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Short Communication

Simultaneous estimation of asymptotic value of absorption plot and absorption rate constant

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In a previous report methods of estimating asymptotic values of absorption plots from early data points of the plots as well as the advantages of the methods were discussed (Barzegar-Jalali, 1981). These methods require blood samples taken according to particular time schemes (i.e. equal time and t, 2t schemes).

In this communication an equation is derived from early data points of the absorption plot which can be applied to any time scheme. When the equation is solved graphically, it would give both the asymptotic value and the absorption rate constant.

The absorption plot of linear open-compartment models is described by Eqn. 1 (Wagner, 1975a)

$$\frac{A}{V}=\frac{FD}{V}(1-e^{-k_a t}) \tag{1}$$

where A is the cumulative drug amount absorbed up to time t, V is the volume of distribution of drug, F is fraction of dose D absorbed, and k_a is a first-order absorption rate constant. The term FD/V is an asymptotic value of the plot.

Eqn. 1 may be written as:

$$\frac{A}{V}=\frac{FD}{V}-\frac{FD}{V}e^{-k_a t} \tag{2}$$

The integration of Eqn. 2 between times 0 and t yields:

$$\int_0^t (A/V)\cdot dt=\frac{FD}{V}t+\frac{FD}{k_a V}e^{-k_a t}-\frac{FD}{k_a V} \tag{3}$$

Eqn. 3 is rearranged to give:

$$\int_0^t (A/V)\cdot dt=\frac{FD}{V}t-\frac{FD}{k_a V}(1-e^{-k_a t}) \tag{4}$$

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But according to Eqn. 1 the term $FD/V(1-e^{-k_a t})$ is equal to $(A/V)_t$. Therefore, Eqn. 4 can be written as Eqn. 5

$$\int_0^t (A/V) \cdot dt = \frac{FD}{V} t - \frac{1}{k_a}\left(\frac{A}{V}\right)_t \tag{5}$$

Dividing both sides of Eqn. 5 by t will result in Eqn. 6

$$\left[\frac{\int_0^t (A/V) \cdot dt}{t}\right] = \frac{FD}{V} - \frac{1}{k_a}\left[\frac{(A/V)_t}{t}\right] \tag{6}$$

where $\int_0^t (A/V) \cdot dt$ is the area under the absorption plot between times 0 and t. The intercept and slope of the line resulting from plotting left-hand side of Eqn. 6 vs. $[(A/V)_t/t]$ will be equal to FD/V and $-1/k_a$, respectively.

Eqn. 6 was applied to 0.4, 0.8, 1.2, 1.6 and 2 h data points of the Table 3 of a Wagner's paper (1975b), using the set 3 data. The asymptote and k_a obtained were 100.7 units and 0.4905 h^{-1}, respectively. These values were very close to the actual values (i.e. 100 units and 0.5 h^{-1}) given by the author.

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