On the quantitative evaluation of routes of glucose metabolism by the use of radioactive glucose

In a recent paper[1] we sought to interpret the ^{14}C content of pyruvate derived from variously labelled [^{14}C]glucose in terms of the relative amounts of glucose catabolized by the Embden-Meyerhof glycolytic sequence and the hexose monophosphate oxidative pathway. For considerations of brevity, we did not detail the methods employed in arriving at those systems of evaluation (cases *a* and *b* in Fig. 1) which were not used in our experiments with *Sarcina lutea*. However, the interest evinced in this approach makes it desirable to clarify cases *a* and *b* in more detail since they do, in effect, set the limits within which this method is applicable.

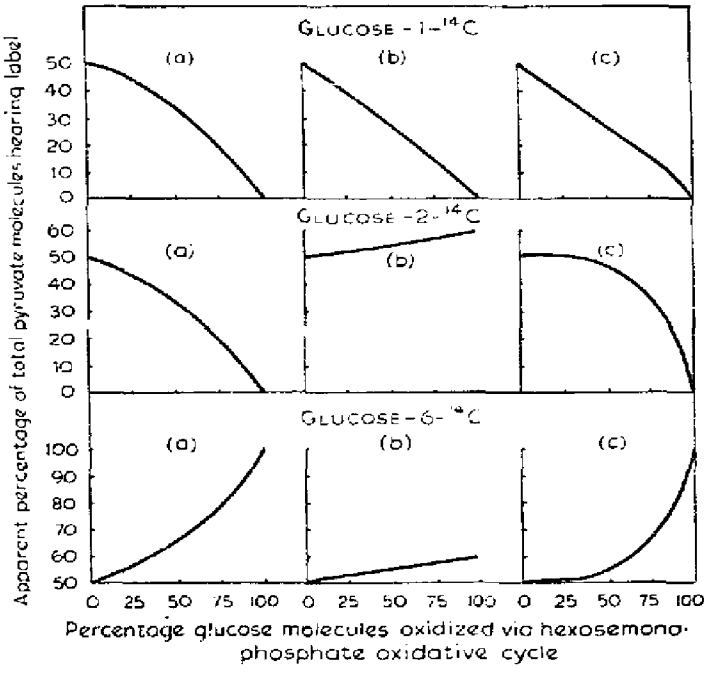

Fig. 1. Relationship between the apparent percentage of pyruvate molecules bearing label and the percentage of glucose molecules oxidized via the hexosemonophosphate oxidative pathway when only this route and the Embden-Meyerhof pathway are operative. The three cases are described in the text.

Cases *a* and *b* are derived in a manner similar to that used by earlier workers in this field at a time when the cyclic operation of the hexose monophosphate oxidative pathway had not been fully established (see, for example, BLUMENTHAL *et al.*[2]) and the principal factor considered was the *initial* attack on the glucose molecule. That is to say, if a C_6 unit is attacked by the oxidative pathway to give a C_5 unit the whole glucose molecule is considered to have been degraded by this pathway. Pyruvate is assumed to arise from C-4, C-5 and C-6 of the original glucose and C-2 and C-3 are assumed either to yield pyruvate (case *b*) or not (case *a*), without specifying the mechanisms involved in these processes. Case *a* has been most commonly employed

(*e.g.* ref. [2]) but both *a* and *b* can be described in terms of the operation of the hexose monophosphate pathway by the following assumptions:

Case a. (i) The Embden-Meyerhof glycolytic sequence degrades glucose to yield pyruvate equally from C-1 to C-3 and C-4 to C-6. (ii) The hexose monophosphate pathway yields pyruvate from glucose C-4 to C-6. (iii) The phosphorylated hexose formed by the operation of the hexose monophosphate pathway is degraded completely by the action of this pathway. This has the effect that the original C-2 and C-3 of glucose yield CO_2 and C-4, C-5 and C-6 form pyruvate.

Case b. Assumptions (i) and (ii) are as in case *a*. (iii) The phosphorylated hexose formed by the operation of the hexose monophosphate pathway is degraded completely by the action of the Embden-Meyerhof sequence. This means that all the carbon atoms of the original glucose (except C-1) attacked by the hexose monophosphate pathway yield pyruvate.

Both sets of assumptions are possibly unlikely in respect of points *a* (iii) and *b* (iii). Nevertheless *b* (iii) is perhaps feasible on the grounds that the phosphorylated hexose formed is fructose-6-phosphate and might therefore, for reasons of enzyme location, be preferentially disposed to the Embden-Meyerhof pathway rather than to conversion to glucose-6-phosphate followed by direct oxidation.

In our derivation (case *c*) we accept assumptions (i) and (ii) but consider it more likely that the phosphorylated hexose formed in the hexose monophosphate pathway is subject to further degradation by both routes in the same proportion as the original glucose, *i.e.*, there exists a pool of hexose monophosphate common to both pathways. This makes full use of our present knowledge regarding the cyclic nature of the hexose monophosphate pathway and give values for the degree participation in this pathway from [1-^{14}C], [2-^{14}C] and [6-^{14}C]glucose which are in reasonably good agreement. All the assumptions inherent in this derivation have already been listed[1] and, while on present knowledge we consider these to be justified, we do not exclude the possibility of change in the light of future data on the cyclic operation of this pathway.

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[1] E. A. DAWES AND W. H. HOLMS, *Biochim. Biophys. Acta*, 29 (1958) 82.
[2] H. J. BLUMENTHAL, K. F. LEWIS AND S. WEINHOUSE, *J. Am. Chem. Soc.*, 76 (1954) 6093.

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