHA-FA.

Energy values associated with DL-Met and MHA-FA

The matrix can contain further information, such as energy content, which is important in this context. Of course, DL-Met and MHA-FA contain energy which contributes — although little — to the overall energy content of the diet, and there are well-established concepts about metabolizable and net energy in poultry and swine nutrition. It is often assumed that the discussion on relative efficacy considers dietary energy and respective utilization because growth responses, as determined in growth response trials, are net effects of all nutrients and energy together. Therefore, a bioefficacy of 65% should be reflected in the energy values entered into the matrices in LCF, too. However, if the energy ratio between the products is higher than 65% the relative attractiveness of MHA-FA compared to DL-Met increases. Adisseo released a publication in which metabolizable energy for MHA-FA is suggested to be as high as for DL-Met for birds; with net energy even 4-5% higher [49,50]. Similar numbers were reported for mammals. Using such values in LCF would overrule the effect of lower Met+Cys value for MHA-FA and thus largely pull MHA-FA into the diet instead of DL-Met, regardless of the lower Met+Cys activity. That makes MHA-FA attractive for price negotiations. However, while these proposed energy values were not determined in animal trials but by calculations on molecular level, it should be noted that (supplemental) amino acids and their hydroxy analogs are fed for effective incorporation into body protein and are, therefore, not meant for oxidation. In this context it should be emphasized that Met+Cys are first limiting factors in many diets, which consequently indicates maximized utilization. If this is taken into account, the picture would change as all MHA-isomers need to be converted into L-methionine which is actually — indeed small — an energetic burden.

MHA-FA as acidifying agent

A further attempt to increase the relative attractiveness of MHA-FA against DL-Met in LCF is suggested with the “ABC-4 Acidsaver” by Adisseo. This web application calculates how much of an acidifier can be saved purely with MHA-FA supplementation, which itself is indeed a strong organic acid with a pH of one. Replacing (a certain amount of) organic acid products in feed would reveal an economic advantage. The question whether MHA-FA can act as acidifier in feed remains. When the disappearance of MHA-FA and DL-Met from digesta in gnotobiotic chicken and swine was evaluated, it was concluded that intestinal microbes utilize a considerable amount of MHA-FA in contrast to DL-Met, which then was not available to the host [51,52]. However, while these studies did not allow for assessing whether microbes consuming MHA-FA died, they suggest that MHA-FA would not have a double functionality. An investigation of the impact of formic acid, DL-Met, MHA-FA and gradual replacement of formic acid by MHA-FA on microbial activity in swine ileum and colon revealed no impact of MHA-FA on microbial

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density nor on short chain fatty acid production [53]. Data reported by Smith et al. confirms that MHA-FA does not modulate microbiota or gut characteristics in swine and broilers [54]. Locatelli et al. concluded that MHA-FA is ineffective for feed preservation such as controlling salmonella [55]. Analogous to the dietary energy, growth responses for determining bioefficacy would include any impact on both gut microbiota and health. Moreover, validation trials challenging the recommended bioefficacy of 65% were conducted under controlled and field conditions and did not suggest any difference between environments and, therefore, beneficial health effects of MHA-FA in monogastric farm animals [13,12,8].

MHA-FA as antioxidative agent

Oxidative stress is another relevant challenge in animal production. It is triggered by various stressors such as heat stress, but also stocking density and dietary insufficiencies. The so-called reactive oxygen species (ROS) molecules are at the center of this discussion because the organisms need to counteract those with various antioxidative strategies. Among many other compounds, sulfur containing amino acids have been reported to ameliorate oxidative stress [56]. As summarized by Magnuson et al., the sulfur group of methionine can be oxidized to sulfoxide at oxidative stress enabling methionine to counteract ROS [57]. Moreover, via the transsulfuration pathway methionine can be transformed into cysteine, which in turn is a precursor of glutathione (GHS) being an effective antioxidant [57]. In their questionable review (see above) Becquet et al. emphasized the beneficial effects of MHA-FA against ROS. While they reported studies where ratios of reduced GHS to total or oxidized GHS were higher with MHA-FA than with DL-Met, suggesting a higher capacity for oxidative stress defense [58–60], they did not mention other studies reporting a higher anti-oxidative efficiency for DL-Met [61,62] or studies that could not differentiate the products in this context [63,64]. A recent publication addresses the origin of ROS and it could be shown in muscle cell (myoblast) models that particularly D-MHA is transformed to L-Met in mitochondria rather than in peroxisomes resulting in higher concentration of H_2O_2, which is a strong ROS, in extracellular space and which would stimulate a defense against oxidative stress [65]. Accordingly, MHA-FA metabolism itself adds to oxidative stress at cell level. Again, as pronounced earlier, application of the recommended bioefficacy of 65% for MHA-FA is successful under any environmental, nutritional and husbandry condition which therefore excludes an extra-benefit of MHA-FA under such conditions [13,32,8,12].

Summary and conclusion

To summarize, multi-exponential regression of simultaneous dose-response data allows for determination of the bioefficacy of MHA-FA relative to DL-Met as well as for validation of the method. Accordingly, a bioefficacy of 65% is recommended. This is similar to the findings of Adisseo’s predecessor company Rhône-Poulenc – AEG, which concluded in 1983 on a bioefficacy of 70% on product level [4]. Particularly MHA-FA producers and scientists supported by those companies introduced various statistical approaches in order to establish nutritional equivalency of MHA-FA and DL-Met. Moreover, in a couple of examples it could clearly be demonstrated that such publications and even so-called reviews ignored other research that is inconvenient for the MHA producers in this context. In addition to the discussion about bioefficacy, several attempts are made to increase the nutritional value of MHA-FA relative to DL-Met by suggesting a higher dietary energy value, acidifying properties or anti-oxidative capacity for MHA-FA. However, not one single approach can negate practical applicability of our recommended 65% bioefficacy and related savings for the user, because more than 150 challenge tests under any production condition prove validity of our recommendation.

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6. Utilization of methionine sources for growth and Met+Cys deposition in broilers

Open Access Article

Utilization of Methionine Sources for Growth and Met+Cys Deposition in Broilers

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Simple Summary

Methionine (Met) is the first limiting amino acid in broiler feeds and for balancing dietary Met and methionine+cysteine (Met+Cys) levels. DL-2-hydroxy-4-methylthio butanoic acid (HMTBA) and DL-methionine (DLM) are typical feed additives. The relative bioavailability value (RBV) describes the nutritional value of HMTBA relative to DLM and is important for adequate, precise, and cost-effective broiler nutrition. The current broiler feeding trial revealed an average RBV of 63% compared to DLM and the inclusion of an internal standard into the experimental design allowed for validation of the methodological approach. Evaluation of the utilization of supplemental Met sources for Met+Cys deposition in body protein provided further evidence for a higher efficiency and, thus, nutritional value of DLM over HMTBA.

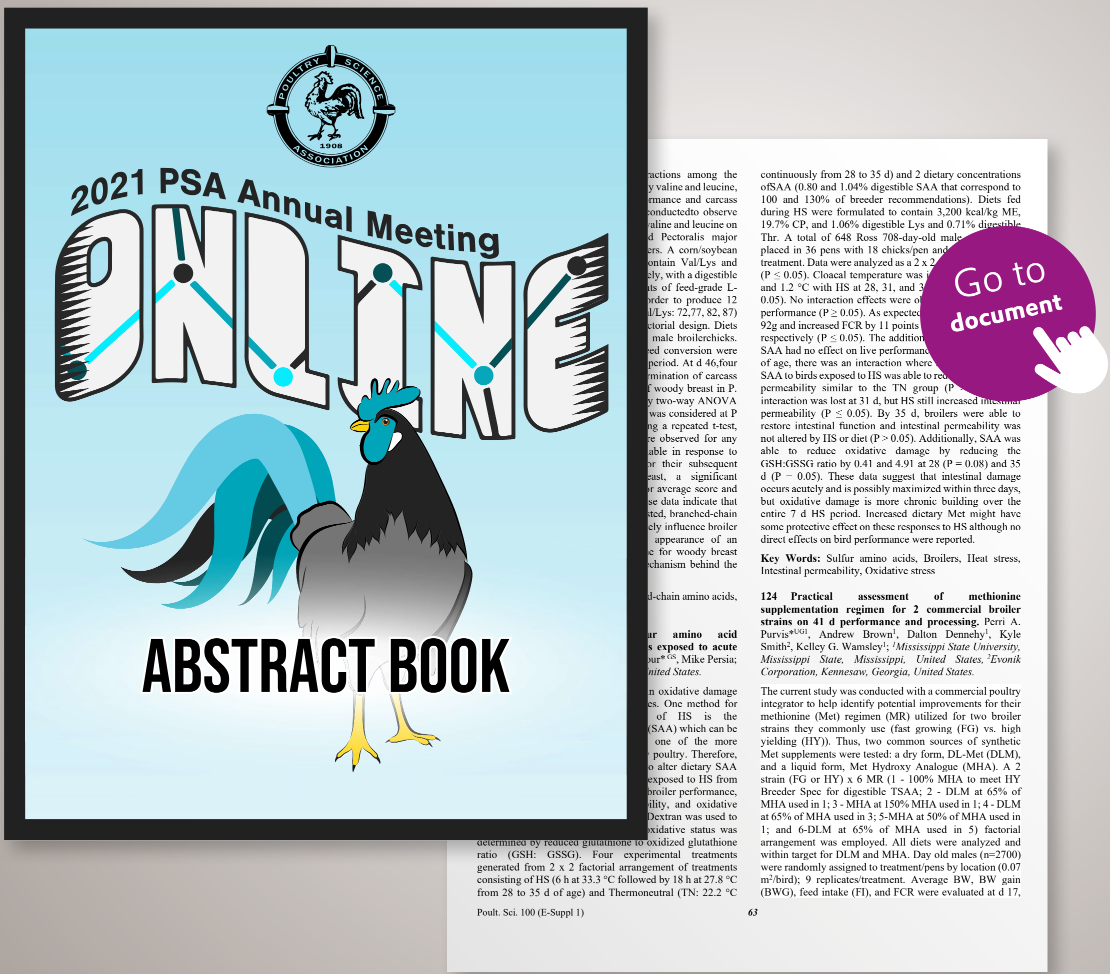
Abstract

Knowledge about the nutritional value of methionine sources is highly important for their appropriate application in terms of animal and economic performance. Therefore, a broiler feeding trial was conducted to determine the relative bioavailability value (RBV) of DL-2-hydroxy-4-methylthio butanoic acid (HMTBA) compared to DL-methionine (DLM). DLM diluted to 65% purity (DLM65) served as the internal standard, with a known RBV of 65%. A total of 1920 d-old male broilers were used in the three-phase feeding trial comprising 16 treatments including a basal, Met+Cys-deficient diet and 5 graded DLM, HMTBA, or DLM65 levels. Growth performance and carcass quality data were subjected to multi-exponential regression analysis. Increasing levels of any Met source significantly improved all performance parameters compared to the negative control ($p < 0.05$). Across all performance parameters, the RBV of HMTBA was 63% and that of DLM65 was 58%. All RBV estimates of HMTBA and DLM65 were significantly lower than 88% ($p < 0.05$). Cumulative efficiency of DLM for Met+Cys deposition in body protein was higher than that of HMBTA at any dose, confirming the determined RBV. Using DLM65 as an internal marker allowed for validation of the methodology.

Keywords: broiler; relative bioavailability; methionine; methionine hydroxy analogue; utilization

SECTION 2, VIDEO NO. 6

7. Practical assessment of methionine supplementation regimen for 2 commercial broiler strains on 41 d performance and processing



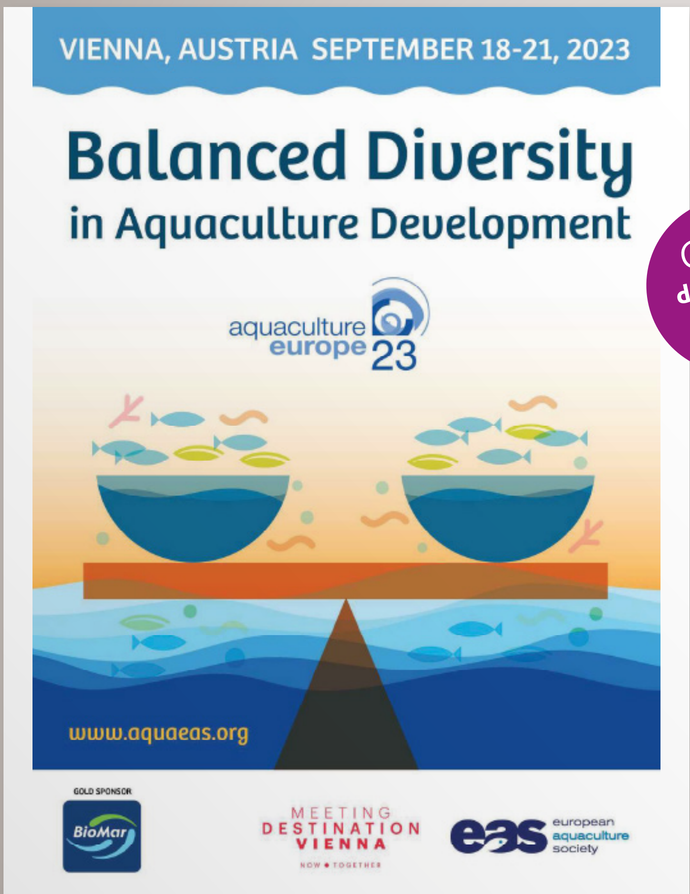
Mississippi State University, Mississippi, USA in collaboration with a commercial poultry integrator

SECTION 1, TRIAL NO. 4

8. Effects of methionine supplement sources and crude protein on Ross 708 male broiler performance

SECTION 1, TRIAL NO. 5
SECTION 2, VIDEO NO. 4

9. Validating biological efficacy of methionine sources in nile tilapia



Validating Biological Efficiency of Methionine Sources in Nile tilapia.

Aquaculture Europe 23. Sep 18-21. Vienna, Austria. Abstract Book, pp: 872-873.

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SECTION 1, TRIAL NO. 6

10. Effects of supplemental methionine sources in finishing pig diets on carcass characteristics, cutting yields, and meat quality

Go to document

GROWTH, DEVELOPMENT, MUSCLE BIOLOGY AND MEAT SCIENCE

PSV-14 Performance and Consumer Preference Between Bone-In and Boneless Striploins Using a Precision Dry-Aging System (Agenator).

Nicolas Herrera[1], Joseph Sonderman[1], David Velazco[1], Chris Calkins[1], [1]*University of Nebraska-Lincoln*

Abstract: To determine effects of moisture loss on dry-aged beef, strip loins from 12 low Choice carcasses were collected. One loin from each carcass side was randomly assigned to bone-in or boneless treatment. Loins were assigned to 1 of 4 aging treatments: bone-in-wet (BW), bone-in-dry (BD), boneless-wet (bW), or boneless-dry (bD). Dry-aging loins were placed in individual dry-aging chambers for 40 d, precisely controlling relative humidity (70%), air velocity, temperature (2°C) and mass (±5 g). Data were continuously recorded to calculate percent and rate of moisture loss. After aging, bone-in loins were de-boned, and dry-aged loins were trimmed of dried surfaces. Percent moisture loss, trim loss, and yield were calculated. Two steaks per dry-aged loin were cooked to 71°C, one for Warner-Bratzler Shear Force (WBSF), and one for consumer evaluation of tenderness, juiciness, and flavor and preference ranking. Percent and rate of moisture loss of dry-aged loins were analyzed as a completely randomized design (CRD), with day as repeated measures. Mean separations were conducted using LSMEANS with SLICEDIFF function at $P < 0.05$. Percent trim loss, total moisture loss, yield, and WBSF were analyzed as a CRD. Affective consumer testing utilized a Tukey HSD adjustment at $P < 0.05$. A treatment-by-day effect occurred ($P < 0.05$) for percent and rate moisture loss. Lower moisture loss in BD loins occurred after 2 d aging and daily rate of moisture loss through 31 d aging compared with bD. The bD loins had the greatest ($P < 0.05$) total moisture loss, trim loss, and lowest yield. The BD loins had higher degree of liking ($P < 0.05$) for tenderness and preference ratings compared with bD. No differences ($P > 0.05$) were seen in WBSF. Intact bone reduces rate of moisture loss in dry-aged loins, increasing total yield and consumer preference compared with boneless loins.

Keywords: beef, dry-aging, preference

PSV-9 Effects of Supplemental Methionine Sources in Finishing Pig Diets on Carcass Characteristics, Cutting Yields, and Meat Quality.

Hannah Remole[1], J. Caroline González-Vega[2], John K. K. Htoo[2], Anna Dilger[1], Bailey Harsh[3], [1]*University of Illinois,* [2]*Evonik Operations GmbH,* [3]*University of Illinois at Urbana-Champaign*

Abstract: While supplemental methionine (Met) is widely used within the swine industry, data are limited regarding the effect of Met sources on carcass cutability and meat quality. The objective was to determine the effects of DL-methionine (DLM, 99%), L-methionine (LM, 99%), or calcium salt of DL-methionine hydroxyanalogue (MHA-Ca, 84%) in finishing pig diets on carcass characteristics and meat quality. Pigs (n = 240) were allocated to 60 single-sex pens. For the final 7 wk of the finisher phase, pigs (BW= 79.9 ± 0.80 kg) were fed diets containing DLM, LM, or MHA-Ca, with the supplemental methionine source providing 25% of the sulfur amino acid requirement. One pig per pen was slaughtered, and left sides of carcasses were fabricated into subprimal cuts to determine carcass-cutting yields. Loin quality including proximate composition and shear force was measured. Data were analyzed using the MIXED procedure of SAS. Hot carcass weight was not different ($P= 0.34$) between treatments (DLM 103.0 kg; LM 104.5 kg; MHA-Ca 101.5kg), moreover loin eye area was not different ($P= 0.98$) between treatments (DLM 52.49 cm^2; LM 52.65 cm^2; MHA-Ca 52.81 cm^2). Boneless carcass cutting yield was not different ($P = 0.56$) between treatments (DLM 54.82 kg; LM 54.97 kg; MHA-Ca 54.52 kg). Loin pH was not different ($P = 0.24$) between treatments (DLM 5.48; LM 5.45; MHA-Ca 5.45). However, drip loss tended to be reduced ($P = 0.11$) by the DLM treatment (5.58%) compared with LM (7.03%) and MHA-Ca (6.68%) treatments. Shear force was not different ($P = 0.85$) between treatments (DLM 3.06 kg; LM 3.03 kg; MHA-Ca 3.10 kg). However, cook loss tended to be reduced ($P = 0.06$) by the DLM treatment (16.20%) compared with LM (18.18%) and MHA-Ca (18.50%) treatments. These data suggest that only minimal differences in carcass cutability and meat quality can be attributed to methionine sources in finishing pig diets.

Keywords: carcass characteristic, meat quality, methionine; pig

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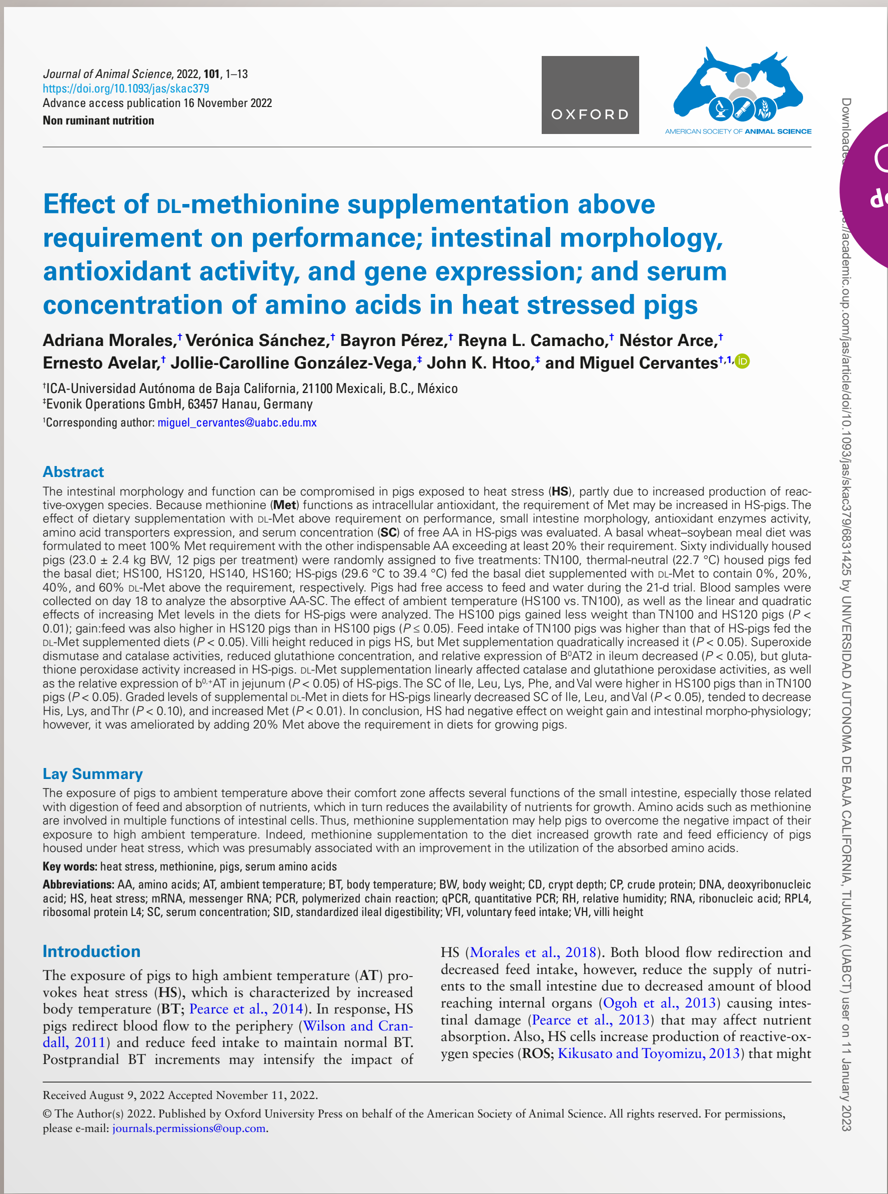
11. Effect of dl-methionine supplementation above requirement on performance, intestinal morphology, antioxidant activity, and gene expression, and serum concentration of amino acids in heat stressed pigs



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Non ruminant nutrition

Effect of DL-methionine supplementation above requirement on performance; intestinal morphology, antioxidant activity, and gene expression; and serum concentration of amino acids in heat stressed pigs

Adriana Morales,[†] Verónica Sánchez,[†] Bayron Pérez,[†] Reyna L. Camacho,[†] Néstor Arce,[†] Ernesto Avelar,[†] Jollie-Carolline González-Vega,[‡] John K. Htoo,[‡] and Miguel Cervantes[†,1]

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Abstract

The intestinal morphology and function can be compromised in pigs exposed to heat stress (**HS**), partly due to increased production of reactive-oxygen species. Because methionine (**Met**) functions as intracellular antioxidant, the requirement of Met may be increased in HS-pigs. The effect of dietary supplementation with DL-Met above requirement on performance, small intestine morphology, antioxidant enzymes activity, amino acid transporters expression, and serum concentration (**SC**) of free AA in HS-pigs was evaluated. A basal wheat–soybean meal diet was formulated to meet 100% Met requirement with the other indispensable AA exceeding at least 20% their requirement. Sixty individually housed pigs (23.0 ± 2.4 kg BW, 12 pigs per treatment) were randomly assigned to five treatments: TN100, thermal-neutral (22.7 °C) housed pigs fed the basal diet; HS100, HS120, HS140, HS160; HS-pigs (29.6 °C to 39.4 °C) fed the basal diet supplemented with DL-Met to contain 0%, 20%, 40%, and 60% DL-Met above the requirement, respectively. Pigs had free access to feed and water during the 21-d trial. Blood samples were collected on day 18 to analyze the absorptive AA-SC. The effect of ambient temperature (HS100 vs. TN100), as well as the linear and quadratic effects of increasing Met levels in the diets for HS-pigs were analyzed. The HS100 pigs gained less weight than TN100 and HS120 pigs ($P < 0.01$); gain:feed was also higher in HS120 pigs than in HS100 pigs ($P \leq 0.05$). Feed intake of TN100 pigs was higher than that of HS-pigs fed the DL-Met supplemented diets ($P < 0.05$). Villi height reduced in pigs HS, but Met supplementation quadratically increased it ($P < 0.05$). Superoxide dismutase and catalase activities, reduced glutathione concentration, and relative expression of B^0AT2 in ileum decreased ($P < 0.05$), but glutathione peroxidase activity increased in HS-pigs. DL-Met supplementation linearly affected catalase and glutathione peroxidase activities, as well as the relative expression of $b^{0,+}AT$ in jejunum ($P < 0.05$) of HS-pigs. The SC of Ile, Leu, Lys, Phe, and Val were higher in HS100 pigs than in TN100 pigs ($P < 0.05$). Graded levels of supplemental DL-Met in diets for HS-pigs linearly decreased SC of Ile, Leu, and Val ($P < 0.05$), tended to decrease His, Lys, and Thr ($P < 0.10$), and increased Met ($P < 0.01$). In conclusion, HS had negative effect on weight gain and intestinal morpho-physiology; however, it was ameliorated by adding 20% Met above the requirement in diets for growing pigs.

Lay Summary

The exposure of pigs to ambient temperature above their comfort zone affects several functions of the small intestine, especially those related with digestion of feed and absorption of nutrients, which in turn reduces the availability of nutrients for growth. Amino acids such as methionine are involved in multiple functions of intestinal cells. Thus, methionine supplementation may help pigs to overcome the negative impact of their exposure to high ambient temperature. Indeed, methionine supplementation to the diet increased growth rate and feed efficiency of pigs housed under heat stress, which was presumably associated with an improvement in the utilization of the absorbed amino acids.

Key words: heat stress, methionine, pigs, serum amino acids

Abbreviations: AA, amino acids; AT, ambient temperature; BT, body temperature; BW, body weight; CD, crypt depth; CP, crude protein; DNA, deoxyribonucleic acid; HS, heat stress; mRNA, messenger RNA; PCR, polymerized chain reaction; qPCR, quantitative PCR; RH, relative humidity; RNA, ribonucleic acid; RPL4, ribosomal protein L4; SC, serum concentration; SID, standardized ileal digestibility; VFI, voluntary feed intake; VH, villi height

Introduction

The exposure of pigs to high ambient temperature (**AT**) provokes heat stress (**HS**), which is characterized by increased body temperature (**BT**; Pearce et al., 2014). In response, HS pigs redirect blood flow to the periphery (Wilson and Crandall, 2011) and reduce feed intake to maintain normal BT. Postprandial BT increments may intensify the impact of HS (Morales et al., 2018). Both blood flow redirection and decreased feed intake, however, reduce the supply of nutrients to the small intestine due to decreased amount of blood reaching internal organs (Ogoh et al., 2013) causing intestinal damage (Pearce et al., 2013) that may affect nutrient absorption. Also, HS cells increase production of reactive-oxygen species (ROS; Kikusato and Toyomizu, 2013) that might

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12.

DL-Methionine: The first methionine source

Fernanda Castro[1], Victor Naranjo[2], Andreas Lemme[3]

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.

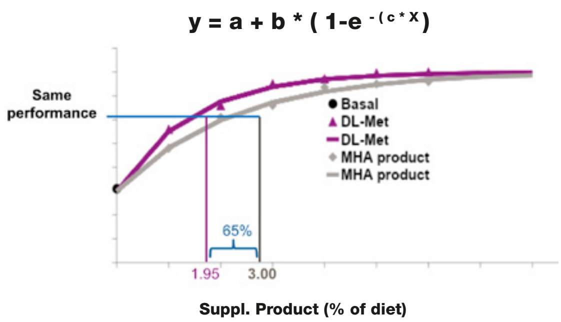

Figure 1: *Simultaneous multi-exponential regression analysis to determine relative bioeficacy.*

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).

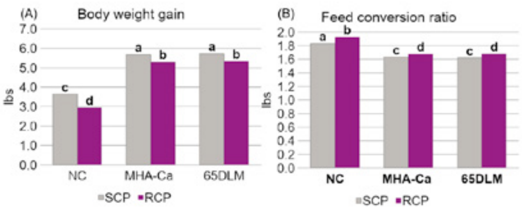

Figure 2: *(A) Body weight gain and (B) feed conversion ratio results from 1 to 42 days. (A) CP level: P<0.001; Met source: P<0.001; Interaction: P<0.001; SEM: 0.016; (B) CP level: P<0.001; Met source: P<0.001; Interaction: P<0.001; SEM: 0.015. NC – Negative control diet, no methionine supplemented; 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

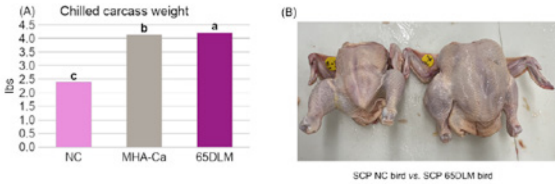

Figure 3: *(A) Chilled carcass weight from 1 to 42 days and (B) chilled carcass visual comparison between standard crude protein negative control bird (left) and standard crude protein 65DLM-fed bird (right). (A) CP level: P<0.01; Met source: P<0.01; Interaction: P=0.120; SEM: 0.212. NC – Negative control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

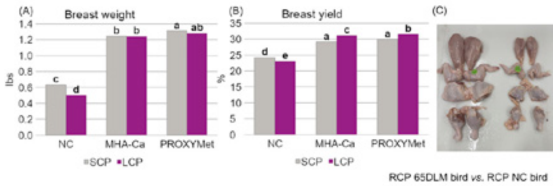

Figure 4: *(A) Chilled carcass weight from 1 to 42 days and (B) chilled carcass visual comparison between standard crude protein negative control bird (right) and standard crude protein 65DLM-fed bird (left). (A) CP level: P<0.01; Met source: P<0.01; Interaction: P=0.120; SEM: 0.212. NC – Negative control 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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13. Are the main methionine sources equivalent? A focus on DL-Methionine and DL-Methionine Hydroxy Analog reveals differences on rainbow trout hepatic cell lines functions

International Journal of *Molecular Sciences*

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Article

Are the Main Methionine Sources Equivalent? A Focus on DL-Methionine and DL-Methionine Hydroxy Analog Reveals Differences on Rainbow Trout Hepatic Cell Lines Functions

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Abstract: The replacement of fishmeal by plant proteins in aquafeeds imposes the use of synthetic methionine (MET) sources to balance the amino acid composition of alternative diets and so to meet the metabolic needs of fish of agronomic interest such as rainbow trout (RT-*Oncorhynchus mykiss*). Nonetheless, debates still exist to determine if one MET source is more efficiently used than another by fish. To address this question, the use of fish cell lines appeared a convenient strategy, since it allowed to perfectly control cell growing conditions notably by fully depleting MET from the media and studying which MET source is capable to restore cell growth/proliferation and metabolism when supplemented back. Thus, results of cell proliferation assays, Western blots, RT-qPCR and liquid chromatography analyses from two RT liver-derived cell lines revealed a better absorption and metabolization of DL-MET than DL-Methionine Hydroxy Analog (MHA) with the activation of the mechanistic Target Of Rapamycin (mTOR) pathway for DL-MET and the activation of integrated stress response (ISR) pathway for MHA. Altogether, the results clearly allow to conclude that both synthetic MET sources are not biologically equivalent, suggesting similar in vivo effects in RT liver and, therefore, questioning the MHA efficiencies in other RT tissues.

Keywords: aquaculture; nutrition; rainbow trout; cell lines; metabolism; methionine

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Citation: Pinel, K.; Heraud, C.; Morin, G.; Dias, K.; Marcé, A.; Beauclair, L.; Fontagné-Dicharry, S.; Masagounder, K.; Klünemann, M.; Seiliez, I.; et al. Are the Main Methionine Sources Equivalent? A Focus on DL-Methionine and DL-Methionine Hydroxy Analog Reveals Differences on Rainbow Trout Hepatic Cell Lines Functions. *Int. J. Mol. Sci.* **2022**, 23, 2935. https://doi.org/10.3390/ijms23062935

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1. Introduction

By 2050, the global population will reach 9 billion humans. Hence, providing a sustainable food supply to that exponentially growing human population is one of the core challenges for the future. Aquaculture can definitely play an important role in fulfilling this goal. Indeed, over the last four decades, aquaculture production has multiplied by five to finally provide more than half of the fish consumed worldwide in 2014 [1]. Nonetheless, and despite the intrinsic capacities of aquaculture farmers and industries to sustain and improve production levels, new economic and ecological issues have arisen. One of these problems, related to the increase demand for fish feeds, is the soaring prices of fishmeal (FM), which is still considered the most nutritious and digestible ingredient for farmed fish. Of particular concern are salmonids such as rainbow trout, which use a balanced set of amino acids for protein synthesis as other species but are adapted to use amino acids (AAs) as their preferred energy source over carbohydrates (as most carnivorous fish). Therefore, they require high levels of dietary proteins (35–45% of their meal) that can no longer be supplied by FM due to their limited availability and high demand. Multiple strategies

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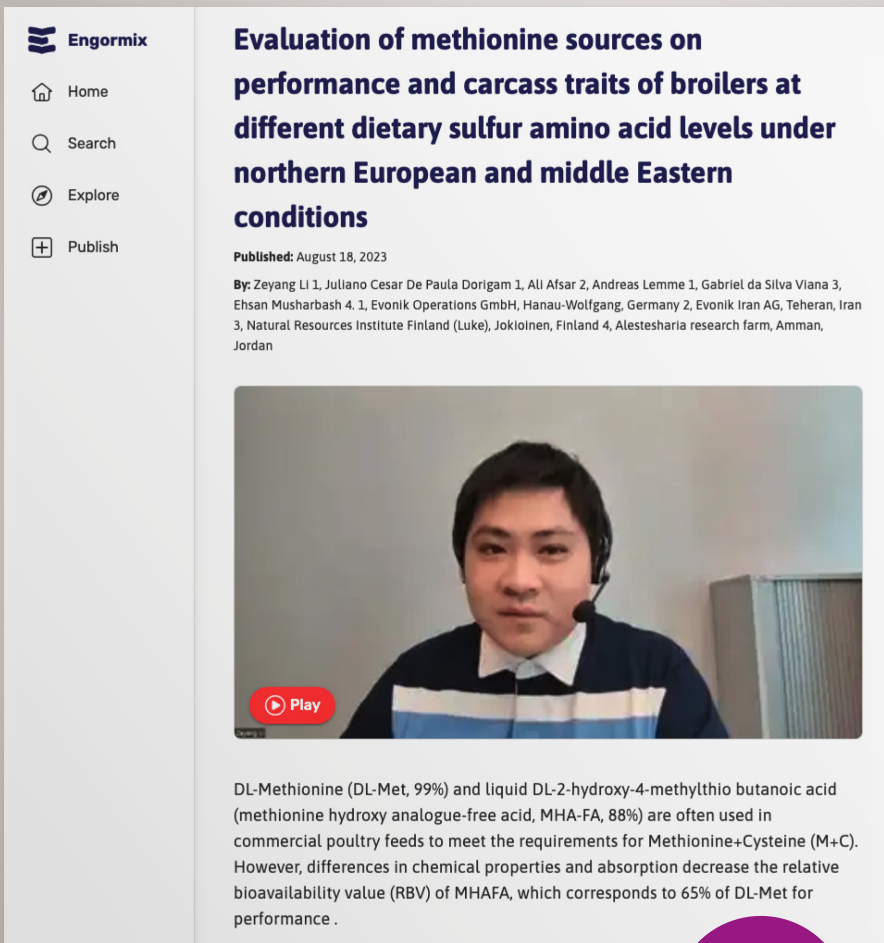
14. DL-methionine can replace methionine-hydroxy analog products in a ratio of 65:100 in laying hen feed

SECTION 1, TRIAL NO. 3

METAMINO® ATLAS 2022, SECTION 1, TRIALS NO. 3 AND NO. 5

15. Evaluation of methionine sources on performance and carcass traits of broilers at different dietary sulfur amino acid levels under northern European and middle Eastern conditions



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Evaluation of methionine sources on performance and carcass traits of broilers at different dietary sulfur amino acid levels under northern European and middle Eastern conditions

Published: August 18, 2023

By: Zeyang Li 1, Juliano Cesar De Paula Dorigam 1, Ali Afsar 2, Andreas Lemme 1, Gabriel da Silva Viana 3, Ehsan Musharbash 4. 1, Evonik Operations GmbH, Hanau-Wolfgang, Germany 2, Evonik Iran AG, Teheran, Iran 3, Natural Resources Institute Finland (Luke), Jokioinen, Finland 4, Alesteshaira research farm, Amman, Jordan

Play

DL-Methionine (DL-Met, 99%) and liquid DL-2-hydroxy-4-methylthio butanoic acid (methionine hydroxy analogue-free acid, MHA-FA, 88%) are often used in commercial poultry feeds to meet the requirements for Methionine+Cysteine (M+C). However, differences in chemical properties and absorption decrease the relative bioavailability value (RBV) of MHAFA, which corresponds to 65% of DL-Met for performance .

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SECTION 1, TRIAL NO. 9

SECTION 1, TRIAL NO. 13

SECTION 2, VIDEO NO. 7

16. Evaluation of methionine sources on performance and carcass traits of broilers at different dietary sulfur amino acid levels under northern European and middle Eastern conditions

SECTION 1, TRIAL NO. 9

SECTION 1, TRIAL NO. 13

17. An investigation of the assumed efficacy of methionine hydroxy analogue compared to DL-methionine by measuring growth performance, carcass traits, and GHR and IGF-I expression in broilers

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RESEARCH ARTICLE

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An investigation of the assumed efficacy of methionine hydroxy analogue compared to DL-methionine by measuring growth performance, carcass traits, and GHR and IGF-I expression in broilers

Engin Yenice, Ali Anıl Çenesiz, İsmail Yavaş, Neşe Nuray Toprak, İbrahim Çiftci and Necmettin Ceylan

Department of Animal Science, Faculty of Agriculture, Ankara University, Ankara, Türkiye

ABSTRACT

This experiment was conducted to investigate the assumed efficacy of 65% on the product basis of methionine hydroxy analog (OH-Met, 88% aqueous solution of DL-2-hydroxy-4-(methylthio) butanoic acid) relative to DL-methionine (DL-Met) in broiler chickens. A total of 792-day-old male chickens were randomly allotted to 7 dietary treatments consisting of a methionine deficient-basal diet based on corn-soybean meal and 6 different diets obtained by supplying the basal diet with methionine at 3 levels (25, 100 and 125%; levels of addition relative to the required amount of additional Met to meet SID Met + Cys requirements) from either DL-Met or OH-Met at a ratio of 65:100 (DL-Met to OH-Met on a product basis) in the corresponding treatments.

Regardless of the source, methionine supplementation enhanced ($p < .05$) growth performance, carcase and breast meat yield. Supplemental level and the source of Met had no significant effect on the proximate chemical composition of breast meat ($p > .05$). Comparison of effects of OH-Met and DL-Met supplemented at 100–65% weight ratio revealed no differences at any Met + Cys level and for performance criterion confirming the applied concept. Expression of growth hormone receptor (GHR) mRNA, which showed a positive correlation with body weight gain, carcase yield and breast percentage, in broiler liver significantly increased with 100% and 125% relative addition of DL-Met, while only 100% of OH-Met addition did ($p < .05$) when compared to the basal diet. The expression of the insulin-like growth factor-I (IGF-I) gene was not significantly affected by either Met source or supplementation level.

In conclusion, our data indicated that DL-Met can be substituted with a 1.54 times higher amount of OH-Met in corn-soybean meal based broiler diets.

HIGHLIGHTS

- Methionine supplementation enhanced growth performance, carcase and breast meat yield of broiler chickens fed corn-soybean meal based diets.
- DL-Met and OH-Met showed similar growth performance, carcase and cuts yields and breast meat traits when a 1.54 times higher amount of OH-Met, on a product basis, was added.
- DL-Met can be substituted with a 1.54 times higher amount of OH-Met in corn-soybean meal based broiler diets.

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KEYWORDS
Broiler; gene expression; efficacy of methionine hydroxy analog

Introduction

Methionine (Met) is an essential amino acid that plays a crucial role in protein synthesis and is considered to be the first limiting amino acid in corn-soybean-based broiler diets. Supplemental Met sources, including crystalline DL-methionine (DL-Met; 99% of active substance) and methionine hydroxy analog (OH-Met; 88% of active substance), are thus used to meet the sulphur amino acid requirements of broiler chickens. Both sources must be converted to L-Met after being absorbed in the small intestine to be used for protein synthesis and other metabolic pathways (Dibner and Knight 1984). Compared to DL-Met, OH-Met has a hydroxy group instead of an amino group and thus undergoes a different enzymatic process during conversion to L-Met. Furthermore, while some studies have reported comparable or even higher absorption of OH-Met compared to DL-Met (Dibner et al. 1992;

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SECTION 1, TRIAL 12

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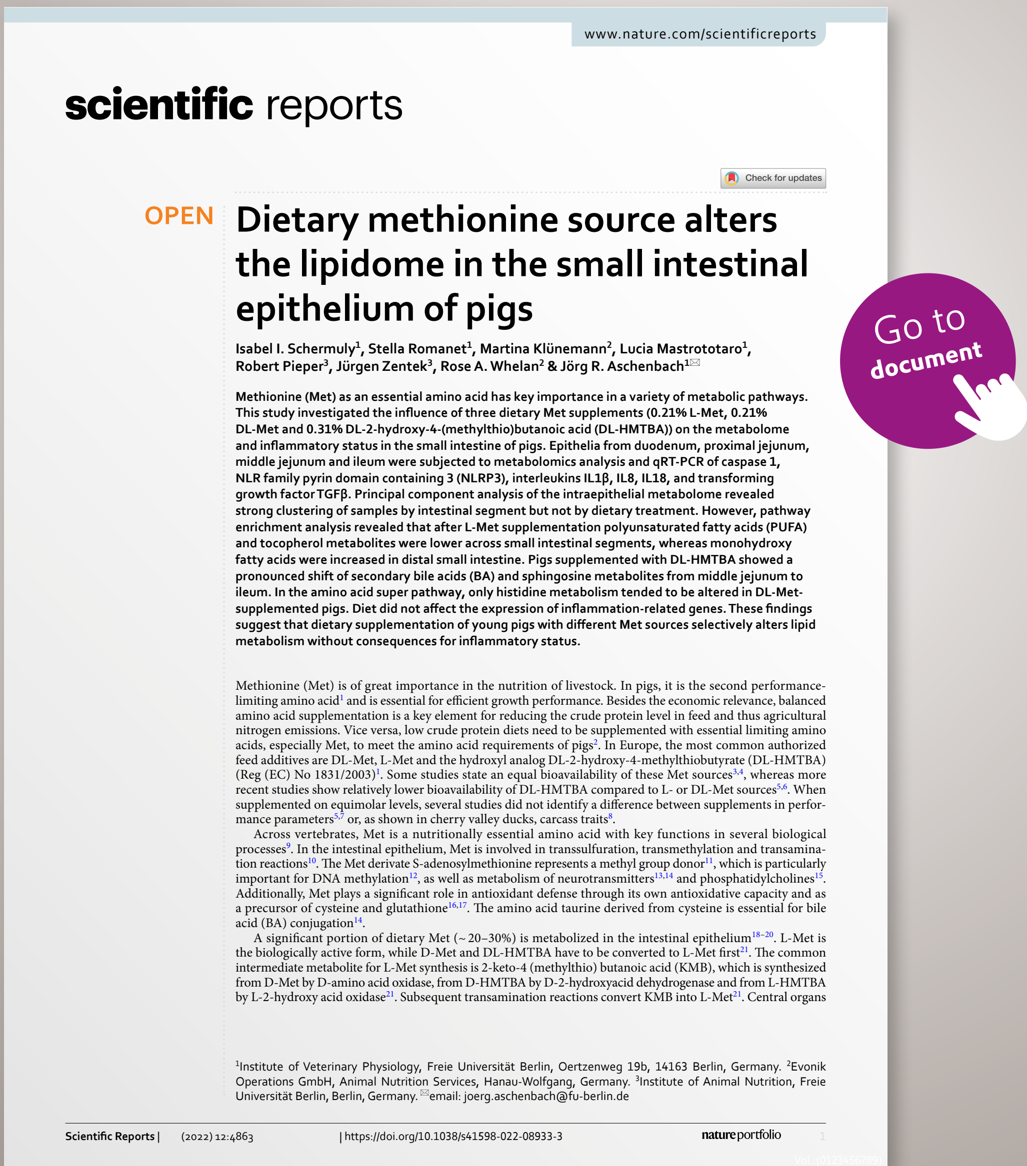
18. Dietary methionine source alters the lipidome in the small intestinal epithelium of pigs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Dietary methionine source alters the lipidome in the small intestinal epithelium of pigs

Isabel I. Schermuly[1], Stella Romanet[1], Martina Klünemann[2], Lucia Mastrototaro[1], Robert Pieper[3], Jürgen Zentek[3], Rose A. Whelan[2] & Jörg R. Aschenbach[1]✉

Methionine (Met) as an essential amino acid has key importance in a variety of metabolic pathways. This study investigated the influence of three dietary Met supplements (0.21% L-Met, 0.21% DL-Met and 0.31% DL-2-hydroxy-4-(methylthio)butanoic acid (DL-HMTBA)) on the metabolome and inflammatory status in the small intestine of pigs. Epithelia from duodenum, proximal jejunum, middle jejunum and ileum were subjected to metabolomics analysis and qRT-PCR of caspase 1, NLR family pyrin domain containing 3 (NLRP3), interleukins IL1β, IL8, IL18, and transforming growth factor TGFβ. Principal component analysis of the intraepithelial metabolome revealed strong clustering of samples by intestinal segment but not by dietary treatment. However, pathway enrichment analysis revealed that after L-Met supplementation polyunsaturated fatty acids (PUFA) and tocopherol metabolites were lower across small intestinal segments, whereas monohydroxy fatty acids were increased in distal small intestine. Pigs supplemented with DL-HMTBA showed a pronounced shift of secondary bile acids (BA) and sphingosine metabolites from middle jejunum to ileum. In the amino acid super pathway, only histidine metabolism tended to be altered in DL-Met-supplemented pigs. Diet did not affect the expression of inflammation-related genes. These findings suggest that dietary supplementation of young pigs with different Met sources selectively alters lipid metabolism without consequences for inflammatory status.

Methionine (Met) is of great importance in the nutrition of livestock. In pigs, it is the second performance-limiting amino acid[1] and is essential for efficient growth performance. Besides the economic relevance, balanced amino acid supplementation is a key element for reducing the crude protein level in feed and thus agricultural nitrogen emissions. Vice versa, low crude protein diets need to be supplemented with essential limiting amino acids, especially Met, to meet the amino acid requirements of pigs[2]. In Europe, the most common authorized feed additives are DL-Met, L-Met and the hydroxyl analog DL-2-hydroxy-4-methylthiobutyrate (DL-HMTBA) (Reg (EC) No 1831/2003)[1]. Some studies state an equal bioavailability of these Met sources[3,4], whereas more recent studies show relatively lower bioavailability of DL-HMTBA compared to L- or DL-Met sources[5,6]. When supplemented on equimolar levels, several studies did not identify a difference between supplements in performance parameters[5,7] or, as shown in cherry valley ducks, carcass traits[8].

Across vertebrates, Met is a nutritionally essential amino acid with key functions in several biological processes[9]. In the intestinal epithelium, Met is involved in transsulfuration, transmethylation and transamination reactions[10]. The Met derivate S-adenosylmethionine represents a methyl group donor[11], which is particularly important for DNA methylation[12], as well as metabolism of neurotransmitters[13,14] and phosphatidylcholines[15]. Additionally, Met plays a significant role in antioxidant defense through its own antioxidative capacity and as a precursor of cysteine and glutathione[16,17]. The amino acid taurine derived from cysteine is essential for bile acid (BA) conjugation[14].

A significant portion of dietary Met (~20–30%) is metabolized in the intestinal epithelium[18–20]. L-Met is the biologically active form, while D-Met and DL-HMTBA have to be converted to L-Met first[21]. The common intermediate metabolite for L-Met synthesis is 2-keto-4 (methylthio) butanoic acid (KMB), which is synthesized from D-Met by D-amino acid oxidase, from D-HMTBA by D-2-hydroxyacid dehydrogenase and from L-HMTBA by L-2-hydroxy acid oxidase[21]. Subsequent transamination reactions convert KMB into L-Met[21]. Central organs

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19. Methionine sources differently affect production of reactive oxygen species, mitochondrial bioenergetics, and growth of murine and quail myoblasts in vitro

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Article

Methionine Sources Differently Affect Production of Reactive Oxygen Species, Mitochondrial Bioenergetics, and Growth of Murine and Quail Myoblasts In Vitro

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Abstract: An optimal supply of L-methionine (L-Met) improves muscle growth, whereas over-supplementation exerts adverse effects. To understand the underlying mechanisms, this study aims at exploring effects on the growth, viability, ROS production, and mitochondrial bioenergetics of C2C12 (mouse) and QM7 (quail) myoblasts additionally supplemented (100 or 1000 µM) with L-Met, DL-methionine (DL-Met), or DL-2-hydroxy-4-(methylthio)butanoic acid (DL-HMTBA). In both cell lines, all the supplements stimulated cell growth. However, in contrast to DL-Met, 1000 µM of L-Met (C2C12 cells only) or DL-HMTBA started to retard growth. This negative effect was stronger with DL-HMTBA and was accompanied by significantly elevated levels of extracellular H_2O_2, an indicator for OS, in both cell types. In addition, oversupplementation with DL-HMTBA (1000 µM) induced adaptive responses in mitochondrial bioenergetics, including reductions in basal (C2C12 and QM7) and ATP-synthase-linked (C2C12) oxygen consumption, maximal respiration rate, and reserve capacity (QM7). Only QM7 cells switched to nonmitochondrial aerobic glycolysis to reduce ROS production. In conclusion, we found a general negative effect of methionine oversupplementation on cell proliferation. However, only DL-HMTBA-induced growth retardation was associated with OS and adaptive, species–specific alterations in mitochondrial functionality. OS could be better compensated by quail cells, highlighting the role of species differences in the ability to cope with methionine oversupplementation.

Keywords: methionine; HMTBA; muscle; growth; satellite cell; metabolic rate; viability; ROS

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1. Introduction

In postnatal muscle, so-called satellite cells (SCs) and their progeny are the primary mediators of hypertrophic growth, muscle maintenance, and regeneration, and therefore, their number and molecular and functional properties are crucial in muscle development and plasticity [1–3]. SC activation, proliferation, and differentiation have a high requirement for ATP and are, thus, essentially dependent on mitochondrial energy production through aerobic metabolism (respiratory chain and citric acid cycle). Basically, SC functional processes and lineage determination are specifically regulated by myogenic genes, e.g., *Pax7*, *MyoD*, *Myf5*, and *MyoG* [4]. However, metabolic signaling by mitochondria, e.g., via the regulation of Ca^{2+} levels, the release of metabolic intermediates, and the production of reactive oxygen species (ROS) [5–7], is also known to play a crucial role. Mitochondria-derived signals affect SC gene expression and functionality, especially with regard to SC differentiation and fate [8,9]. ROS, in particular, function under physiological conditions to adjust cellular activity to available bioenergetic resources,

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SECTION 4, ARTICLE 24

20. Issues with a meta-analysis assessing the efficacy of different sources of methionine supplementation

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Issues with a meta-analysis assessing the efficacy of different sources of methionine supplementation

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The article "Evaluating growth response of broiler chickens fed diets supplemented with synthetic DL-methionine or DL-hydroxy methionine: a meta-analysis" by Uddin et al. (2022, Poult. Sci. 101:101762 https://doi.org/10.1016/j.psj.2022.101762) analyzed literature data on methionine supply for broilers to derive requirement figures as well as to compare two methionine sources. We have concerns regarding both the reported results and the data analysis methodology. First, the data compilation is incomplete to achieve the objectives of the paper including determination of requirements and comparison of methionine supplement efficiencies. Second, the paper suggests Met and Met+Cys requirements of broilers but makes no attempt to discuss them in the context of nutrition of modern broiler strains. Third, the data preparation for methionine source comparison as well as the mathematical approach includes weaknesses resulting in misleading conclusions.

Selected data were incomplete: The authors analyzed 480 records from 39 studies comparing DL-Methionine (**DL-Met**) and DL-Hydroxy analogue of methionine (**DL-OH-Met**) in simultaneous dose-response experiments with broilers. While the supplementary material suggests 39 publications, more than 39 studies were available as for example, Lemme et al. (2002) and Payne et al. (2006) reported 2 and 3 studies, respectively. While the reported studies were found according to the process described, the authors also referenced another meta-analysis (Sauer et al., 2008) on the same subject. The second meta-analysis referenced at least 16 additional studies which were not considered by Uddin et al. (2022), providing 144 records from nine peer-reviewed papers (Buresh und Harms, 1986; Balnave und Oliva, 1990; Groote et al., 1990; van Weerden et al., 1992; Huyghebaert, 1993; Rostagno und Barbosa, 1995; Roemer und Abel, 1999; Wallis, 1999; Hoehler et al., 2005). All records meet the requirements as defined (Uddin et al., 2022) meaning that at least 30% records for analysis were missing. Interestingly, most of the missing studies reported DL-Met to be advantageous over DL-OH-Met with respect to biological effectiveness. Moreover, the selected studies were used for the determination of Met and Met + Cys requirements. Valuable research from 100 papers reporting studies with only one methionine source were excluded. This significant data omission appears deliberate but the rationale for this exclusion was not given. The power, outcome, and conclusions of the meta-analysis with respect to requirements would change when including such studies. We see no reason for excluding studies with just a single methionine source, because meta-analysis allows integrating such information with studies comparing both sources (Salanti et al., 2010). This is particularly relevant when the studies have a control, the usual situation, because the controls serve as a common reference to connect studies with just a single methionine source. Even without a control, the random-coefficient approach taken by the authors would have allowed including such studies, making use of inter-study information (van Houwelingen et al., 2002).

Reported requirement figures are questionable: Uddin et al. (2022) reported digestible Met+Cys requirements of 0.314 (LP; linear-plateau) or 0.379 g/d (QP, quadratic plateau), 0.932 g/d (LP), and 0.953 g/d (LP) for starter (11 days of age), grower (21 days of age) and finisher broilers (35 days of age), respectively. No statistical information on goodness of fit is provided except for the LOOIC which is only used to compare models but gives no easily interpretable absolute indication of fit to data. Figures 3 and 4 do not suggest a particularly suitable fit for the regression models, nor would they suggest break

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21. “Absorption of methionine sources in animals—is there more to know?” — Yes, there is more to know!

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Letter to the Editor

Reply to: “Absorption of methionine sources in animals—is there more to know?” — Yes, there is more to know!

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Recently, above mentioned paper compiling and discussing literature concerning the absorption of DL-methionine (DL-Met) and two forms of the hydroxy analogue of methionine (2-hydroxy-4-methylthiobutyric acid [HMTBa], Ca-salt of HMTBa [HMTBa-Ca]) was published in Animal Nutrition (https://doi.org/10.1016/j.aninu.2022.09.004). We would like to comment on this article regarding the aim of the study as expressed in the introduction: “This critical review provides an understanding of diverging studies and provides insights into how further evaluation should be conducted when the bioefficacy of the two molecules is discussed”.

While methods in physiology research have indeed been further developed and improved in many respects over time, those methods are seldomly appropriate for quantifying impact on performance indicators such as body growth, meat deposition or feed and nutrient utilization. Insofar, research on absorption of methionine or its analogues helps to understand and explain effects determined empirically but would not be suitable to change the conclusions out of growth studies. The mentioned “conflicting” results of bioefficacy studies are indeed a matter of experimental setups which are, in fact, not discussed in the present publication. Moreover, recently the lower bioefficacy of HMTBa and HMTBa-Ca as well as the methodology for determination have been reported and validated, respectively (Elwert et al., 2008; Lemme et al., 2020). After a meticulous examination of literature, the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) also concluded that HMTBa shows a lower bioefficacy (75% on molar level) than DLM-Met in monogastric animals which was associated especially with lower efficacy of dimers, trimers and oligomers of HMTBa (Rychen et al., 2018).

In Chapter 2, references and results are reported which should indicate that HMTBa is absorbed to a high degree before feed/digesta enters the duodenum in chicken and other farm animals suggesting high if not identical absorption of this compound compared to DL-Methionine. While it is notable that only references from sponsored research of the co-authors of the present review were considered, authors did not include other studies that reported considerable and higher concentrations of HMTBa compared to methionine at proximal duodenum in broilers and swine (Drew et al., 2003; Maenz and Engele-Schaan, 1996; Malik et al., 2009) which ingested experimental feeds with labelled methionine sources. Accordingly, the papers concluded a remarkably lower absorption of HMTBa at terminal ileum. In a later chapter (3.1) authors discredit the use of ^{3}H-labelling and it was suggested that ^{3}H-labelled compounds would bear the risk of instability. Furthermore, authors devoted more than 60 lines to this subject. In addition, they argued that ^{14}C labelled compounds were also unstable. However, neither research by Saunderson (1985) nor that by Lingens and Molnar (1996) were mentioned. Instructively, these researchers used ^{14}C-labelled methionine and HMTBa or HMTBa-Ca, respectively, and were able to detect and quantify the label in various tissues and the excreta of broiler chickens. Saunderson (1985) reported twice the residual radiation for HMTBa in excreta compared to DL-Met fed broilers which is almost identical to Esteve-Garcia and Austic (1993) findings. Indeed, in Esteve-Garcia and Austic (1993) data would suggest a relative bioefficacy of 64% for HMTBa-Ca compared to DL-Met on weight basis (72% on equimolar comparison). Lingens and Molnar (1996) reported even three-to four-fold residual radiation in excreta of broilers. All these studies would, thus, consistently report substantially higher concentration of HMTBa and HMTBa-Ca compared to the methionine label in excreta (Drew et al., 2003; Lingens and Molnar, 1996; Maenz and Engele-Schaan, 1996; Malik et al., 2009; Saunderson, 1985). Contrary to the data reported by Becquet et al., (2022), these findings are not in agreement with almost complete absorption of HMTBa. Indeed, the detected labels were not necessarily associated with the methionine or HMTBa (Maenz and Engele-Schaan, 1996) and other studies suggested that a large portion of particularly HMTBa has been catabolized by microbiota (Drew et al., 2003; Malik et al., 2009). Therefore, HMTBa available for uptake and further transformation into L-methionine had been shown to be lower than uptake of DL-Met. The entire chapter 3.2 discusses the inappropriateness of the rooster assay for digestibility evaluation as the respective paper by Rostagno and Barbosa (1995) reported a 7% lower apparent digestibility for HMTBa compared to DL-Met and the respective growth study suggested an average bioefficacy of about 66% on weight basis (75% on molar level). In Rostagno and Barbosa (1995), compounds as opposed to labels were analysed and this effect on digestibility would be in addition to the disappearance due to micro-

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22. Noninferiority of the hydroxy analog of methionine compared to DL-methionine not confirmed in a broiler trial

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LETTER TO THE EDITOR

Noninferiority of the hydroxy analog of methionine compared to DL-methionine not confirmed in a broiler trial

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Concerning: "New statistical approach shows that hydroxy-methionine is non-inferior to DL-methionine in 35-day old broiler chickens" by D. I. Batonon-Alavo, C. Manceaux, J. T. Wittes, F. Rouffineau, and Y. Mercier.

In the paper by Batonon-Alavo et al. (2023) a noninferiority test was used to provide evidence that broiler performance achieved by supplementing feed with DL-hydroxy-methionine (**OH-Met**) is not worse than that achieved with DL-methionine (**DL-Met**). The purpose of this letter is to point out that the noninferiority test was not applied correctly, and therefore the respective conclusions are not correct, and the paper ignores fundamental nutritional principles.

The authors do not explain in detail the process for selecting broiler studies for the meta-analysis required for the determination of the lower confidence limit according to the 95-95 approach suggested by Schumi and Wittes (2011). It appears that feeding studies with final age of 35 d and feeding corn-wheat-soybean meal based were selected. Studies testing liquid OH-Met or OH-Met-Ca in comparison to DL-Met were included but criteria for selecting particular treatments out of the dose-response trial remain unclear. While referring to Lemme et al. (2020) in the discussion, data reported in that paper were not considered for this exercise although in that study corn-wheat-soybean meal-based diets were fed until 35 d of age. Accordingly, a response of 963 g body weight gain (1.2 g/kg DL-Met vs. unsupplemented basal diet) was reported. Adding this to the meta-analysis would have even increased M_1 and, thus, increased the range of acceptable difference.

It turns out that Batonon-Alavo et al. (2023) have applied the 95-95 method described in Schumi and Wittes (2011) incorrectly. Here, we will briefly state the 95-95 method as proposed by Schumi and Wittes (2011) and also refer back to the original proposal of the 95-95 method given in Rothmann et al. (2003) and Rothmann and Tsou (2003). The method proposed first uses a meta-analysis to estimate the effect of the reference treatment compared to the control treatment. This effect is estimated as the difference between the reference treatment mean and the control treatment mean. The estimate will be referred to as D_1 (our notation). A conservative estimate of the effect that is likely to be observed in a new study is obtained by computing the 1-sided lower limit of a 95% confidence interval of that difference (Rothmann et al., 2003). The lower limit is denoted as M_1. The user then determines a predetermined lower fraction of M_1 that corresponds to the largest loss of effect, that is, the largest inferiority the user is prepared to consider acceptable. That smaller value is denoted as M_2. For example, if a reduction of the effect by 5% of M_1 is deemed acceptable, the value is $M_2 = 0.05{*}M_1$. M_2 is denoted as the noninferiority margin (Rothmann et al., 2003). To establish noninferiority of a new treatment compared to the reference treatment, it then needs to be shown that the difference of the new treatment to the reference treatment mean is significantly larger than M_2. We denote the estimate of this difference as D_2. Note that D_2 is expected to be negative, assuming that the reference treatment is superior to the new treatment. The difference D_2 corresponds to the estimated loss of effect when using the new treatment instead of the reference treatment. The decision is based on the lower 1-sided 95% confidence interval for the difference D_2 (Rothmann et al., 2003).

Batonon-Alavo et al. (2023; Table 1) find $M_1 = 467$ for body weight based on the difference of DL-Met compared to a basal diet. This calculation is correct, apart from the fact that the authors used a 2-sided 95% interval in place of a 1-sided 95% interval prescribed by Rothmann et al. (2003). The calculation of the noninferiority margin (M_2), however, seems to be in error. According

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23. Data for meta-analysis need standardization – A response to "Assessing the nutritional equivalency of DL-methionine and L-methionine in broiler chickens: A meta-analytical study"

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Poultry Science

Data for meta-analysis need standardization—a response to "Assessing the nutritional equivalency of DL-methionine and L-methionine in broiler chickens: a meta-analytical study" by Asasi et al.

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Letter to the editor,—Concerning "Assessing the nutritional equivalency of DL-methionine and L-methionine in broiler chickens: A meta-analytical study" by Roya Asasi, Hamed Ahmadi, Mohammad Amir Karimi Torshizi, Karimi Torshizi, Rasoul Vaez Torshizi, Farid Shariatmadari.

For a meta-analysis for evaluating the nutritional value of L-methionine vs. DL-methionine in broiler nutrition data from 13 feeding experiments were analyzed by simultaneous regression (linear, exponential) and visualization. While this is an appreciated objective, we have concerns with respect to data selection and preparation.

Original performance data (daily gain; feed conversion ratio) were put into one plot while it was not considered that data within study are more correlated than between studies. Approaches like mixed-models would be more suitable for such analysis.

A major concern is that responses were plotted only to supplemented methionine although the magnitude of responses in single trials are largely dependent on the overall (digestible) methionine+cysteine level. For example, the total Met+Cys levels of basal diets varied between 0.17% and 0.52% in assay 1 of Dilger and Baker (2007) and highest sulfur amino acid level was reported for assay 4 by Dilger et al. (2007; 0.89%). While the sulfur amino acid level of the basal diet would affect performance and magnitude of response, regressing against Met+Cys levels would impact position of data points of different publications in the plot. Moreover, also the methionine to cysteine ratio within sulfur amino acids impact responsiveness to methionine supplementation. Data by Dilger and Baker (2007) clearly provide evidence for this interaction. However, Asasi et al. (2023) did not put attention to this interaction and all data of this publication were included in the meta-analysis and certainly biased its outcome. For example, in assay 1 of Dilger and Baker (2007) methionine to sulfur amino acid ratio decreased from 70% to 23%. Finally, intake of sulfur amino acids is more suitable as basis for comparison than "% in diet" and would be impacted by feed intake as well. Therefore, studies are hardly comparable without normalizing data.

While not all studies included a basal, nonsupplemented diet (e.g., Rehman et al., 2019), trials reported by Dilger and Baker (2007; assay 2) and Dilger et al. (2007; assay 3) included more L-Met than DL-Met treatments which would imbalance the data base.

Therefore, it might be doubted whether the reported relative bioavailability figure for DL-methionine compared to L-methionine remains when the above would be adequately considered.

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DISCLOSURES

Authors declared no conflict of interest. This can be questioned as second author is representant of an L-methionine producer /agent in Iran.

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24. Bioavailability of calcium salt of hydroxy analogue of methionine relative to DL-methionine to support growth performance of 11 to 20 kg pigs

SECTION 1, TRIAL NO. 7

25.

META-ANALYSIS

IMPORTANCE OF MEASURING RELATIVE BIOAVAILABILITY IN METHIONINE SOURCES

Juliano C. P. Dorigam, Zeyang Li, and Andreas Lemme

Methionine (Met) is an essential amino acid of particular importance because it cannot be synthesized by broilers and because it can be converted to the other sulfur amino acid, cysteine (Cys). Due to low levels in ingredients, Met and Cys are usually the first performance limiting amino acids in broiler feeds and commonly DL-methionine (**DL-Met**, 99% purity) or methionine hydroxy analog (**MHA**; free acid: MHA-FA, 88% purity; to a much smaller extent calcium salt: MHA-Ca; 84% purity) is supplemented to meet requirements. Due to the chemical differences between the two compounds, their nutritional values differ. Nutritional value is expressed as the relative bioavailability (**RBV**) of MHA compared to DL-Met, which indicates the replacement ratio of these products in feed.

A recent publication indicated an RBV at or close to 65% for MHA-FA compared to DL-Met in broilers on a product-to-product basis [1], and a scientific opinion published in 2018 in the EFSA journal concluded an RBV of 75% on an equimolar basis for both forms of MHA (64 (MHA-Ca) - 67% (MHA-FA) on a product basis) based on the available literature at that time [2]. The principle behind the RBV determination is to compare dose-response data for both products simultaneously [3]. In this approach, the starting point (basal diet) of the curve and the asymptote are the same for both products while the difference between the slopes (regression coefficient) of the curves is used to calculate the RBV.

The multiple exponential regression method was validated in a meta-analysis, which provided statistical evidence that both methionine sources would allow for the same maximal performance (asymptote), while the steepness of the curve indicates their nutritional value [4]. Earlier experiments [5–8] provided additional evidence for the appropriateness of the simultaneous dose-response approach by introducing diluted DL-Met (diluted to a purity of 65%; **DLM65**) as an internal standard. In a recent meta-analysis, Lemme et al. [1] found that DLM65 was 62% as efficient as DL-Met on average across six experiments, while MHA-FA was 63% as efficient. This result validates the methodology because the RBV of DLM65 was almost exactly as expected for DL-Met diluted to 65% purity. The RBV value in the cited studies is less than 88%, which is contrary to claims made by MHA producers and may have implications not only for animal performance but also for economics and purchasing decisions.

Based on this, an RBV of 65% is recommended for MHA products relative to DL-Met. Indeed, this finding should be reflected in the pricing of products to realize the full value. A recent challenge test at a commercial farm with 408,500 broilers suggested savings of >11,000 €/year just by applying our recommendation to a feed volume of 10,000 t/year [9].

The validation of the recommendation on relative bioavailability value

In addition to the dose-response studies, there is a more practical and simple experimental protocol that can be applied to challenge and validate the recommended RBV of 65% for MHA as compared with DL-Met (on product basis). The simplest test comprises two treatments with either MHA or DL-Met supplemented up to 65% as MHA, i.e. considering that 100 units of MHA are replaced by 65 units of DLM. The same animal performance at a lower cost is expected with DL-Met.

The application of such a performance test is exemplified by a recent publication, where both products were compared at different dietary Met+Cys levels under Northern European and Middle Eastern conditions [10]. The first study was conducted in Finland and consisted of 5 treatments with 9 replicates with 16 male Ross 308 broilers per replicate. Diets were wheat-soybean meal based. The second study was conducted in Jordan and consisted of 5 treatments with 10 replicates and 50 mixed-sex (1:1) Ross 308 broilers per replicate. In this case, corn-soybean based feeds were fed.

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In both trials, broilers received a basal diet (**BD**) formulated to meet all nutritional requirements except for Met+Cys (60-66% of Met+Cys requirements), or BD supplemented with MHA-FA to meet either 75% or 100% of Met+Cys requirements. In two further treatments, MHA-FA was replaced by DL-Met on a weight basis, but only up to 65% of the MHA-FA inclusion level, according to the recommended RBV of 65% for MHA-FA relative to DL-Met. Broilers were fed *ad libitum* from 0-35 days (Trial 1) or from 0-32 days (Trial 2) in 3-phase programs under standard housing conditions. The final results from trials 1 and 2 are presented in **Tables 1 and 2**, respectively.

Table 1.
Growth performance of male Ross 308 broilers fed with adequate and reduced Met+Cys levels and supplemented with either DL-Methionine (DL-Met) or liquid methionine hydroxy analogue free acid (MHA-FA) at a ratio of 65:100 during 35 days period

Performance parameters	Basal	At reduced Met level (75%)		At recommended Met Level (100%)		SEM	*P-value*
		100 MHA-FA	65 DL-Met	100 MHA-FA	65 DL-Met		
ADFI, g/d	62.19[a]	110.04[b]	108.53[b]	109.25[c]	110.46[b]	0.923	<0.01
ADG, g/d	35.85[a]	74.50[b]	73.94[b]	77.56[c]	77.95[c]	0.660	<0.01
FCR, g/g	1.735[a]	1.477[b]	1.468[b]	1.409[c]	1.417[c]	0.012	<0.01
BW, g	1260[a]	2574[b]	2555[b]	2678[c]	2691[c]	22.51	<0.01

ADFI=average daily feed intake, ADG=average daily gain, FCR=feed conversion ratio.
Data was analyzed using one-way ANOVA with GLM procedure of SAS (ver. 9.4). Significances were considered if P<0.05 (Tukey test).

Table 2.
Growth performance of mixed Ross 308 male and female broilers fed with adequate and reduced Met+Cys levels and supplemented with either DL-Methionine (DL-Met) or liquid methionine hydroxy analogue free acid (MHA-FA) at a ratio of 65:100 during 32 days period

Performance parameters	Basal	At reduced Met level (75%)		At recommended Met Level (100%)		SEM	*P-value*
		100 MHA-FA	65 DL-Met	100 MHA-FA	65 DL-Met		
FI, g	2592[b]	2879[a]	2855[a]	2867[a]	2933[a]	22.69	<0.05
BW, g	1586[c]	1914[b]	1916[b]	1980[a]	2014[a]	16.17	<0.05
WG, g	1545[c]	1873[b]	1874[b]	1938[a]	1972[a]	16.09	<0.05
FCR, g/g	1.673[a]	1.524[b]	1.510[bc]	1.470[c]	1.480[bc]	0.012	<0.05
CY, % of BW	70.75[b]	72.34[ab]	72.69[ab]	73.67[a]	72.88[a]	0.508	<0.05
BY, % of carcass	35.89[c]	38.75[b]	39.07[b]	41.60[a]	42.12[a]	0.417	<0.05

FI=feed intake, BW=body weight, WG=weight gain, FCR=feed conversion ratio, CY= carcass yield, BY= breast meat yield.
**Data was analyzed using one-way ANOVA with GLM procedure of SAS (ver. 9.4). Significances were considered if P<0.05 (Tukey test).*

In both studies, average feed intake was significantly lower in broilers fed the basal diet (indicated by different superscripts [a,b,c]) but there were no differences between the other treatments. In contrast, marginal dietary Met+Cys supply (75%) resulted in significantly lower weight gain and final body weight than treatments at 100% Met+Cys. These effects were reflected in feed conversion ratio, particularly, in trial 1 and breast meat yield in trial 2. However, there were no differences between the corresponding MHA-FA and DL-Met treatments at marginal or adequate Met+Cys supply, or between different performance parameters. This provides evidence that the recommended RBV of 65% for MHA-FA relative to DL-Met is applicable without compromising performance. Moreover, the observed lower performance at 75% of the recommended Met+Cys levels indicates a performance limitation by Met+Cys, which makes the 65:100 test more sensitive, and thus the results provide strong support for the recommendation.

Compilation and Meta-Analysis of previous preformance tests

While the above reports of the most recent trials challenge and confirm our recommendation, many such 65:100 trials have been conducted in recent years that can be analyzed by meta-analysis. For this compilation, we used the classical meta-analysis by using Hedges' *g* to estimate the effect size with a 95% confidence interval. This methodology is well established in animal science and has been used to integrate and determine the overall effect from several studies to provide more accurate insights [11]. Therefore, we conducted a meta-analysis to assess the performance responses of broilers to DL-Met when replacing MHA at a 65:100 ratio. Moreover, especially scientists and authors who favor – in contrast to us - a high nutritional value of MHA-FA, repeatedly state that the nutritional value of MHA-FA is higher, especially at or above Met+Cys requirement, while lower dietary Met+-Cys levels would interfere with the efficiency of MHA [12,13]. Therefore, we split the current meta-analysis of the 65:100 trials into experiments operating at marginal Met+-Cys supply (below recommendations), at recommended levels, and clearly above recommended levels to see if any differences in responses could be observed.

In order to perform the meta-analysis, the mean values of the performance criteria, the respective standard deviations and sample sizes (replicates per treatment) were extracted from each included study. The target variable reported in this article is the feed conversion ratio (**FCR**), but results for other performance parameters were almost identical. When more than one Met+Cys level was used in a study, each corresponding treatment pair (65:100) was coded individually. Additionally, the study groups were separated according to the Met+Cys level and classified in relation to the requirement (below, at or above requirement). In the case of dose-response studies, the requirement was determined by the exponential equation presented in the publication.

Data analysis was performed using Meta-Essential version 1.4. The estimated effect size (the difference between DL-Met and MHA treatment) was quantified using Hedges' g with a 95% confidence interval (CI) [14]. Data were pooled using a fixed-effect model due to the lack of heterogeneity, after being pre-checked using the I^2 statistic. An effect was declared significant when the overall estimated effect size was $P < 0.05$.

As shown in Figures 1, 2 and 3 no substantial heterogeneity was found for feed conversion ($I^2 = 0.00\%$), indicating that all studies in these subgroups produced an estimate of the same true effect size in a homogeneous population. In fact, the graphs demonstrate that all mean effect size values were close to zero and no single experiment had confidence intervals excluding zero, indicating very homogenous data with no exception. Moreover, with respect to the overall results indicated by the purple dots (and results shown in the last line in bold), the mean effect size was almost zero and the overall confidence interval was very small, providing clear evidence that replacement of MHA with DL-Met at a ratio of 100:65 always results in the same performance.

Study name	Hedges'g (95% CI)
Elwert et al. (2008)	-0.06 (-1.55 to 1.42)
Hoehler et al. (2005)	-0.07 (-1.56 to 1.41)
Hoehler et al. (2005)	0.18 (-1.58 to 1.94)
Hoehler et al. (2005)	1.02 (-0.85 to 2.88)
Lemme et al. (2020)	1.11 (-0.48 to 2.71)
Lemme et al. (2002)	1.25 (-0.67 to 3.17)
Payne et al (2006)	0.08 (-1.11 to 1.26)
Sangali et al. (2014)	-0.64 (-2.44 to 1.16)
Goes et al. (2017)	0.53 (-0.57 to 1.64)
Purohit et al. (2018)	-0.82 (-2.36 to 0.73)
Purohit et al. (2018)	0.19 (-1.30 to 1.68)
Purohit et al. (2018)	-0.30 (-1.80 to 1.19)
Purohit et al. (2018)	0.08 (-1.40 to 1.57)
Purohit et al. (2018)	0.75 (-0.79 to 2.28)
Purohit et al. (2018)	0.50 (-1.01 to 2.00)
Murakami et al (2017)	0.09 (-1.21 to 1.40)
Murakami et al (2017)	-0.66 (-2.00 to 0.68)
Murakami et al (2017)	-0.50 (-1.83 to 0.82)
Murakami et al (2017)	-0.18 (-1.49 to 1.13)
Overall (P = 0.488)	**0.10 (-0.17 to 0.38)**
Heterogeneity (I^2=0.00%)	

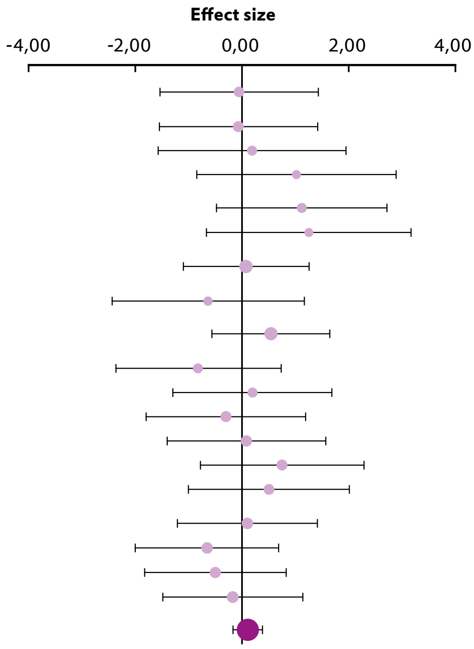

Figure 1. Forest plot showing the effect of dietary replacement of 100 parts MHA with 65 parts of DL-Met on feed conversion ratio of broilers when dietary Met+Cys is above the requirement.

Study name	Hedges'g (95% CI)
Lemme et al. (2020)	0.03 (-1.46 to 1.51)
Lemme et al. (2020)	-0.37 (-1.87 to 1.13)
Payne et al (2006)	-0.11 (-1.30 to 1.07)
Li et al. (2019)	0.22 (-0.87 to 1.31)
Li et al. (2019)	0.26 (-0.75 to 1.28)
Viana et al. (2009)	0.08 (-1.11 to 1.26)
Goes et al. (2017)	-0.07 (-1.16 to 1.01)
Boontarue et al. (2023)	-0.68 (-1.46 to 0.09)
Boontarue et al. (2023)	0.07 (-0.69 to 0.82)
Purohit et al. (2018)	0.60 (-0.92 to 2.12)
Purohit et al. (2018)	0.19 (-1.30 to 1.68)
Purohit et al. (2018)	-0.09 (-1.57 to 1.40)
Purohit et al. (2018)	0.92 (-0.64 to 2.48)
Purohit et al. (2018)	-0.95 (-2.51 to 0.62)
Purohit et al. (2018)	-1.18 (-2.79 to 0.43)
Lemme (2022)	-0.23 (-1.99 to 1.53)
Murakami et al (2017)	-0.44 (-1.76 to 0.88)
Murakami et al (2017)	0.05 (-1.26 to 1.36)
Fact&Figures n°15166	0.41 (-1.09 to 1.91)
Fact&Figures n°15133	0.15 (-1.61 to 1.91)
Fact&Figures n°15123	0.26 (-1.23 to 1.75)
Fact&Figures n°15120	-0.52 (-2.03 to 0.99)
Fact&Figures n°15119	-0.95 (-2.02 to 0.12)
Fact&Figures n°15116	-0.35 (-1.55 to 0.84)
Overall (P = 0.676)	**-0.13 (-0.33 to 0.07)**
Heterogeneity (I^2=0.00%)	

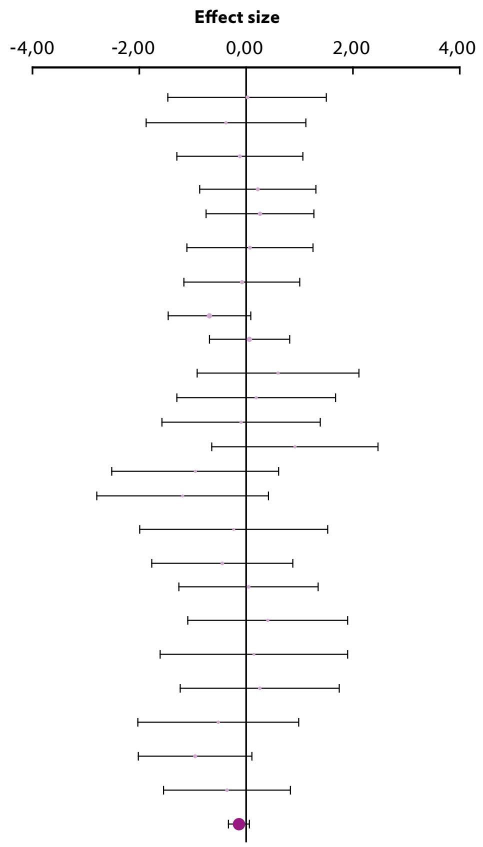

Figure 2. Forest plot showing the effect of dietary replacement of 100 parts MHA with 65 parts of DL-Met on feed conversion ratio of broilers when dietary Met+Cys is at the requirement.

In addition, analyzing all trials reported in Figures 1,2 and 3 together (not shown) also confirms that application of the recommended RBV of 65% for MHA-FA is always successful. Splitting, however, the data into various Met+Cys supply categories revealed that this conclusion applies for marginal, adequate and luxury Met+Cys levels, thus refuting claims that there would be different efficiencies at different dietary Met+Cys levels.

Conclusion

Two studies conducted under Northern European or Middle Eastern conditions confirmed that 100 units of liquid MHA-FA could be replaced by 65 units of DL-Met without compromising performance, regardless of, for example, the choice of ingredients. A more comprehensive evaluation involving 76 pairs of treatments provides evidence that not only can MHA be replaced by DL-Met in a 100:65 ratio with no risk, but also that this conclusion is valid for any general dietary Met+Cys supply status.

Study name	Hedges'g (95% CI)
Elwert et al. (2008)	0.82 (-0.72 to 2.37)
Elwert et al. (2008)	0.00 (-1.48 to 1.48)
Elwert et al. (2008)	0.14 (-1.35 to 1.63)
Elwert et al. (2008)	-0.46 (-1.97 to 1.04)
Hoehler et al. (2005)	0.99 (-0.58 to 2.56)
Hoehler et al. (2005)	1.04 (-0.54 to 2.62)
Hoehler et al. (2005)	-0.70 (-2.23 to 0.83)
Hoehler et al. (2005)	0.12 (-1.36 to 1.61)
Hoehler et al. (2005)	0.16 (-1.59 to 1.92)
Hoehler et al. (2005)	-1.27 (-3.19 to 0.66)
Hoehler et al. (2005)	0.15 (-1.34 to 1.64)
Hoehler et al. (2005)	0.10 (-1.39 to 1.58)
Hoehler et al. (2005)	-0.44 (-1.94 to 1.06)
Hoehler et al. (2005)	0.00 (-1.48 to 1.48)
Hoehler et al. (2005)	0.62 (-0.90 to 2.14)
Lemme et al. (2020)	1.03 (-0.55 to 2.61)
Lemme et al. (2002)	0.11 (-1.65 to 1.87)
Lemme et al. (2002)	1.37 (-0.58 to 3.32)
Lemme et al. (2002)	0.45 (-1.33 to 2.22)
Mandal et al. (2004)	-0.47 (-1.50 to 0.55)
Payne et al (2006)	-0.75 (-1.98 to 0.47)
Sangali et al. (2014)	0.00 (-1.76 to 1.76)
Sangali et al. (2014)	-0.16 (-1.92 to 1.60)
Li et al. (2019)	-0.25 (-1.34 to 0.84)
Li et al. (2019)	-0.37 (-1.39 to 0.65)
Viana et al. (2009)	-0.11 (-1.30 to 1.07)
Goes et al. (2017)	-0.29 (-1.39 to 0.80)
Goes et al. (2017)	0.00 (-1.09 to 1.09)
Murakami et al (2017)	-0.19 (-1.50 to 1.12)
Murakami et al (2017)	0.02 (-1.29 to 1.32)
Murakami et al (2017)	-0.31 (-1.63 to 1.00)
Murakami et al (2017)	-0.16 (-1.47 to 1.15)
Fact&Figures n°15119	0.63 (-0.40 to 1.67)
Overall (P = 0.629)	**−0.01 (-0.17 to 0.20)**
Heterogeneity (I^2=0.00%)	

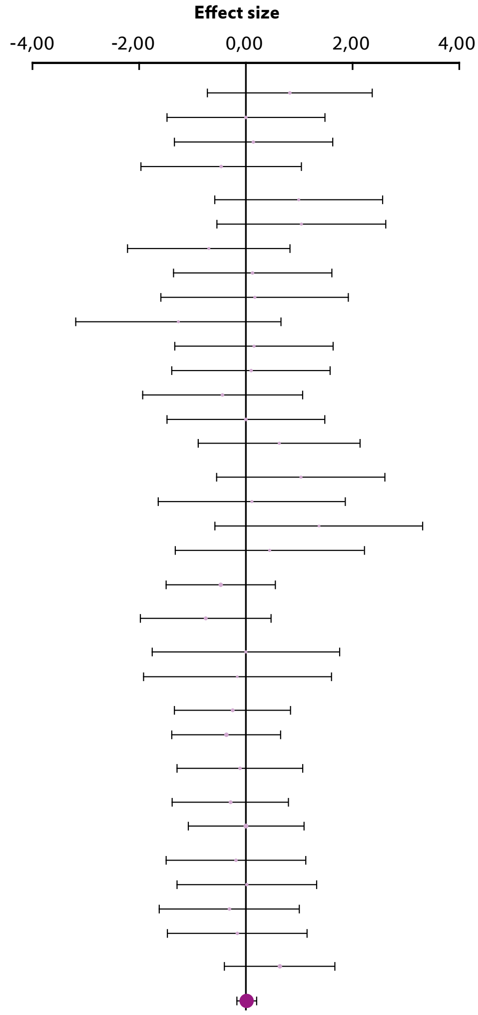

Figure 3. Forest plot showing the effect of dietary replacement of 100 parts MHA with 65 parts of DL-Met on feed conversion ratio of broilers when dietary Met+Cys is below the requirement.

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Sustainability

26.

MetAMINO® Carbon Footprint

Choose MetAMINO® to reach your greenhouse gas emission targets

Ambitious emission reduction targets verified by the Science Based Targets initiative

Scope 1 & 2: **25%** absolute reduction by 2030, relative to 2021.

In accordance with a well-below 2 °C warming pathway.

SCIENCE BASED TARGETS
DRIVING AMBITIOUS CORPORATE CLIMATE ACTION

Scope 3: **11%** absolute reduction by 2030, relative to 2021.

In the near future, Evonik aims to revalidate its targets to support a pathway that limits warming to 1.5°C by 2050.

Find out more about Evonik's greenhouse gas emission reduction strategy here.

Sustainability data you can trust: Product LCAs conducted according to a certified process

When buying from Evonik, you can access Product Environmental Footprint data for almost all our animal nutrition products.

Our in-house lifecycle assessment experts use a calculation methodology externally certified by TÜV Rheinland against ISO standards and Together for Sustainability Product Carbon Footprint guidelines.

This data enables you to:

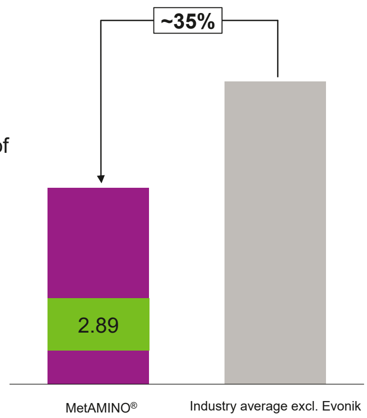
- prove to your customers and other stakeholders that you are sourcing sustainable ingredients with credible and reliable lifecycle assessments
- use primary data for your company's greenhouse gas emission calculations, reporting, and reduction goals.

Contact your sales representative for more information.

A low-emission source of DL-Methionine

When weighted according to bioavailable methionine content, one unit of MetAMINO® typically emits only 65% of the CO_2 of the industry average.

Global Warming Potential (GWP) of MetAMINO® versus global industry average



Thanks to Evonik's cutting-edge technology, energy-efficient processes and raw materials, as well as our continuous increase in the use of lower-emission energy sources, we are able to provide a more sustainable supply of DL-Methionine.

Contact your sales representative for more information.

Methodology for MetAMINO® GWP: Product Environmental Footprint Category Rules (PEFCR), excluding biogenic carbon, cradle to gate (Scope 1, 2 and Scope 3 upstream). LCA calculation and reporting follow the ISO 14040/44, ISO 14067 and TfS guidelines.

Methodology for global industry averages: estimated internally by Evonik's market intelligence, technology and lifecycle assessment experts. The global industry average is estimated based on producers covering >90% of total global production volume. Industry methionine sources include DL-methionine, L-methionine and methionine hydroxy analogue (MHA). GWP is estimated accounting for higher bioavailability of methionine in MetAMINO® versus MHA.

Data valid as of February 2026.

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27.

Handprint of low crude protein concepts powered by MetAMINO®

Evonik's nutritional expertise improves environmental outcomes in livestock production

Sciencing the Global Food Challenge

Evonik's Next Generation Solutions enable positive sustainability impacts for our customers

Lifecycle assessment study

- We conducted a comparative lifecycle assessment (LCA) of Evonik's recommended diets to quantify the environmental benefits of Evonik solutions versus market reference diets for broilers, layers and swine in North America, Brazil, Europe, China and Asia South.
- The study was conducted by Evonik nutritionists and LCA specialists, critically reviewed by external experts, and independently certified by TÜV Rheinland against quality standards ISO 14040 and 14044.

Study results

- The study demonstrates that compared to reference diets, Evonik's full-service recommendation on optimal amino acid supplementation of animal feed reduces greenhouse gas (GHG) emissions, land use and eutrophication potential in broiler, layer and swine production.
- The majority of the GHG savings arise from lower use of soy enabled by higher amino acid supplementation. Similarly, the land use savings arise from the lower use of crude protein sources such as soy, corn and wheat. The improvements in eutrophication potential are largely driven by decreased nitrogen in animal excretions resulting from lower crude protein diets.
- Overall the study demonstrates that amino acid-balanced, low crude protein diets enable positive sustainability impacts without compromising animal performance.

Potential of low protein diets

TÜVRheinland CERTIFIED
Comparative Life Cycle Assessment
www.tuv.com
ID 0000027153

	GHG emissions reduction	Land use impact reduction	Eutrophication potential reduction
Broilers	up to -11%	up to -10%	up to -18%
Layers	up to -28%	up to -14%	up to -17%
Pigs	up to -12%	up to -7%	up to -30%

Data displayed represent maximum reduction potentials identified.

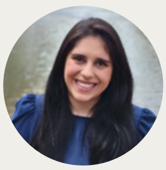
The assessments for each species consider regional variations with respect to available feed raw materials and protein levels in feed.

Making sustainability tangible – inoSust®

- inoSust® is Evonik's service offer that helps clients to calculate and improve the environmental footprint of feed and animal protein production.
- The results, achieved through semi-automated lifecycle analysis, can be third-party certified and used to communicate credible and reliable performance improvements to stakeholders.

Contact

Find out how Evonik can help you calculate, optimize and communicate nutritional and sustainability outcomes in animal production.



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EVONIK Leading Beyond Chemistry

SEE SECTION 2, VIDEO NO. 5

SEE SECTION 2, VIDEO NO. 14


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