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Short Communication

Calculating absorption rate constant of linear one-compartment open models using peak blood level or peak urinary excretion rate and postabsorptive data

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The absorption rate constant is widely used as a measure of the rate of drug bioavailability. The classical methods for graphical determination of this parameter require frequent samplings at the absorptive phase of the blood level and/or urinary excretion profile of the drug. The frequent sampling during the absorptive phase in the urinary excretion studies is difficult. For this reason Pidgeon and Pitlick (1980) have derived an equation for determining absorption rate constant of the linear one-compartment open model using peak urinary excretion rate and postabsorptive urinary excretion data. They also derived a similar equation from the peak and postabsorptive blood level data (1977).

In this communication 3 additional simple equations for calculating the absorption rate constant of the model are derived using the peak blood level or peak urinary excretion rate and the postabsorptive data. Details of the derivation of the equations are as follows:

(1) *From the blood level data.* The linear postabsorptive phase of the blood level vs time for the model is described by Eqn. 1 (Gibaldi and Perrier, 1975)

$$\ln C = \ln\left[\frac{k_a FD}{(k_a - K)V}\right] - Kt \qquad (1)$$

where C is drug concentration in blood at time t, k_a and K are first-order absorption and elimination rate constants of the drug, F is fraction of dose D absorbed, and V is the apparent volume of distribution of the drug.

According to Eqn. 1, the concentration $C_{t_{max}}$, corresponding to t_{max} (the time of peak blood level) on the extrapolated linear phase is given by the following

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equation:

$$\ln C_{t_{max}} = \ln\left[\frac{k_a FD}{(k_a - K)V}\right] - Kt_{max} \tag{2}$$

or

$$C_{t_{max}} = \frac{k_a}{k_a - K} \times \frac{FD}{V} \cdot e^{-Kt_{max}} \tag{3}$$

The peak blood level, C_{max}, of drug is calculated from Eqn. 4 (Gibaldi and Perrier, 1975):

$$C_{max} = \frac{FD}{V} \cdot e^{-Kt_{max}} \tag{4}$$

It is evident from Eqns. 3 and 4 that $C_{t_{max}} > C_{max}$. Substitution of C_{max} for the term $FD/V \cdot e^{-Kt_{max}}$ into Eqn. 3 will give:

$$C_{t_{max}} = \frac{k_a C_{max}}{k_a - K} \tag{5}$$

Solving Eqn. 5 for k_a will result in the following equation:

$$k_a = \frac{KC_{t_{max}}}{C_{t_{max}} - C_{max}} \tag{6}$$

where K is the slope of a best-fit line describing the postabsorptive phase and $C_{t_{max}}$ is calculated by inserting the value of t_{max} in the equation of the best-fit line.

(2) *From the urinary excretion data.* (a) From the urinary excretion rate data. Similar to the blood level plot, the drug excretion rate, $\dot{U}_{t_{max}}$, corresponding to t_{max} on the extrapolated linear phase of the drug urinary excretion rate vs time plot can be written as:

$$\dot{U}_{t_{max}} = \frac{k_a}{k_a - K} \cdot k_e FD \cdot e^{-Kt_{max}} \tag{7}$$

in which k_e is a first-order urinary excretion rate constant. Applying a similar technique of derivation given by Gibaldi and Perrier (1975) for the blood level equation to the equation describing the urinary excretion rate profile, the following equation for calculating $\dot{U}_{max}$ (the maximum value of the urinary excretion rate of the drug) may be derived:

$$\dot{U}_{max} = k_e FD \cdot e^{-Kt_{max}} \tag{8}$$

Substitution of $\dot{U}_{max}$ from Eqn. 8 into Eqn. 7 and solving the resulting equation for k_a will give Eqn. 9

$$k_a = \frac{K\dot{U}_{t_{max}}}{\dot{U}_{t_{max}} - \dot{U}_{max}} \tag{9}$$

As with the equations of Pidgeon and Pitlick (1977, 1980), the accuracy of the k_a value calculated from Eqns. 6 and 9 will depend largely on the accuracy of determined t_{max}, C_{max}, and $\dot{U}_{max}$ values.

(b) From the urinary sigma-minus data. The zero time intercept, P, of postabsorptive phase of the urinary sigma-minus plot is given by Eqn. 10 (Gibaldi and Perrier, 1975)

$$P = \frac{k_a U_\infty}{k_a - K} \tag{10}$$

Solving Eqn. 10 for k_a gives Eqn. 11

$$k_a = \frac{KP}{P - U_\infty} \tag{11}$$

U_∞ is the cumulative amount of unchanged drug excreted via urine between times 0 and ∞ (infinity) and its value can be estimated from the postabsorptive data using the rapid method given by Niebergall et al. (1975).

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