The cost of the conversion of L-methionine precursors in mammals and birds

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Abstract
To fulfil the requirements for methionine, animal diets are widely supplemented with synthetic methionine sources such as L-Methionine (L-Met), DL-Methionine (DL-Met), and DL-2-hydroxy-4-(methylthio)-butanoic acid (DL-OH-Met). The objective of this study is to calculate the energy cost of the different conversion steps leading to L-Met and to propose energy equivalence values for DL-Met and DL-OH-Met, relative to that of L-Met. The conversion of DL-OH-Met to L-Met involves a nitrogen-sparing effect, because excess nitrogen can be used for the transformation of DL-OH-Met to L-Met, rather than being excreted as urea or uric acid Consequently, the ME-to-GE ratio of DL-OH-Met is 109% in mammals and 114% in birds, compared to the value of DL-Met. Because of differences in metabolism and the formation of hydrogen peroxide in the conversion to L-Met, the NE-to-ME ratios are 96% for DL-Met and 100% for DL-OH-Met in both mammals and birds. The conversion of DL-OH-Met to L-Met is therefore energetically less costly than the conversion of DL-Met. The stoichiometric approach presented here only considers the biochemical conversion steps, without considering the cost of transport and further transformation steps.

Keywords: metabolisable energy, net energy, stoichiometry

Introduction

Animals can only use L-amino acids for protein synthesis. D-amino acids can be fed to animals, but they have to be converted to the L-enantiomer through an oxidative deamination, followed by a transamination. The efficiency with which this conversion occurs varies widely among amino acids and among species. Today, L-Met, DL-Met, and DL-OH-Met are widely used in animal nutrition. The energy cost of the conversion of D-Met and DL-OH-Met to L-Met has been questioned and raises debate on the relative efficiency of methionine sources. Although conflicting results abound in the literature (Agostini *et al*., 2016; Sauer *et al*., 2008), surprisingly little attention has been paid on the biochemical aspects of the conversion. The objective of this study is to quantify the contribution of biochemistry to the cost of the conversion of DL-Met and DL-OH-Met to L-Met.

Materials and methods

Dibner and Knight (1984) described the conversion of D-Met and of D- and L-OH-Met to L-Met. The conversion occurs in two steps and involves the conversion of the three precursors to 2-keto-4-methylthio-butanoic acid (KMB), followed by the transamination of KMB to L-Met. The conversion of D-Met to KMB is catalysed by an oxidase and yields hydrogen peroxide (H_2O_2) and ammonia (NH_3). The H_2O_2 needs to be reduced, for example by reducing glutathione (i.e., GSH to GSSG); the reduction of GSSG back to GSH requires 1 NADPH. The released NH_3 is converted to an amino acid, which requires 1 ATP. The conversion of L-OH-Met to KMB is similar to that of D-Met without the formation of NH_3, while the conversion of D-OH-Met to KMB is catalysed by a dehydrogenase yielding NADH.

Based on the stoichiometry of these reactions and using the framework developed by van Milgen (2002), the theoretical energy costs of the conversion of D-Met, D-OH-Met, and L-OH-Met to L-Met are calculated.

Results and discussion

The conversion of D-Met to L-Met is an oxidative deamination followed by a transamination so that no nitrogen is gained or lost in the process. The ME-to-GE ratio of D-Met is therefore equal to that of L-Met. In contrast to D-Met, DL-OH-Met does not have an amino group and the latter has to be provided by other amino acids. Since this amino group originates from amino acids available in excess, it will induce a nitrogen and energy sparing effect, because less urea or uric acid will be excreted. Urea has 2 N-atoms and an energy value of 635 kJ/mol, whereas uric acid has 4 N-atoms and an energy value of 1926 kJ/mol. The energy value of DL-OH-Met is 3,366 kJ/mol so that its ME-to-GE ratio, compared to that of L-Met, is (3,366 + 635 x 0.5)/3,366 = 109% in mammals and (3,366 + 1,926 x 0.25)/3,366 = 114% in birds. The stoichiometry of the different reactions can also be used to calculate theoretical net energy values for the different Met sources. 1 glucose (2,820 kJ/mol) yields 31 ATP, so that 91 kJ of glucose is required to synthesize 1 ATP. For D-Met, 1 ATP is required in the oxidative deamination (for the synthesis of an amino acid from NH_3) and 2.5 ATP for the reduction of H_2O_2 (through NADPH). Given that the GE value of L-Met is 3,522 kJ/mol, the NE-to-ME ratio of D-Met is thus (3,522 - 3.5 x 91)/3,522 = 91%, relative to that of L-Met. Consequently, the NE-to-ME ratio of DL-Met is 95.5%. Similarly, the NE-to-ME ratio for L-OH-Met is then (3,366 + 635 x 0.5 - 2.5 x 91)/(3,366 + 635 x 0.5) = 93.8% in mammals and 94.1% in birds. For D-OH-Met, the NE-to-ME ratios are 106.2% and 105.9% in mammals and birds, respectively, so that the NE-to-ME ratio for DL-OH-Met equals 100%. Not all biochemical aspects of the metabolism of Met sources have been included in the calculations given above. For example, to calculate the ME-to-GE ratios, only the energy values of urea and uric acid are considered, but not the cost of urea and uric acid synthesis (i.e., the energy value of a product is less than the energy values of its constituents). Also, the energy cost of transport (i.e., active vs passive transport) has not been considered. The stoichiometric analysis does not allow making statements about the dietary efficiency of DL-OH-Met and DL-Met relative to L-Met. The metabolism of DL-OH-Met and D-Met passes through KMB and the main pathway to metabolize KMB is by the (reversible) transamination to L-Met. Although KMB (and thus all sources of Met) can also be catabolised by a dehydrogenase, its role is minor in physiological conditions (Wu, 2013). In conclusion, the metabolic conversion of DL-OH-Met to L-Met is energetically equal compared to that of L-Met, whereas this conversion is more costly for DL-Met. However, the dietary inclusion rates of the precursors of L-Met are low (i.e., 0.1 to 0.4%) and the contribution of amino acids to the energy values of feeds is small.

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