PRESYSTEMIC ELIMINATION AND MEAN RESIDENCE TIME

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In a recent publication, Midha *et al.*[1] outlined how statistical moments of residence times can be used to distinguish between different models of drug absorption. I agree with the authors' conclusion that one can read from the mean residence time of propranolol and its glucuronide alone that propranol undergoes an extensive first pass metabolisation. Unfortunately, however, the equations the authors used to demonstrate the validity of the alternative pharmacokinetic model are not correct: Equation (6) should read

$$\mathrm{MRT_m} = f\left(\frac{1}{K_a^1} + \frac{1}{K_{me}}\right) + (1-f)\left(\frac{1}{K_a^1} + \frac{1}{\beta} + \frac{1}{K_{me}}\right) \qquad (1)$$

and consequently, equation (8) should read

$$(\mathrm{MRT_m} - \mathrm{MRT_p}) = (\mathrm{MRT_m})_{i.v.} - f\,(\mathrm{MRT_p})_{i.v.} \qquad (2)$$

The validity of the latter equation (2) is obvious and contradicts that given by Midha *et al.*: If f approaches zero, i.e. no first pass effect, equation (2) would be identical to equation (4) in the paper by Midha *et al.* However equation (8) in their paper would not be identical.

It is this very equation (4) in the article in question which expresses the most useful property of the mean time concept: The additivity of mean times, which has been demonstrated by several authors.[2–4]

Although it is well known that propranol undergoes first pass metabolization, the idea of discriminating between different pharmacokinetic models by

moments is most useful for the evaluation of drugs under development usually first given only orally.

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