Meet swine sulfur amino acids requirements correctly using a modern, a more sustainable and a healthier source : L-methionine

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Introduction

Methionine (Met) is an essential amino acid in pigs. It is considered as a second or third limiting amino acid in swine diets. Thus, supplementing Met to the feed in order to balance sulfur amino acids (SAA) has a long history in swine nutrition. Methionine deficiency not only has negative impacts on pig performance but it also drastically reduces redox potential in tissues (Bauchart-Thevret et al. 2009). Methionine deficiency reduces protein and DNA synthesis in most of the important organs (gut, liver, spleen and stomach) (Bauchart-Thevret et al. 2009). Ingested Met starts to be metabolized in the intestine: gut utilizes 20% of ingested Met (called first pass metabolism), 49% of ingested Met will be used for methylation (transmethylation) and 32% of the ingested Met will be transformed to cysteine (transsulfuration) in the whole body (Riedijk et al. 2007).

Bioavailability of methionine sources

Methionine can be provided via raw feed ingredients or by adding supplemental Met to the feed. The first Met sources which became commercially available were DL-Met and its liquid hydroxy analogue (DL-HMTBA) which is available in two forms: liquid fatty acid (MHA-FA) or powder calcium salt (MHA-Ca). These Met sources are produced from nonrenewable resources through chemical synthesis. Because the L-Met is the natural form of Met (the only form which the animal can utilize it directly), the D-Met and DL-HMTBA must be transformed to L-Met by the animal itself which requires energy, enzyme activities, amino acids (for amination of Keto-methionine) and cellular capacities (Fig. 1).

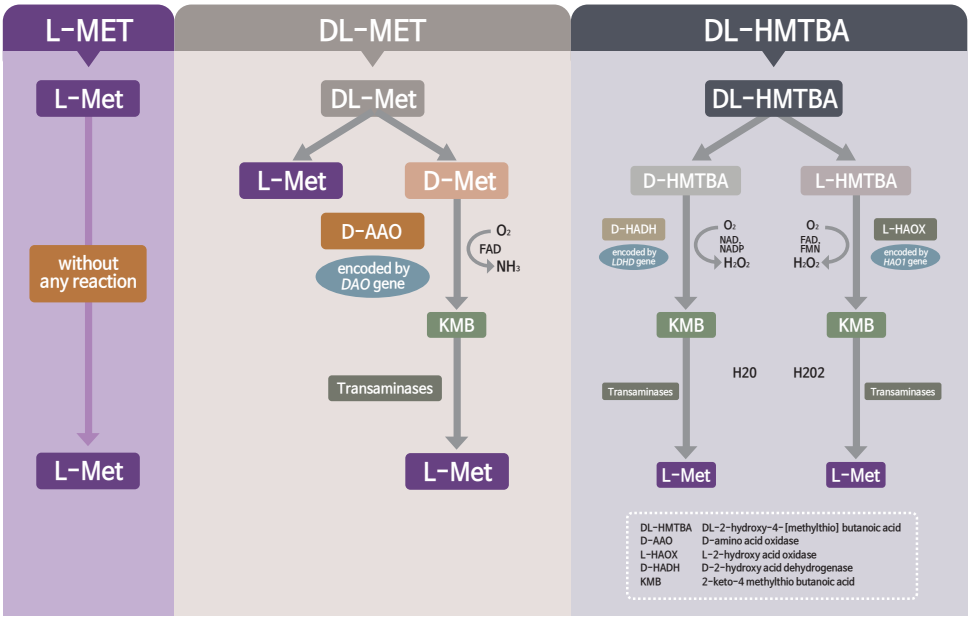

Figure 1. Metabolism of different dietary methionine (Met) sources. Met isomer D-Met and Met precursor DL-2-hydroxy-4-(methylthio) butanoic acid (DL-HMTBA) must be converted to L-Met for utilization. Different enzymes and cofactors play roles in this process (adapted from Zhang et al. 2018).

Since 2015, L-Met has been commercially available (in high volumes) which is produced from renewable resources. Crystalline L-Met provides the opportunity of relieving farm animals from the extra unnecessary energy expenditure to convert the D isomer and the precursors to L-Met. End-users are always confronted with the question of relative bioavailability (RBA) of Met sources because of commercial and nutritional interests. There is a huge controversy in literature about RBA of Met sources. One needs to examine the whole picture to be able to decide about the correct effectiveness of Met sources. Professor Baker is the major cited scientist when it comes to RBA of Met sources (Katz and Baker, 1975).
"L-Met is a better source of sulfur amino acids than D-methionine" Baker wrote (Baker, 1994). Nevertheless, in a more recent publication, Baker thinks that the RBA is a matter of species (Baker 2006). For example, RBA of D-Met is 90% in chicks, but 100% in pigs although RBA of DL-HMTBA is 80% in both species (Table 1).

Table 1. Relative utilization of methionine isomers and the OH analogue [1](Baker, 2006)

Amino acid	Rat	Mouse	Pig	Chick	Dog	Human
L-Met	*100*	*100*	*100*	*100*	*100*	*100*
D-Met	90	75	100	90	100[2]	30[3]
DL-Met	95	88	100	95	100	65
DL-HMTBA	70	70	80	80	NA	NA

DL-HMTBA, hydroxy analogue of methionine: NA, data unclear or not available.

(1) Values are expressed as percentages of the growth efficacy (molar or isosulphurous basis) of the L-isomer, which in all cases is presumed to represent 100% oral utilization.

(2) Efficacy of D-Met is also almost 100% in growing kittens.

(3) Efficacy is also about 30% in non-human primates.

Running RBA trials has evolved through years and nowadays looks quite different. For example, the basis for pig RBA values in table 1 is an experiment where two doses (0.025% and 0.050%) of either L-Met or DL-Met is compared with one single dose (0.057%) of DL-HTMBA (Chun and Baker, 1992). No surprise that no differences between Met sources were detected. It is now known that at least a basal diet (containing no supplementary Met source) which is deficient in Met plus Cys and 4 graded levels of each source of Met are needed to conduct a proper estimation of bioavailability. Controversy in results are also happening in more recent data. Even a lower RBA value is claimed for L-Met compared with D-Met irrespective of how questionable such data are, claiming a D isomer being better than the natural L form. Herein, the published data in pigs are summarized (Table 2) and on average RBA of L-Met is 113%, 115%, and 121% compared with DL-Met in pigs for nitrogen utilization, gain to feed, and average daily gain, respectively.

Table 2. Summary of publications about bioavailability of L-Met compared with DL-Met

Paper	Average daily gain	Gain to Feed	Nitrogen utilization
Baker 1992	100	100	
Htoo 2016	99.6		
Htoo 2015	89		
Kong 2015			114 and 111
Kong 2016			114 and 112
Lim 2015 (1)	368.4 and 111.1		
Lim 2015 (2)	61.8 and 63	73.2 and 75.3	
Lim 2015 (3)	95.9 and 100.4	104.6 and 147.3	
Lim 2015 (4)	88.9 and 92.9	135.3 and 139.6	
Shen 2015	144 and 159	123 and 139	
Average	121	115	113

Remus et al. (2015) meta-analysis with data from 4406 weaning pigs and found that performance is always at a higher level with L-Met compared to the other Met sources (Fig. 2).

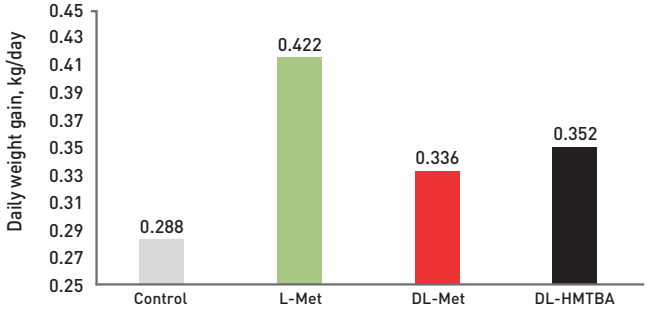

Figure 2. L-Met outperformed DL-Met and DL-HMTBA (adapted from Remus et al. 2015)

Cho (1980) measured the appearance of D-Met in urine and found out that 63% of Met excreted in urine is in the D form. Thus, the ingested D-Met which is absorbed in the intestine but not transformed into L-Met is not utilized and consequently excreted in the urine. Rasch et al. (2019) demonstrated that L-Met is better (56%) converted to L-cysteine (transsulfuration) as compared with DL-Met and DL-HMTBA (44% and 46%, respectively) and DL-HMTBA is resembling a Met deficient condition. Moreover, the highest rate of transmethylation (62%) was in L-Met fed piglets as compared with DL-Met and DL-HMTBA fed piglets (59% and 42%, respectively). L-Met enrichment in liver tissue was also higher than DL-Met and DL-HMTBA. L-Met fed piglets had the highest body weight (Rasch et al. 2016). Overall, this shows that L-Met is more efficiently used in different sulfur amino acid demanding physiological processes.

Gut morphology and oxidative status:

Additional to improved performance results with L-Met, the gut morphology and oxidative status of pigs fed with L-Met are also improved when compared with DL-Met (Shen et al. 2014). Conversion of D-Met to L-Met is possible because D-Amino acid oxidase (DAAO) which exist in the peroxisomes (a cell organelle responsible for fat oxidation) to oxidize D-amino acids. DAAO has a high affinity for D-proline followed by hydrophobic amino acids and neutral amino acids. DAAO oxidation of D-Met is a hydrogen peroxide (H_2O_2) producing enzymatic reaction (Appendino et al. 2010; Equation 1). H_2O_2 as an oxidant or reactive oxygen species (ROS) can damage the peroxisomes. H_2O_2 can also damage the other organelles within cells because H_2O_2 is the only oxidant which can flow out of the cells and move through the body fluids into other tissues and organs.

Equations 1:

Moreover, the entire conversion of the ingested D-Met must occur within the peroxisomes. Peroxisomes are well prepared to fight back against oxidants (H_2O_2 or free radicals) because fat oxidation which is the major function of peroxisomes creates ROS compounds. There are different enzymatic and nonenzymatic pathways to neutralize ROS within the peroxisomes. However, it is not known if peroxisomes are able to tolerate extra load of ROS which is produced via D-Met conversion into L-Met. With L-Met as a supplemental source of Met, one may avoid the extra ROS load in this small organelle.

Conclusion

DL-HMTBA and DL-Met could be easily replaced with lower amount of L-Met without compromising performance of the animal. L-Met also provides a better redox condition for the pigs. Thus, customers can save money by using L-Met as their supplemental source of methionine and can support their pigs with a healthier and a more sustainable solution.

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