Species Body Size and Liver Glutamine Synthetase, Glutaminase and Glutamine Aminotransferase

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Previous work on various mammalian species has shown that as adult body size diminishes certain liver enzymes concerned with amino acid metabolism increase greatly in activity: pyruvate aminotransferases (Lin, Rivlin & Knox, 1959; Rowsell & Carnie, 1964), L-alanine-2-oxoglutarate aminotransferase (Cornelius, 1963) and serine dehydratase (Rowsell, Carnie & Wahbi, 1965). We are surveying for other enzymes in liver homogenates with the prospect that more will be found having a similar dependence on body size; the significance of this phenomenon may then become clearer.

Glutamine synthetase was assayed as described by Elliott (1955), by calculating rates from Wu's (1963) extinction coefficient value for the Fe^{+++} complex of L-glutamyl- γ -hydroxamate; glutaminase in 0.05M-potassium phosphate buffer, pH 7.8, with 0.02M-L-glutamine, the glutamate liberated being measured in heat-inactivated incubation samples with ninhydrin after chromatographic separation; and glutamine amino-transferase as described by Buttery, Rowsell & Carnie (1969). In all cases initial rates were obtained from linear progress curves under conditions where rate was proportional to liver concentration.

Assays with fresh liver from the local abattoir were included and there were delays in transport (never more than 45 min.) before these could be started. Some attempt was made to gauge what losses in activity this might involve. When freshly obtained chopped rat liver was stored ice-cold in the appropriate buffer for homogenization (as in conveying abattoir samples), the activities measured after 2 hr. for glutamine synthetase, glutaminase and glutamine aminotransferase were respectively (compared with immediate assay) 87%, 77% and 98%.

Glutamine aminotransferase activities [μ moles of 2-oxoglutarate/hr/g. of liver $\pm$ S.E.M. (no. of animals)] were: mouse, 67 ± 2 (12); red-backed vole, 75 and 77; hamster, 26 ± 2 (7); rat, 18 ± 1 (18); guinea pig, 3.1 ± 0.5 (5); rabbit, 3.3 ± 1.6 (4); cat, 4.7 ± 0.4 (5); pig, sheep and ox, 1.6-2.8 (each 2). There is a fairly systematic acute rise in activity with diminishing body size.

This was not found with glutaminase activities (μ moles of glutamate/hr./g.): mouse, 319 ± 43 (8);

rat, 244 ± 6 (6); guinea pig, 190 ± 13 (5); cat, 380 ± 26 (4); pig, 245 and 113.

For glutamine synthetase it appears that activity (μ moles of glutamyl- γ -hydroxamate/hr./g.) is of a higher order in the smaller mammals: mouse, 517 ± 18 (4); red-backed vole, 224 ± 23 (4); rat, 398 ± 38 (6); guinea pig, 18 ± 3 (3); rabbit, 24 ± 2 (3); cat, 46 ± 2 (4); sheep, 52 ± 4 (3); goat, 58 ± 7 (3); pig 65 ± 16 (3); ox, 36 ± 9 (5).

The significance of these findings will be discussed in relation to the variation of basal metabolism with adult body size.

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Investigation of the Cathepsins of Human Gastric Carcinomata

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Extracts of gastric carcinomata are devoid of pepsin (Greenstein & Stewart, 1942), but proteolytic activity near pH 3.5 has been demonstrated (Taylor, 1960a) that appears similar to the proteolytic activity of normal intestinal mucosa (Taylor, 1960b).

The construction of pH-activity curves with tumour extracts, by a modification of the Anson (1938) method of assay, gave a maximum ranging from pH 3.3 to 3.8 and curves that were asymmetrical. Electrophoresis of the extracts on agar gel at pH 8.2 revealed a cationic and at least one anionic proteolytic zone at positions corresponding respectively to cathepsins D and E of rabbit tissues (Lapresle & Webb, 1960, 1962).

Chromatography of one extract on DEAE-cellulose (Lapresle & Webb, 1962) gave three peaks of activity. The first peak (proteinase 1) eluted from the column was chromatographically and electrophoretically similar to rabbit cathepsin D. The pH-activity curve for this proteinase was symmetrical, with the maximum at pH 3.7. The second and third peaks (proteinases 2a and 2b) were only partially resolved, and emerged from the column

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