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Polymorphic hydroxylation of debrisoquine in Ghanaians

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The alicyclic hydroxylation of debrisoquine exhibits genetic polymorphism in Caucasians (Mahgoub, Idle, Dring, Lancaster & Smith, 1977). About 5–6% of British White Caucasians are defective in respect of this reaction (PM phenotype) while the remainder (EM phenotype) extensively 4-hydroxylate the drug. One feature of polymorphisms of drug metabolism reactions is that there can occur considerable inter-ethnic differences in the occurrences of the various phenotypes. Accordingly, we have been examining the metabolic hydroxylation of debrisoquine in a variety of different ethnic groups including, Egyptians, Nigerians, Gambians, Ghanaians, Malaysians and Chinese. In this communication we report on our studies with Ghanaians.

Eighty healthy Ghanaian medical students, male and female each took a single tablet of Declinax (10 mg debrisoquine) early morning after an overnight fast and the urine collected for a 0–8 h period. This was analysed by g.c. for debrisoquine and 4-hydroxydebrisoquine. A metabolic ratio was calculated for each subject this being derived as follows: % dose excreted unchanged/% dose as 4-hydroxydebrisoquine in the urine in the 0–8 h period. A frequency histogram was constructed from the results (Figure 1).

The data obtained indicates that the 4-hydroxylation of debrisoquine is polymorphic with an incidence of 'poor metabolisers' (PM) similar to that found for Caucasians. There is also an indication that the metabolic ratio frequency distribution in Ghanaians is trimodal, suggesting that homozygous and heterozygous EM subjects are distinguishable, a situation not evident with our Caucasian subjects (Figure 1).

Further studies revealed strong positive rank-correlation between the alicyclic and aromatic hydroxylation of debrisoquine in both Ghanaians and Caucasians ($r_{(s)} = 0.82$ and 0.83 respectively, $P < 0.01$) indicating the involvement of the same single gene in the two types of carbon-centre oxidation.

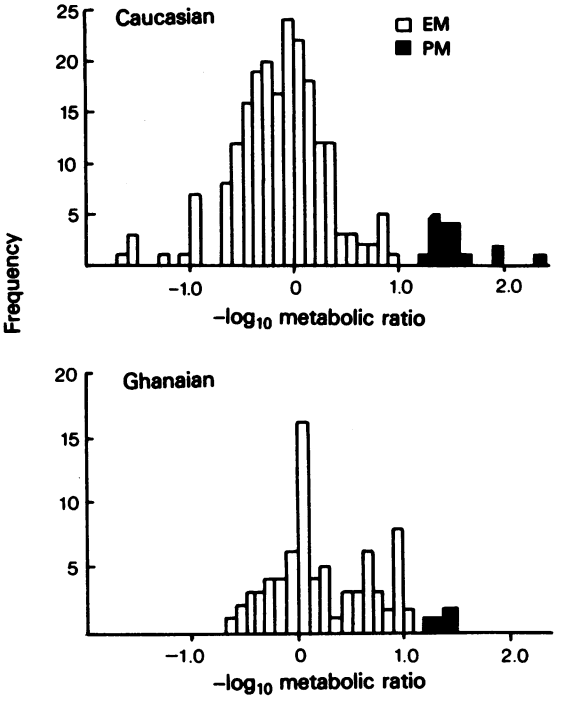

Figure 1 Frequency distribution of $\log_{10}$ metabolic ratios in Ghanaian and Caucasian study populations.

$$\left(\text{Metabolic ratio} = \frac{\%\text{ Dose eliminated as debrisoquine}}{\%\text{ Dose eliminated as 4-hydroxydebrisoquine}} \text{ in 0–8 h}\right).$$

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