DNA synthesis particularly in Ehrlich ascites-tumour cells are less sensitive to inhibition by (–)-emetine than are the corresponding biosynthetic activities in HeLa cells.

We find that much higher concentrations of (–)-emetine are needed to interfere with RNA biosynthesis. The incorporation of [2-¹⁴C]uridine into RNA *in vitro* is inhibited by 50% in the presence of (–)-emetine (0.7 mM) in the incubation medium. However, the inhibition of RNA synthesis brought about by incubation with (–)-emetine (1 mM) could be reversed when cell suspensions were washed free of (–)-emetine and reincubated with labelled uridine in fresh medium.

We find, further, that inhibitory concentrations of (–)-emetine have no effect on the release of radioactivity from Ehrlich ascites-tumour cells with prelabelled DNA, RNA or protein. This implies that the inhibitory effects above are not related to increased breakdown of macromolecules.

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Measurement of Liver Protein-Synthetic Rate

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The rate of protein synthesis in rat liver has been measured by constant intravenous infusion of radioactively labelled amino acids. The results from [¹⁴C]glycine and [¹⁴C]tyrosine infusions are compared.

This technique enables the protein-synthetic rate to be determined from measurement of the specific radioactivity of free and protein-bound amino acid in the tissue at a single point of time. Although the specific radioactivity of the amino acid in the blood and tissues reaches a plateau, except for very long infusions, the early time-course must be known. In practice the early time-course of specific radioactivity of the precursor amino acid is assumed to approximate to a single exponential (Waterlow & Stephen, 1968). The rate constant for this exponential need only be known approximately. It depends very largely on the turnover rate of the intracellular pool of

free amino acid, which in turn depends, not only on the rate of protein synthesis occurring within the tissue, but also, to an important extent, on the ratio of protein bound to free amino acid (*R*). This ratio differs greatly for different amino acids. For glycine *R* lies close to 25, whereas for tyrosine it is near to 400. This means that the nature of the approximation for the exponential rate constant will differ for these two amino acids.

It will be demonstrated how the value of this rate constant may be determined for glycine and tyrosine in rat liver and how this may be used to determine the protein-synthetic rate.

Rats (100 g body wt.) were infused for periods of 6 h into the internal jugular vein with either [¹⁴C]glycine or [¹⁴C]tyrosine, after which time their livers were removed. The protein-bound and free amino acids were separated by homogenizing the tissue in 10% trichloroacetic acid and by centrifugation. The specific radioactivity of glycine was determined by separation of its 2,4-dinitrophenyl derivative by t.l.c. (Garlick, 1969) and tyrosine by enzymic decarboxylation and fluorimetry (Garlick & Marshall, 1972).

Glycine gave a protein synthetic rate of 40 ± 7%/day and tyrosine 45 ± 12%/day; the difference between these two values is insignificant. Variations in synthetic rate between animals occurred, but different lobes from the same liver gave the same value. Infusions of different amino acids with widely differing properties therefore can be used to determine protein-synthetic rate in rat liver, giving very similar results.

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The Inhibition of Amino Acid-Activating Enzymes and Leucine Aminopeptidase by Chloromethyl Ketone Analogues of Amino Acids

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The amino acid-activating enzymes catalyse the following reaction:

They show a high substrate specificity, in that each enzyme will react only with the corresponding amino acid. This makes a study of their active sites of particular interest. We have now synthesized chloromethyl ketone analogues of amino acids that retain the free amino group. Such compounds may exhibit