Aspartic Acid as a Precursor for Ribonucleic Acid Pyrimidines

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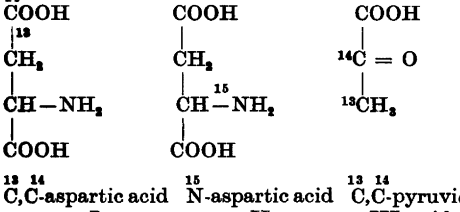
While the precursors of the carbon atoms of the purines seem to be well established [1], very little is known about the possible corresponding precursors of the pyrimidines.

Heinrich et al. [1] and Lagerkvist [2] have shown that carbon atom nr. 2 in uracil is derived from CO_2. As to carbon atoms 4—6 the work of Mitchell *et.al.* [3] and Wright *et.al.* [4] with microorganisms makes it appear possible that these are formed from some intermediate of the citric acid cycle. The present investigation was carried out both in order to test this possibility and in order to investigate the ability of aspartic acid as a whole molecule to act as precursor for pyrimidines. For this purpose slices from regenerating liver where used in the same way as described previously [5]. In three different experiments the tested precursors were added to the medium in 0.01 molar concentration. The precursors used were as follows:



In each experiment slices from 10—30 regenerating livers were incubated for 8 hours. Polynucleotides were prepared from the livers according to Hammarsten's [6] method. From pentose nucleic acid both pyrimidines were prepared as uracil by a combination of ion exchange chromatography [7] and starch chromatography [8]. Details of the method will be described later.

The results of the different experiments indicated that compounds II and III can hardly be direct precursors for pyrimidines, since in these experiments the dilution of the isotope from the precursor to uracil was about 500—1500 fold. Compound I, however, gave corresponding dilution factors of 100—400 for C^{14} and 30—70 for C^{13}. We believe that aspartic acid, after loss of the NH_2-group is relatively directly used for the synthesis of uracil. That this transformation is probably very extensive could be shown in the experiment with II, since at the end of the incubation large amounts of N^{15}-glutamic acid could be isolated from the medium, while practically no aspartic acid was left. *

In order to explain the difference in isotope incorporation from the carboxyl and methylene groups, and in order to get a clearer picture of the paths of their incorporation, we hope to degrade uracil from this experiment and to obtain the isotope content from each of its carbon atoms. A more detailed description of the experiments will be given in connection with publication of the degradations.

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