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Influence of Optical Activity on Utilization of Lysine for Growth.

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Recent studies on the relative value for growth of the optical isomers of 2 essential amino acids have yielded divergent results. Thus, *dl*-tryptophane promotes growth as readily as the natural *l* form¹ and the *d* form is likewise as efficient as the *l* form^{2, 3}. On the other hand, *i*-cystine is less effective than *l*-cystine⁴ and neither *d*-cystine⁵ nor one half of the meso form⁶ is available for growth. Several years ago McGinty, Lewis and Marvel⁷, in studying the replaceability of lysine by related hydroxy compounds, fed control rats both natural (*d*) lysine and synthetic (*dl*) lysine. In the one experiment in which equal amounts of the 2 compounds were employed, the natural amino acid promoted somewhat better growth. As an initial step in evaluating the growth-promoting ability of *l*- and *d*-lysine, we undertook a more exact comparison of the *d* isomer and the *dl* mixture.

d-Lysine was prepared as the dihydrochloride by the method of Cox, King, and Berg⁸ and racemized essentially as directed by Fisher and Weigert⁹. The *dl*-lysine was isolated as the dihydrochloride. $[\alpha]_D^{20}$ for the former dihydrochloride (3% solution in water) was +15.64, for the latter 0.0. Analyses for N and Cl agreed with the calculated values. Zein served as the lysine-deficient protein and was prepared essentially according to the method of Brazier¹⁰. The diet was composed of zein, 14.6; tryptophane, 0.2; cystine, 0.2; starch, 39.5; sucrose, 15.0; Crisco, 19.0; cod liver oil,

¹ Berg, C. P., and Potgieter, M., *J. Biol. Chem.*, 1931-32, **94**, 661.

² du Vigneaud, V., Sealock, R. R., and Van Etten, C., *J. Biol. Chem.*, 1932, **98**, 565.

³ Berg, C. P., *J. Biol. Chem.*, 1934, **104**, 373.

⁴ Lawrie, N. R., *Biochem. J.*, 1932, **26**, 435.

⁵ du Vigneaud, V., Dorfmann, R., and Loring, H. S., *J. Biol. Chem.*, 1932, **98**, 577.

⁶ Loring, H. S., Dorfmann, R., and du Vigneaud, V., *J. Biol. Chem.*, 1933, **103**, 399.

⁷ McGinty, D. A., Lewis, H. B., and Marvel, C. S., *J. Biol. Chem.*, 1924-25, **62**, 75.

⁸ Cox, G. J., King, H., and Berg, C. P., *J. Biol. Chem.*, 1929, **81**, 755.

⁹ Fisher, E., and Weigert, F., *Ber. chem. Ges.*, 1902, **35**, 3772.

¹⁰ Brazier, M. A. B., *Biochem. J.*, 1930, **24**, 1188.

5.0; salt mixture¹¹, 4.5; and agar, 2.0%. In each case the lysine supplement replaced an amount of zein. In addition, 200 mg. of yeast was supplied separately to each animal daily. Twelve rats were divided into 4 groups of 3 each. One group received no lysine supplement; the second, 0.125%; the third, 0.25%; and the fourth 0.5%, in the form of an equivalent amount of the dihydrochloride. During the first and third 20 days 2 animals of the second and fourth groups and one of the third received the *dl* modification. The others were fed *d*-lysine. On the second and fourth 20 day periods those animals which had received the *d*-lysine were fed *dl*-lysine, and *vice versa*.

The accompanying table summarizes the findings which indicate that only the dextro component of *dl*-lysine can be used by the rat for purposes of growth. Further studies are in progress.

TABLE I.
Comparative Average Growth of Animals on a Lysine-Deficient Basal Diet Supplemented with *d*- and *dl*-Lysine.*

| Rat No., Sex | Aver. daily gain on <i>d</i> -Lysine gm. | Aver. daily gain on <i>dl</i> -Lysine gm. | Lysine Supplement % |
|---------------|--|---|---------------------|
| 137 ♀ | 1.20 | .60 | .5 |
| 138 ♂ | 1.03 | .78 | .5 |
| 144 ♂ | .90 | .48 | .5 |
| Aver. | 1.04 | .62 | |
| 135 ♀ | .63 | .23 | .25 |
| 136 ♀ | .70 | .38 | .25 |
| 143 ♂ | .68 | .20 | .25 |
| Aver. | .67 | .27 | |
| 133 ♀ | .53 | .20 | .125 |
| 140 ♀ | .55 | .35 | .125 |
| 134 ♂ | .45 | .33 | .125 |
| Aver. | .51 | .29 | |
| Grand average | .74 | .39 | |

¹¹ Hawk, P. B., and Oser, B. L., *Science*, 1931, **74**, 369.

* The average daily growth of the 3 rats on the unsupplemented basal diet was 0.17 gm.