Phenylethylamine formation in perfused rat liver

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Phenylethylamine is a sympathomimetic amine which can be formed via decarboxylation of L-phenylalanine or derived from dietary constituents (Nakajima, Kakimoto & Sano, 1964; Sandler, Youdim & Hanington, 1974). This amine can pass the blood-brain barrier and has been implicated in the pathogenesis of certain affective disorders (Sandler & Reynolds, 1976). There is little quantitative information concerning the formation of phenylethylamine from L-phenylalanine and the aim of the present experiments was to determine the extent of its formation from L-phenylalanine in rat liver.

When livers from fed female Wistar rats were perfused (Hems, Ross, Berry & Krebs, 1966) with glucose (5 mmol/l) and L-phenylalanine (0–30 mmol/l), at amino acid concentrations above 5 mmol/l there was a substantial decarboxylation of L-phenylalanine (Youdim, Mitchell & Woods, 1975) measured by the accumulation of phenylacetic acid and mandelic acid. These acids which were identified and measured by gas chromatography and mass spectrometry (Goodwin, Ruthven & Sandler, 1974, 1975) accounted for 0.6% of the L-phenylalanine removed at initial concentrations below 5 mmol/l. This figure rose to 2.2% at 10 mmol/l and reached 8% above 20 mmol/l (Figure 1).

Phenylethylamine is a substrate for hepatic monoamine oxidase (MAO) 'type B' (Youdim, 1975) and thus these figures represent an under-estimate of phenylethylamine formation. Treatment of the rats with the MAO inhibitor tranylcypromine (20 mg/kg i.p.) 2 h before perfusion resulted in the accumulation of phenylethylamine. When the initial L-phenylalanine concentrations were 0, 1, 5 and 30 mmol/l the amounts of phenylethylamine formed in 2 h were 1.0, 1.72, 18.4 and 32.8 μg/g wet liver respectively. In the absence of tranylcypromine only trace amounts of phenylethylamine were detected. This fact, taken together with the accumulation of mandelic and phenylacetic acids under these conditions suggests that normally phenylethylamine is a transient intermediate.

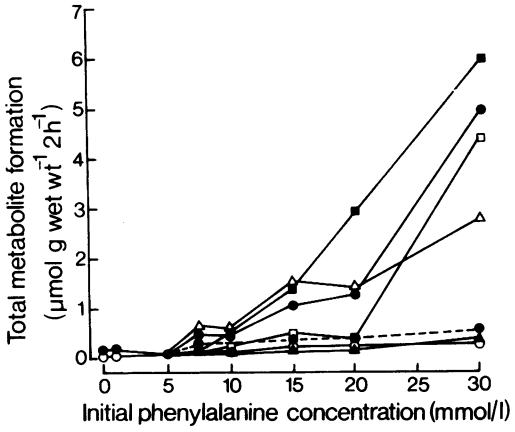

Figure 1 Formation of metabolites from L-phenylalanine in the isolated perfused rat liver.

●——● Phenylpyruvic acid, ○——○ O-Hydroxyphenylacetic acid, □——□ Phenyl lactic acid, △——△ Phenylacetic acid, ■——■ Mandelic acid, ●---● *P*-Hydroxyphenyl lactic acid, ▲——▲ *P*-Hydroxyphenylacetic acid. The figures are means for between two and five estimations.

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