Utilization of methionine isomers and analogs by the pig


Key words: Pigs, methionine isomers and analogs, growth performance


Mots clés: Porcelets, isomères et analogues de la méthionine, performance de croissance

There is a consensus of opinion that the levels of sulfur amino acids (SAA) contained in practical corn-soybean meal diets are not limiting for growth of swine. However, use of feed ingredients other than corn and soybean meal could potentiate methionine deficiency in swine diets. Commercial (chemical) synthesis results in the racemic DL mixture of either methionine (Met) or methionine hydroxy analog (HMB) (L-Met, D-Met and DL-Met were provided by Degussa Corporation, Allendale, NJ; DL-HMB was provided by Monsanto Corporation, St. Louis, MO). An amino acid oxidation study conducted by Kim and Bayley (1983) indicated that D-Met was only 50% efficacious relative to L-Met in reducing phenylalanine catabolism in young pigs fed liquefied skim milk diets. Young miniature pigs utilized D-Met with 100% efficiency when DL-Met was administered as part of a parenteral solution (Cho et al. 1980). Pig hepatocytes isolated from 24-h-old piglets were shown to incorporate more L-Met than DL-HMB into protein (Reifsnyder et al. 1983).

DL-HMB was parallel to L-Met as indicated by growth performance of 3-wk-old pigs receiving low protein liquid diets (Reifsnyder et al. 1984). Discrepancies in the estimates of Met isomer and analog utilization are attributed primarily to use of different types of diets and different response criteria.

A Met-deficient feather meal-corn-soybean meal-dried whey (FM-C-SBM-DW) basal diet was recently developed in our laboratory. A preliminary study indicated that pigs fed the Met-deficient basal diet when fortified adequately with Met could produce excellent weight gains similar to those of pigs fed a 20% crude protein practical corn-soybean meal-dried whey diet (Chung and Baker 1991). Growth rate was reduced dramatically without Met fortification, however, indicating that a broad Met response range was possible. This diet was, therefore, used in our study to evaluate the oral efficacy of D-Met, DL-Met and DL-HMB relative to L-Met set at 100%.

The Met-deficient FM-C-SBM-DW basal diet was formulated to meet or exceed all National Academy of Sciences — National Research Council (NAS-NRC) (1988) nutrient requirements of 10- to 20-kg pigs.
with the exception of Met. The composition of the Met-deficient basal diet was: 26.77% cornstarch, 15.51% feather meal, 15.21% corn, 15.00% dried whey, 10.21% soybean meal, 5.00% sucrose, 0.77% L-lysine·HCl, 0.23% L-histidine·HCl·H₂O, 0.10% L-tryptophan, 2.00% corn oil, 2.22% dicalcium phosphate, 0.87% limestone, 0.35% trace-mineral mixture (provided per kilogram of diet: 0.1 mg selenium; 0.35 mg iodine; 8 mg copper; 20 mg manganese; 90 mg iron; 100 mg zinc; 0.75 mg cobalt; 2.73 g sodium chloride), 0.25% vitamin mixture (provided per kilogram of diet: 8250 IU vitamin A; 825 IU vitamin D₃; 55 IU vitamin E; 5 mg vitamin K; 2.75 mg riboflavin; 16.38 mg d-pantothenic acid; 41.25 mg niacin; 412.5 mg choline chloride; 43.88 μg vitamin B₁₂), 0.50% antibiotic mixture (provided per kilogram of diet: 110 mg chlortetracycline; 110 mg sulfamethazine; 55 mg procaine penicillin) and 0.10% CuSO₄·5H₂O. The diet contained 20% crude protein (determined by macro-Kjeldahl), 13.65 MJ ME kg⁻¹ (NAS-NRC 1988), 0.19% Met and 1.00% cystine (determined by ion-exchange chromatographic analysis of individual feed ingredients following 6N HCl hydrolysis of performic acid (30% hydrogen peroxide: 88% formic acid, 1:9, volume/volume) preoxidized samples. Based on a true Met ideal digestibility estimate of 81.6 ± 2.6%, the basal diet contained 0.155% digestible Met (Chung and Baker 1991). The level of digestible Met required for maximal weight gain of 10-kg pigs fed this diet was determined to be 0.255% of the diet (0.290% total Met) in the presence of excess dietary cystine (Chung and Baker 1991)

A total of 72 crossbred (Duroc × Hampshire × Landrace) weanling pigs with an average initial weight of 9.6 ± 1.4 kg were used. Pigs were assigned randomly to treatments from uniform blocks based upon ancestry and weight. Groups of three pigs (four pens per diet) were housed in 1.22 m² nursery pens with solid partitions and expanded metal floors over an oxidation ditch in a constantly lighted, environmentally controlled nursery. They were fed the basal diet supplemented with 0, 0.025 or 0.05% L-Met, 0.05% D-Met, 0.05% DL-Met or 0.05% DL-HMB for 21 d. The levels of L-Met additions were previously determined to reside on the linear response surface of the growth curve. Pigs averaging 7.5 ± 0.9 kg were pretested on a 20% crude protein corn-soybean meal-dried whey diet to approximately 10 kg for 13 d before experiment initiation. Both feed and water were provided ad libitum. Prior to initiating and terminating the experiment, pigs were fasted overnight and weighed the following morning. Weight gain and feed intake were monitored weekly.

Experimental data were subjected to analysis of variance procedures appropriate for randomized complete-block designs. Single degree-of-freedom comparisons were used to test significance of treatment effects.

Supplementing the Met-deficient diet with 0, 0.025 and 0.05% L-Met resulted in linear (P < 0.05) responses in daily gain, daily feed intake and gain:feed ratio (Table 1). Performance of pigs fed D-Met, DL-Met and DL-HMB did not differ (P > 0.05) from that of pigs fed L-Met at an isomolar level.

D-amino acid oxidase is required for the conversion of a D-amino acid to its α-keto acid, which is then transaminated by aminotransferase to form the corresponding L-isomer. D-methionine is well utilized by chicks (Baker and Boebel 1980). Six-week-old miniature pigs given DL-Met as part of a parenteral solution excreted less than 1% of the infused D-Met in the urine; D-Met was estimated to be 99% as efficacious as L-Met (Cho et al. 1980). Kim and Bayley (1983) suggested that D-Met was only 50% efficacious relative to L-Met in reducing [1-¹⁴C] phenylalanine oxidation in pigs (10–14 d old) fed liquefied skim milk diets. Baker (1986) indicated that poor utilization of D-amino acids is due to one (or more) of several factors: poor absorption from the gut, low D-amino acid oxidase activity and inefficient transamination. Our study showed that D- or DL-Met was utilized with 100% molar efficiency relative to L-Met as indicated by growth performance (Table 1).
D-2-hydroxy acid dehydrogenase (D-HADH) and L-2-hydroxy acid oxidase (L-HAOX) are required for the conversion of D- and L-HMB to L-Met, respectively (Dibner and Knight 1984). Variable efficacy values of HMB have been reported in chick growth studies as reviewed by Van Weerden et al. (1982). Isolated porcine hepatocytes from 24-h-old neonatal pigs were reported to incorporate five times more L-Met than DL-HMB into protein (Reifsnyder et al. 1983). Reifsnyder et al. (1984) nonetheless reported that utilization of DL-HMB was similar to L-Met in 3-wk-old pigs fed low-protein liquid diets. In the latter study, however, daily gain and feed efficiency were neither increased nor decreased by the addition of DL-HMB or L-Met to the 9% protein liquid basal diet, suggesting that an amino acid other than Met may be more growth limiting in the basal diet. Our study indicated that DL-HMB and L-Met were utilized equally on an isomolar basis (Table 1).

Several factors that may have contributed to the disparate efficacy values of Met isomers and analogs: (1) use of diets differing in protein and metabolizable energy levels, (2) use of different response criteria, (3) age of experimental animals and (4) different routes of delivering test compounds. A standardized methodology for evaluating the utilization of Met isomers and analogs (with specified age and weight ranges in pigs) is therefore warranted. The absorption mechanism of D-Met, DL-Met and DL-HMB is yet to be studied in the pig. In addition, the developmental pattern of D-HADH, L-HAOX, D-amino acid oxidase and aminotransferase has not been examined in the pig. The variable utilization of Met isomers and analogs reported in pigs may be a function of age differences or of different methodologies for assessing quantitative efficacy. Nevertheless, our pig growth study clearly showed that L-Met, D-Met, DL-Met and DL-HMB were utilized with the same molar efficiency.

Dibner, J. J. and Knight, C. D. 1984. Conversion of 2-hydroxy-4-(methylthio) butanoic acid to

<table>
<thead>
<tr>
<th>Diet</th>
<th>Daily gain</th>
<th>Daily feed intake</th>
<th>Gain: feed intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. FM-C-SBM-DW basal</td>
<td>268a</td>
<td>605a</td>
<td>439a</td>
</tr>
<tr>
<td>2. As l + 0.025% L-Met</td>
<td>384b</td>
<td>823b</td>
<td>463b</td>
</tr>
<tr>
<td>3. As l + 0.050% L-Met</td>
<td>498c</td>
<td>999c</td>
<td>499c</td>
</tr>
<tr>
<td>4. As l + 0.080% D-Met</td>
<td>498c</td>
<td>969c</td>
<td>513c</td>
</tr>
<tr>
<td>5. As l + 0.050% DL-Met</td>
<td>516c</td>
<td>1019c</td>
<td>507c</td>
</tr>
<tr>
<td>6. As l + 0.057% DL-HMB†</td>
<td>485c</td>
<td>964c</td>
<td>505c</td>
</tr>
<tr>
<td>Pooled SEM</td>
<td>26</td>
<td>53</td>
<td>11</td>
</tr>
</tbody>
</table>

†Data represent means of four pens of three pigs during a 21-d feeding period; average initial weight was 9.6 kg.
3The basal diet contained 0.19% Met and 1.00% cystine.
4Linear (P<0.01) regression (treatments 1–3) of daily gain (g) on daily supplemental Met intake (mg) was Y = 261.3 + 0.519 X (r = 0.87).
50.057% DL-HMB equimolar to 0.050% L-Met.
6Means within a column without common letters differ (P<0.05).


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