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**ACETALDEHYDE METABOLISM IN MAMMALS**

A thesis presented in partial  
fulfilment of the requirements  
for the degree of

Doctor of Philosophy  
in Biochemistry

at

Massey University

New Zealand

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1975

### ABSTRACT

The metabolism of acetaldehyde in mammalian systems has been investigated both with in vitro studies on sheep liver aldehyde dehydrogenase, and by following changes in blood acetaldehyde levels in human volunteers.

The intracellular localisation of aldehyde dehydrogenase was examined, using concurrent assays for marker enzymes. Average results for the distribution of the enzyme showed 30% of the total activity to be mitochondrial, 42% cytosolic, and 10% microsomal. The presence of activity in the microsomes was confirmed in studies where the enzyme was solubilised using sonication and Triton X-100 treatments. The cytoplasmic enzyme was purified by ammonium sulphate fractionations, ion exchange chromatography, and gel filtration, to a reproducible purity of 95%. Molecular weights of the native protein (205,000 - 220,000), subunit molecular weights (51,000 - 55,000) and behaviour during gel electrophoresis have been determined for both the cytoplasmic and mitochondrial sheep liver aldehyde dehydrogenases.

An enzymic assay was developed for measuring very small amounts of acetaldehyde (down to 0.25 nmoles), using purified cytoplasmic sheep liver aldehyde dehydrogenase preparations. This assay has been applied to the determination of levels of acetaldehyde in the blood of human volunteers following ethanol ingestion. Untreated whole blood containing ethanol formed acetaldehyde, and the levels of acetaldehyde determined in either perchlorate-treated or untreated plasma were lower than those in whole blood. Acetaldehyde levels determined enzymically using perchloric acid supernatants of whole blood were reasonably close to the levels determined by gas chromatography, and the range of results (0.05 - 0.25 mg%) correlated well with similar results reported recently in the literature.

A new ion exchange resin, DEAE Protion, was used during this investigation and separations of aldehyde dehydrogenase on forms of this resin and DEAE cellulose have been compared in an Appendix to the thesis.

ACKNOWLEDGEMENTS

I wish to thank my supervisors Professor R.D.Batt and Dr R.M. Greenway for the help they have given me throughout the course of this study.

I would also like to thank other members of the alcohol research group, in particular:

Mr K.Couchman for allowing the use of his gas chromatography results.

Dr T.M.Kitson for supplies of mitochondrial aldehyde dehydrogenase.

Mr A.MacGibbon for help in isolating cytosolic aldehyde dehydrogenase.

Mr T.Braggins for his expert technical assistance.

Thanks are also extended to all members of the Chemistry-Biochemistry Department for their help. In particular I would like to thank Dr J.W.Tweedie, who provided many helpful comments during the course of this study.

I am grateful to all those mentioned above, and also to Dr G.G. Midwinter, Dr J.S.Ayers and Mr A.Stowell for their advice and comments on various parts of the final manuscript.

Finally, I would like to thank Jan Harding for assistance with typing the thesis.

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