STUDIES ON THE FLOWS OF PROPIONATE CARBON TO GLUCOSE IN SHEEP

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by

SHANE WILLIAM CRIDLAND
B. Rural Science (Hons) New England

The Department of Biochemistry and Nutrition
The University of New England
Armidale. N.S.W.
AUSTRALIA

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The studies presented in this thesis were completed by the author whilst a postgraduate student in the Department of Biochemistry and Nutrition, Faculty of Rural Science, the University of New England, Armidale, N.S.W., Australia. Assistance given by other persons is indicated in the text or in the list of acknowledgements. All references cited are included in the bibliography. The work is otherwise original.

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I certify that the substance of this thesis has not already been submitted for any other degree and is not being currently submitted forany other degree.

I certify that any help received in preparing this thesis, and all sources used, have been acknowledged in this thesis.

S. W. Cridland

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Summary

1. In this thesis the flows of ^{14}C to glucose from labelled propionate infused into the rumen of sheep were studied.

2. The pattern of tracer flow does not represent the pattern of net carbon flow because of equilibration of tracer in the symmetrical dicarboxylic acid pools, recycling of tracer, tracer flows via indirect routes and metabolic crossover. The effects of these influences have not been fully appreciated and accounted for in the interpretation of data obtained from many isotope dilution experiments. In this thesis an attempt was made to correct the percentage of the carbon atoms in the glucose pool that originated in the propionate pool (i.e. the transfer quotient) for the above influences and thus, calculate the true percentage of the glucose pool being provided by propionate.

3. The biochemistry of the propionate molecule is given and the effects of interaction with the tricarboxylic acid cycle on the fate of carbon from the middle and carboxyl positions of propionate discussed.

4. The effects of metabolic crossover are proportional to the percentage of the molecules in the oxaloacetate pool that arises from cycling of the tricarboxylic acid cycle. Therefore, equations were developed to estimate this percentage. Two of these equations were based on an approach similar to that used by Weinman, Strisower and Chaikoff (1957): i.e. based on the differences in metabolism of the middle and carboxyl carbons of oxaloacetate and the subsequent labelling

of metabolites synthesised from the oxaloacetate pool. The third equation was based on the incorporation of CO_2 into glucose.

5. The understanding of the tracer flows developed through a series of experiments culminating in the development of 5 pool models (propionate middle or acetate methyl carbon, rumen bicarbonate, blood bicarbonate, glucose and the carboxyl carbon of propionate or acetate).

6. A comparison of the transfer quotients with the relevant values from the models indicated that when ^{14}C-propionate or ^{14}C-acetate was infused into the rumen, a significant proportion of the tracer in glucose was incorporated from the bicarbonate pools.

7. The data for the incorporation of tracer from the middle and carboxyl carbons of oxaloacetate into glucose, their entry into the blood bicarbonate pool and the incorporation of CO_2 into glucose could not be explained simultaneously by the cycling of tracer in the tricarboxylic acid cycle. Nor could all the results be rationalized by taking into account recycling of tracer via the pathways; oxaloacetate, phosphoenol-pyruvate, pyruvate back to oxaloacetate, and/or via; oxaloacetate, phosphoenol-pyruvate, pyruvate, acetyl-CoA, citrate then back to oxaloacetate via the tricarboxylic acid cycle.

8. The incorporation of $^{14}CO_2$ into glucose was much higher than predicted by the pathways of incorporation presently accepted. Therefore, it appears that there is at least one further pathway by which CO_2 can be incorporated into glucose that has

not been accounted for in the interpretation of the results.

9. More basic research is needed to identify all forms of tracer recycling and to quantify their effects on the tracer flows. Until this is done flows calculated from the transfer of tracer from propionate to glucose can not be converted into net carbon flows.