# Effects of the Administration of Single Amino Acids on Ribosome Aggregation in Rat Liver[1] (37167)

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The administration of tryptophan to mice and rats has been reported to promote liver polysome aggregation, whereas administration of methionine, isoleucine or threonine did not (1, 2). On the basis of these reports, others have studied the effects of tryptophan on various aspects of liver protein synthesis, assuming the effects of this amino acid to be unique, without testing other amino acids in a similar way (3, 4). The results reported here demonstrate that administration of some single amino acids other than tryptophan promote aggregation of liver ribosomes, hence, tryptophan is not unique in this respect.

*Methods.* Weanling female rats were fed a laboratory chow diet *ad libitum* and kept under controlled humidity and lighting (lights, 4:30 AM to 4:30 PM). After 4–5 days, when the rats weighed about 85 g, they were fasted for 48 hr and then given 0.125 mmoles L-tryptophan/100 g body weight by stomach tube. A 0.9% saline solution was administered to another group of rats which served as a control. After 1 hr the rats were decapitated and the liver ribosome sedimentation patterns were obtained from the post-mitochondrial supernatant fraction after treatment with antiferritin serum, as described previously (5).

*Results and Discussion.* The administration of 0.125 mmoles of L-tryptophan/100 g body weight did not significantly change the proportion of the ribosomes found as monomers and dimers (Table I, line 1). However, administration of 0.25 mmoles of L-tryptophan/100 g body weight significantly decreased the proportion of ribosomes in the monomers and dimer fractions (Table I, line 2 and Fig. 1). When 0.25 mmoles of L-methionine/100 g body weight was administered by stomach tube, no effect on ribosome aggregation was detected (Table I, line 3). This observation was in agreement with that of Sidransky *et al* (1). However, since it was known that the methionine requirement for polysome maintenance in the perfused rat liver was higher than that for tryptophan (6) 0.50 mmoles of L-methionine/100 g body weight was given by stomach tube and 1 hr later sucrose gradient analysis of ribosome aggregation showed a decrease in the monomer and dimer fraction similar to that seen after

TABLE I. The Effect of Force-Feeding Single Amino Acids on the Aggregation of Fasted Rat Liver Ribosomes.[a]

| L-Amino acid | Dose (mmoles/100 g) | Monomers + dimers (%) Experimental | Control |
|---|---|---|---|
| Tryptophan | 0.125 | 35 (3) [33–39] | 38 (3) [34–41] |
| Tryptophan | 0.25 | 31 ± 6[b] (9) | 43 ± 9 (9) |
| Methionine | 0.25 | 34 (3) [31–39] | 40 (3) [33–45] |
| Methionine | 0.50 | 32 ± 4[b] (18) | 44 ± 4 (18) |
| Phenylalanine | 0.50 | 36 ± 2[b] (12) | 43 ± 2 (12) |
| Threonine | 1.0 | 39 ± 6 (16) | 41 ± 4 (16) |
| Alanine | 0.50 | 39 ± 4 (7) | 39 ± 3 (7) |

[a] The values given represent the mean ± the standard deviation with the number of rats in each group indicated in parentheses. In two cases the range of experimental values is indicated in brackets. The experimental rats were given the amino acid dose indicated in 2–3 ml, adjusted to pH 7.4, whereas, the control rats were given an equal volume of 0.9% NaCl.

[b] Different from control value with $p < .001$ by Student's $t$ test.

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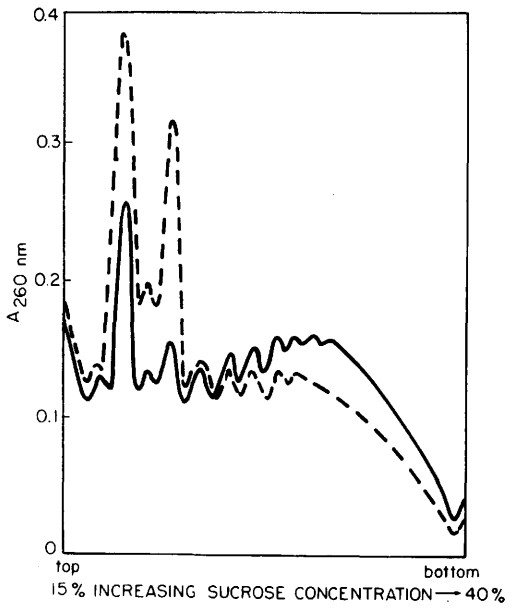


FIG. 1. Effect of force-feeding of L-methionine on the sedimentation of rat liver ribosomes in sucrose gradients. A 2-day fasted, female rat was given 0.50 mmoles L-methionine/100 g body weight (——) or saline (- - - -) by stomach tube. One hour later, the rats were decapitated and the liver was removed. The postmitochondrial supernatant was prepared and ribosome aggregation was determined in sucrose gradients as described previously (5).

administration of L-tryptophan (Table I, line 4). Administration of 0.50 mmoles of L-phenylalanine/100 g body weight also significantly decreased the proportion of ribosomes in the monomer and dimer fractions (Table I, line 5); however, the decrease was not as great as that resulting from administration of tryptophan or methionine. Administration of L-threonine and L-alanine in the amounts tested was without effect on ribosome aggregation (Table I, lines 6 and 7). However, rats receiving 1 mmole of L-threonine/100 g body weight showed some signs of toxicity.

The effects of amino acids at doses other than those shown in Table I have not been investigated. Likewise, the optimum time for examining ribosome aggregation was not determined. The time chosen was that used by previous investigators (1).

Pronczuk, Rogers and Munro (7) have suggested that the administration to fasting rats of a mixture of amino acids, deficient in tryptophan, does not result in ribosome aggregation because tryptophan is already the most limiting amino acid in the rat liver. To provide evidence for this view, they fed rats imbalanced amino acid diets, so that another amino acid would be more limiting than tryptophan, and then administered amino acid mixtures deficient in the limiting amino acid. Liver ribosomes were not aggregated in these rats, whereas, they were aggregated in rats fed an amino acid diet in which the imbalance was corrected.

The studies presented here provide evidence that administration of single amino acids other than tryptophan to rats can result in liver ribosomes aggregation under certain conditions. Thus, it is probable that any one of several amino acids can be critical to ribosome aggregation, depending upon the relative amounts of all the amino acids present. Therefore, the assumption that tryptophan has an unique role in the control of mammalian protein synthesis (1–3) does not appear to be valid.

*Summary.* The administration of 0.25 mmoles of L-tryptophan or 0.50 mmoles of L-methionine/100 g body weight by stomach tube to fasted, female rats decreased the proportion of liver ribosomes found in the monomer and dimer fractions and increased the proportion in polysomes. The same dosage of L-phenylalanine also induced aggregation, but not as much as did tryptophan or methionine. L-Alanine or L-threonine had no effect on the aggregation of liver ribosomes.

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