NUMERICAL ANALYSIS OF APPROXIMATIONS TO THE PLANAR DIFFUSION EQUATION

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Evaluation of drug delivery systems such as polymer matrices, ointments and emulsions usually necessitates the experimental determination of diffusion coefficients (Flynn et al 1974). It has long been established that the general solution to Fick's second law applied to planar diffusion into a perfect sink, Equation 1, can be approximated at short and long times by Equation 2 and 3, respectively, (Crank 1975; Higuchi 1967)

$$Q1 = hC_o\left[1 - \frac{8}{\pi^2} \sum_{n=0}^{\infty} \frac{1}{(2n+1)^2} \exp\left(-\frac{D(2n+1)^2\pi^2 t}{4h^2}\right)\right] \text{ - Eqn. 1}$$

$$Q2 = 2C_o\sqrt{Dt/\pi} \text{ - Eqn 2}$$

$$Q3 = hC_o\left[1 - \frac{8}{\pi^2}\exp\left(-\frac{D\pi^2 t}{4h^2}\right)\right] \text{ - Eqn 3}$$

Q = Amount released per unit area per unit time.
C_o = Initial concentration in donor phase
h = Thickness of donor phase
D = Diffusion coefficient

By dividing Equations 1, 2 and 3 by hC_o, the left hand sides become the dimensionless ratio Q/hC_o representing the fraction, F, of drug released from the matrix at time t. Substitution of χ for $(\pi^2 Dt/4h^2)^{\frac{1}{2}}$ in the above equations gives the following expressions

$$F2 = \frac{4\chi}{\pi^{3/2}} \simeq F1 = \{1 - \frac{8}{\pi^2} \sum_{n=0}^{\infty} \frac{1}{(2n+1)^2} \exp(-(2n+1)^2\chi^2\} \simeq F3 = \{1 - \frac{8}{\pi^2}\exp(-\chi^2)\}$$

- Eqn 4

Hence by inserting suitable values for χ into Equation 4, the fractions released according to Equations 1, 2 and 3 are obtained. Table 1 shows the errors involved in either approximation relative to the 'exact' fraction released, F1. To avoid the use of Equation 1, it is clearly justified to apply Equation 2 for less than 50% release, or a first order plot according to F3 for greater than 50% release. No more than about 0.2% error is thus incurred in values of F.

Table 1

Actual Fraction Released F1	% Error in F2	% Error in F3
0.072	$<10^{-8}$	175
0.143		54.0
0.216		20.3
0.359	4.6×10^{-4}	2.66
0.431	0.013	0.814
0.502	0.103	0.218
0.572	0.414	0.0496
0.639	1.12	9.61×10^{-3}
0.758	4.21	2.22×10^{-4}
0.850	9.81	$<10^{-5}$
0.937	22.6	

In the absence of any further information on the nature of the release process, experimental data in the form log (1-F) might be plotted against time. A linear plot would be consistent with the rate-controlling step being partition at the interface between the 'sink' and the drug delivery system (Higuchi 1967), rather than diffusion in the latter. Linear least mean square regression analysis on 14 'exact' points in the range 0.07 < F1 < 0.89 gives in fact correlation coefficients in excess of 0.99. Thus, analysis of release profiles alone does not appear to provide unambiguous information about the mechanism of rate control.

Crank, J. (1975) "Mathematics of Diffusion", 2nd Ed., Ch. 4, Clarendon Press, Oxford
Flynn, G.L. et al (1974) J. Pharm. Sci. 63:479-510
Higuchi, W.I. (1967) Ibid. 56:315-324

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