A KINETIC TREATMENT OF PURINE SYNTHESIS

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The biosynthesis of purines in pigeon liver homogenates has been very cleverly and carefully worked out by Greenberg (1951). However, it is felt that the kinetics of this mechanism are of equal importance, but up to date they have not been investigated. It is the purpose of this communication to explain quantitatively the following reaction sequence:

$$CO_2 + 3NH_3 + \text{glycine} + \text{“formate”} + \text{ribose-1-phosphate}$$

$$\longrightarrow \text{inosine-5-phosphate} \xrightarrow{-H_3PO_4} \text{inosine} \xrightarrow{+H_3PO_4}$$

$$\text{hypoxanthine} + \text{ribose-1-phosphate.}$$

If the reaction is followed by the use of C^{14}-formate, the kinetics of the C^{14} transfer can be represented very simply, that is,

$$A \xrightarrow{k_1} B \quad \begin{matrix} \overset{k_2}{\nearrow} C \\ \underset{k_3}{\searrow} D \end{matrix}$$

where A = formate (C^{14})
B = I M P-5 (inosine-5-phosphate)
C = HX (hypoxanthine)
D = inosine

The differential equations for the C^{14} transfer are:

$$\frac{dA}{dt} = -k_1A \tag{1}$$

$$\frac{dB}{dt} = k_1A - k_4B \qquad (k_4 = k_2 + k_3) \tag{2}$$

$$\frac{dC}{dt} = k_2B \tag{3}$$

and $$\frac{dD}{dt} = k_3B \tag{4}$$

The solutions of the equations can be given as follows:

$$A = A_0e^{-k_1t} \tag{1a}$$

$$B = \frac{A_0k_1}{k_4-k_1}\left[e^{-k_1t} - e^{-k_4t}\right] \tag{2a}$$

$$C = \frac{A_0k_2}{k_4}\left[1 + \left(\frac{1}{k_4-k_1}\right)\left(k_1e^{-k_4t} - k_4e^{-k_1t}\right)\right] \tag{3a}$$

$$D = \frac{A_0k_3}{k_4}\left[1 + \left(\frac{1}{k_4-k_1}\right)\left(k_1e^{-k_4t} - k_4e^{-k_1t}\right)\right] \tag{4a}$$

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In figure 1, the analytical solution is compared with the experimental results. The curves were calculated from the following rate constants:

$$k_1 = 7.102 \times 10^{-2} \text{ min}^{-1}$$
$$k_2 = 1.048 \times 10^{-2} \text{ min}^{-1}$$
$$k_3 = 6.288 \times 10^{-2} \text{ min}^{-1}$$
$$k_4 = 7.336 \times 10^{-2} \text{ min}^{-1}$$
$$A_O = 21.0 \times 10^{+3} \text{ counts per min per fraction per vessel.}$$

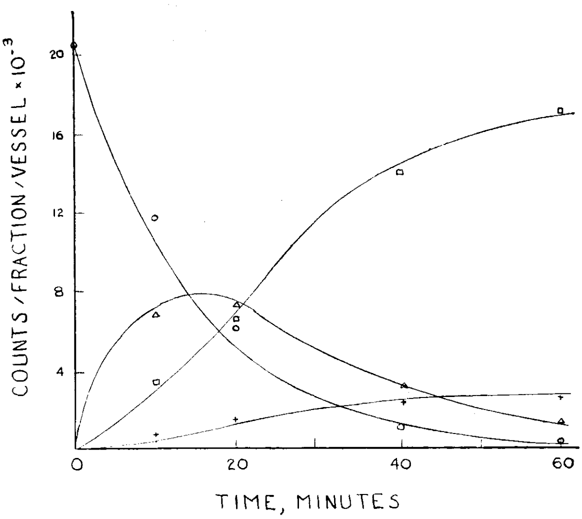

FIGURE 1. Theoretical curves for: o formate; △ IMP–5; □ HX; + inosine.

The agreement appears satisfactory. Further experimental work on this problem will deal with evaluation of the free energy, enthalpy and entropy of activation. Data of this nature for complex reactions are conspicuously missing from the literature.

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