Inhibition of *Tetrahymena* by a new tryptophan analog*

Recently ROBISON AND ROBISON[1] reported the synthesis of a new tryptophan analog, 7-aza-tryptophan. We have tested this compound on the animal micro-organism *Tetrahymena pyriformis* W and found it to be inhibitory to growth. The basal medium used was that previously reported[2], except that the portion designated 4A was omitted. All the ingredients of this medium are chemically defined. When tryptophan is omitted, no growth occurs[3]. For the purposes of this investigation various levels of L-tryptophan were included, and experiments on the response to 7-azatryptophan** were carried out.

The addition of 10 γ/ml of L-tryptophan to the basal medium results in just optimal growth of *Tetrahymena*. At this level of tryptophan slightly over 200 γ/ml of 7-azatryptophan produced half maximum inhibition. Within the limits of the concentrations of the inhibitor used, release of inhibition in a competitive manner is accomplished by tryptophan (Fig. 1). The inhibition index is between 35 and 40 (half maximum). As in the case of most inhibitors, the index is somewhat lower when the normal metabolite is suboptimal or just optimal.

The inhibition index referred to above (35–40) may well be halved, if the isomer of 7-azatryptophan corresponding to D-tryptophan is inert, for the analog was used as a racemic mixture.

This compound should be of considerable interest in other systems, particularly those in which tryptophan synthesis is carried out, for it should be possible there to determine more exactly the point of interference. In *Tetrahymena* the analog appears to interfere with tryptophan utilization. It will be of great theoretical importance to determine whether or not this analog is incorporated into the architecture of the organism, as is the case with a number of inhibitors[4–10] including the methionine analog, ethionine[11].

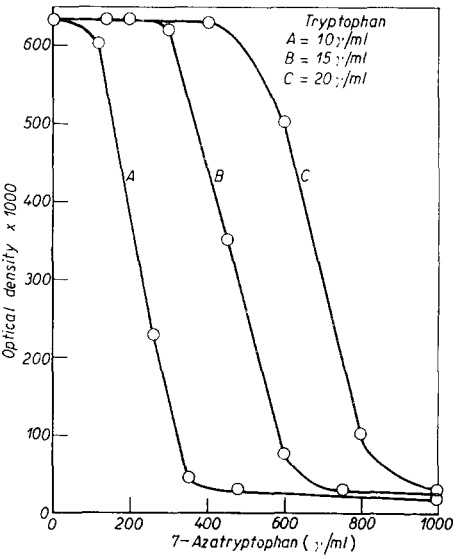

Fig. 1. Dose response of *Tetrahymena pyriformis* W to 7-aza-DL-tryptophan, with varying levels of L-tryptophan.

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[1] M. M. ROBISON AND B. L. ROBISON, *J. Am. Chem. Soc.*, 77 (1955) 457.
[2] V. C. DEWEY, R. E. PARKS, JR., AND G. W. KIDDER, *Arch. Biochem.*, 29 (1950) 281.
[3] G. W. KIDDER AND V. C. DEWEY, *Arch. Biochem.*, 6 (1945) 425;
G. W. KIDDER, V. C. DEWEY, M. B. ANDREWS AND R. R. KIDDER, *J. Nutrition*, 37 (1949) 521.
[4] G. W. KIDDER AND V. C. DEWEY, *J. Biol. Chem.*, 179 (1949) 181.
[5] J. H. MITCHELL, JR., H. E. SKIPPER AND L. L. BENNETT, JR., *Cancer Research*, 10 (1950) 647.
[6] M. R. HEINRICH, V. C. DEWEY, R. E. PARKS, JR., AND G. W. KIDDER, *J. Biol. Chem.*, 197 (1952) 199.
[7] F. WEYGAND, A. WACKER AND H. DELLWEG, *Z. Naturforsch.*, 7b (1952) 19.
[8] R. E. F. MATHEWS, *Nature*, 171 (1953) 1065.
[9] D. B. DUNN AND J. D. SMITH, *Nature*, 174 (1955) 305.
[10] S. ZAMENHOF AND G. GRIBOFF, *Nature*, 174 (1955) 308.
[11] M. LEVINE AND H. TARVER, *J. Biol. Chem.*, 192 (1951) 835.
D. GROSS AND H. TARVER, (in press).

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