HELPING STUDENTS BECOME BETTER MATHEMATICAL MODELERS

Pseudosteady-State Approximations

ANNETTE L. BUNGE, RONALD L. MILLER
Colorado School of Mines • Golden, CO 80401

Undergraduate and graduate students completing their first course in applied engineering mathematics or transport phenomena are often confused about several aspects of modeling physical systems. These may include clearly stating and understanding simplifying assumptions, advantages and limitations of various solution strategies, ways to quickly check that derived solutions seem reasonable using limiting cases, determination of applicable ranges of approximate solutions, how to use limiting cases obtained from exact solutions, and physical interpretation of mathematical results. We have developed a pedagogically sound approach to addressing these issues using a single physical transport problem that can be analyzed with multiple mathematical models. The objective of this paper is to present the problem with two pseudosteady-state solutions and to provide several examples of study questions we pose to students to help them better understand and interpret the results of each solution.

The problem involves mass transfer from topical formulations (ointments or creams applied to skin) containing drugs in suspension. A moving boundary develops in this system and mathematical representations are amenable to pseudosteady-state, similarity transform, and regular perturbation solutions. In this paper we formulate the descriptive differential material balance model and obtain two different pseudosteady-state solutions. We will also present and discuss several study questions to assign students based on results of each model solution (presented in italics).

PROBLEM DESCRIPTION

Delivery of drugs to skin is important for treatment of a number of skin diseases. Many topically applied drugs are solid suspensions in a vehicle consisting of an ointment or cream base. That is, the total amount of active ingredient exceeds the solubility limit of the formulation. In these systems, the solid drug dissolves into the vehicle, diffuses through the vehicle to the skin, establishes local phase equilibrium with the outer layer of skin, diffuses through the skin, and finally is swept away by internal circulation. In many cases, skin represents the rate limiting barrier for mass transfer. Occasionally, particularly for highly insoluble suspension-type formulations or for applications on damaged skin, the primary mass transfer resistance will be the vehicle itself.

Release rates from topical formulations are experimentally measured by spreading the drug suspension on a permeable membrane and then monitoring the appearance of drug in an initially drug-free solution on the opposite side of the membrane, the receiving chamber, as shown in Figure 1. The receiving chamber volume is generally large enough so that drug accumulation can be neglected. Mass transfer resistances in the membrane are usually much smaller than in the formulations, and the system can be treated as if the membrane was not present. Consequently the concentration in contact with the membrane is approximately the same as the concentration of the receiving chamber (*i.e.*, $C = 0$).

If the drug is finely divided, uniformly suspended, and rapidly dissolves, then two zones will develop as illustrated schematically in Figure 2. Far from the receiving chamber ($\delta \le x \le L$), the drug will be present as a solid suspension at the original starting concentration C_0. In the region adjacent to the receiving chamber ($0 \le x \le \delta$), all of the solid will have dissolved and the drug will be present in concentrations below the solubility limit, C_s, as described by Fick's law.[1]

Annette L. Bunge *is Professor of Chemical Engineering and Petroleum Refining at the Colorado School of Mines, where she has taught and conducted research since 1981. Her current research interests include dermal adsorption of chemicals with application to health risk assessment and drug delivery design.*
Ronald L. Miller *is Associate Professor of Chemical Engineering and Petroleum Refining at the Colorado School of Mines, where he has taught and conducted research in educational methods and multiphase fluid flow for twelve years. He has received three university-wide teaching awards and the Helen Plants Award for Best Workshop at the 1992 Frontiers in Education national conference.*

That is,

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} \qquad \text{for} \qquad 0 \le x \le \delta \tag{1}$$

where

$$C = 0 \qquad \text{at } x = 0 \qquad \text{for } t \ge 0 \tag{2}$$

$$C = C_s \qquad \text{at } x = \delta \qquad \text{for } t < 0 \tag{3}$$

The location of the sharp boundary between the fully dissolved and suspended drug zones (δ) will advance in time as required to satisfy the drug material balance at $x = \delta(t)$:

$$(C_o - C_s)\frac{d\delta}{dt} = D\left.\frac{\partial C}{\partial x}\right|_{x=\delta} \tag{4}$$

where

$$\delta = 0 \quad \text{at} \quad t = 0 \tag{5}$$

It is convenient to nondimensionalize the differential equations and restricting conditions using the following definitions:

$$\theta = C/C_s \qquad \eta = x/L \qquad \chi = \delta/L \tag{6}$$

$$\varepsilon = \frac{C_s}{C_o - C_s} = \frac{R}{1-R} \qquad \tau = \frac{C_s}{C_o - C_s}\frac{Dt}{L^2} = \frac{\varepsilon Dt}{L^2}$$

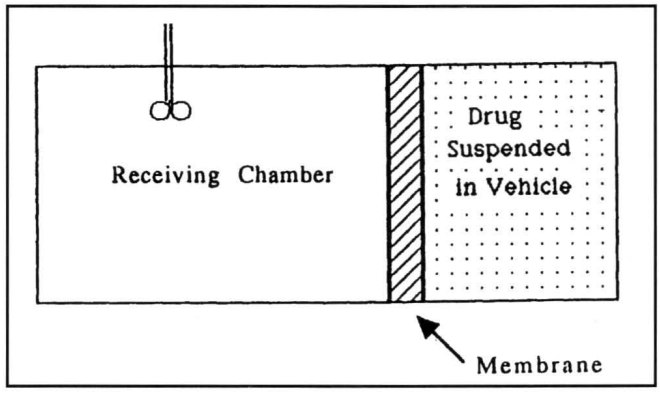

Figure 1. *Schematic diagram of an experiment to measure drug release from a topical formulation containing suspended drug.*

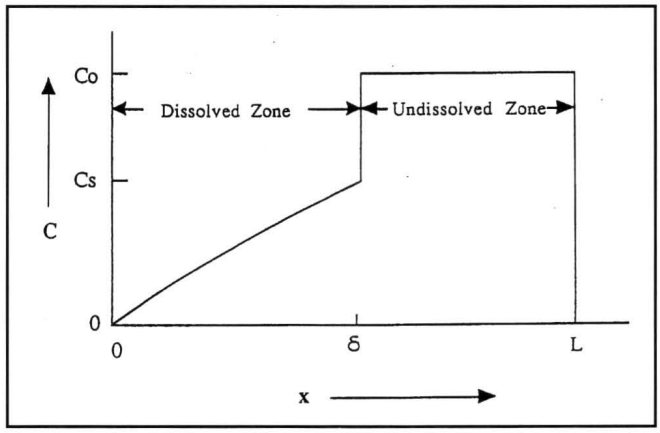

Figure 2. *Schematic diagram of the concentration profile in a vehicle containing suspended drug in contact with an infinite sink.*

where R represents the ratio of C_s/C_o, and ε has been introduced here in anticipation of its use in a regular perturbation solution. In dimensionless form, Eqs. (1) - (5) become

$$\varepsilon\frac{\partial\theta}{\partial\tau} = \frac{\partial^2\theta}{\partial\eta^2} \qquad \text{for } 0 \le \eta \le \chi \tag{7}$$

$$\frac{d\chi}{d\tau} = \left.\frac{\partial\theta}{\partial\eta}\right|_{\eta=\chi} \tag{8}$$

where

$$\theta = 0 \quad \text{at} \quad \eta = 0 \quad \text{for} \quad \tau \ge 0 \tag{9}$$

$$\theta = 1 \quad \text{at} \quad \eta = \chi \quad \text{for} \quad \tau > 0 \tag{10}$$

$$\chi = 0 \quad \text{at} \quad \tau = 0 \tag{11}$$

The concentration profile of drug in the formulation can then be determined by solving two coupled differential equations, Eq. (7) and Eq. (8), for three conditions, Eqs. (9) through (11).

The concentration profile is only occasionally of interest. Practically, it is usually more important to determine quantities such as the mass of drug released as a function of time, the time required for all of the drug to dissolve, and the fraction of the drug that is released when dissolution is complete.

The amount of drug released from the vehicle at $\eta = 0$ per unit of exposed area over a period of time from zero to t is determined by integrating the mass flux at the vehicle receiving chamber interface over time. That is,

$$M_R = A\int_0^t D\left.\frac{\partial C}{\partial x}\right|_{x=0} dt' = ALC_o(1-R)\int_0^\tau \left.\frac{\partial\theta}{\partial\eta}\right|_{\eta=0} d\tau' \tag{12}$$

where t' and τ' are dummy variables of integration. The time required for all of the solid drug to dissolve (τ_f) is the time at which $\chi = 1$, and the mass fraction released when all of the drug dissolves is specified by Eq. (12) when $\tau = \tau_f$.

PSEUDOSTEADY-STATE APPROXIMATION

When C_o is much larger than the drug solubility C_s, the dissolution boundary δ moves slowly relative to diffusion in the dissolved zone. It is then appropriate to assume that the concentration profile in the dissolved zone ($0 \le \eta \le \chi$) is approximately at steady state. That is,

$$\frac{d^2\theta}{d\eta^2} = 0 \qquad \text{for } 0 \le \eta \le \chi \tag{13}$$

which is solved along with the conditions listed in Eqs. (9) and (10) to give

$$\theta = \frac{\eta}{\chi} \tag{14}$$

where the movement of χ in time is determined by substituting for θ in Eq. (8),

$$\frac{d\chi}{d\tau} = \left.\frac{\partial\theta}{\partial\eta}\right|_{\eta=\chi} = \frac{1}{\chi} \tag{15}$$

which is integrated with Eq. (11) to give

$$\chi = \sqrt{2\tau} \tag{16}$$

Thus, the concentration profile of the drug in the formulation is approximately represented by

$$\theta = \frac{\eta}{\sqrt{2\tau}} \tag{17}$$

provided that $C_s << C_o$ (*i.e.*, $R << 1$), guaranteeing that the pseudosteady-state assumption is valid.

The amount of drug released from the vehicle at $\eta = 0$ per unit of exposed area over a period of time from zero to τ is

$$M_R = ALC_o(1-R)\int_0^\tau \frac{1}{\sqrt{2\tau'}}\,d\tau' \tag{18}$$

$$M_R = ALC_o(1-R)\sqrt{2\tau} \tag{19}$$

The time required for all of the solid drug to dissolve (τ_f) is 1/2, during which the mass fraction released is

$$\frac{M_{Rf}}{M_o} = \frac{M_{Rf}}{ALC_o} = 1-R \tag{20}$$

According to Eq. (20), the fraction of the original drug mass remaining in the formulation is R. Thus, according to the pseudosteady-state solution, the average concentration in the formulation when all of the drug has dissolved is C_s, which is not correct. If the concentration profile in the dissolved regions varies linearly from C_s to zero, the average concentration when all the drug is dissolved should be $C_s/2$.

HIGUCHI APPROXIMATION

More than thirty years ago, Higuchi[2] used a variation of the pseudosteady-state solution to obtain a different result. Like the solution just described, Higuchi assumed that the concentration profile had reached its steady-state value rapidly relative to the movement of the dissolution front (*i.e.*, $\theta = \eta/\chi$). He chose, however, to determine the location of the dissolution boundary by requiring that the mass of drug that has left the formulation

$$\frac{M_R}{A} = LC_o - \int_0^L C\,dx = LC_o - \int_0^\delta C\,dx - \int_\delta^L C_o\,dx = C_o\delta - \int_0^\delta C\,dx \tag{21}$$

be equal to the amount that has diffused across the boundary at x=0 into the receptor

$$\frac{dM_R}{dt} = AD\left.\frac{\partial C}{\partial x}\right|_{x=0} \tag{22}$$

Written in dimensionless form, Eqs. (21) and (22) become

$$\frac{M_R}{ALC_o} = \chi - R\int_0^\chi \theta\,d\eta = \chi - R\int_0^\chi \frac{\eta}{\chi}\,d\eta \tag{23}$$

$$\frac{dM_R}{d\tau} = ALC_oR\left.\frac{\partial\theta}{\partial\eta}\right|_{\eta=\chi} \tag{24}$$

Integrating Eq. (23), we obtain

$$M_R = ALC_o(1-R/2)\chi \tag{25}$$

which can be then differentiated

$$\frac{dM_R}{d\tau} = ALC_o(1-R/2)\frac{d\chi}{d\tau} \tag{26}$$

and combined with Eq. (24) to yield

$$\frac{d\chi}{d\tau} = \frac{1-R}{1-R/2}\left.\frac{\partial\theta}{\partial\eta}\right|_{\eta=\chi} = \frac{1-R}{1-R/2}\frac{1}{\chi} \tag{27}$$

Finally, Eq. (27) is integrated with the restriction that $\chi = 0$ at $\tau = 0$ to give

$$\chi = \sqrt{\frac{2(1-R)}{1-R/2}\tau} \tag{28}$$

Substituting Eq. (28) into Eq. (25), we obtain an expression for the cumulative mass released,

$$M_R = ALC_o\sqrt{2(1-R)(1-R/2)\tau} = ALC_o\sqrt{2R(1-R/2)\tau/\varepsilon} \tag{29}$$

which is slightly different than the pseudosteady-state result given in Eq. (19). The dimensionless time required to completely dissolve the drug is

$$\tau_f = \frac{1-R/2}{2(1-R)} \tag{30}$$

at which time the mass fraction released would be

$$\frac{M_{Rf}}{M_o} = \frac{M_{Rf}}{ALC_o} = 1-R/2 \tag{31}$$

According to Eq. (31), the fraction of the original drug mass remaining in the formulation is $1-(1-R/2) = R/2$. Thus, the Higuchi solution correctly predicts that the average concentration in the formulation when all of the drug has dissolved is $C_s/2$. Table 1 summarizes and compares expressions for the pseudosteady-state and Higuchi solutions, respectively.

COMPARING PSEUDOSTEADY-STATE AND HIGUCHI SOLUTIONS

Which of the two pseudosteady-state solutions is likely to be more correct (i.e., more closely match the exact solution) when R is no longer very small?

Based on mass balance, the Higuchi solution is superior. The Higuchi solution required that the mass of drug released into the receptor and the mass remaining in the formulation must always equal the total mass of drug in the original formulation. A similar requirement was not made in the standard pseudosteady-state solution. Most notably, at the moment that all of the drug has completely dissolved, the

pseudosteady-state solution predicts that the average concentration in the formulation is C_s, which is two times larger than the correct value of $C_s/2$.

AFTER THE DRUG HAS COMPLETELY DISSOLVED

What happens after the drug has completely dissolved? Are the two pseudosteady-state solutions valid for all times? If the solution is not always valid, when does its validity expire? What happens then? How would you describe the new situation?

The drug will continue to be released until the concentration reaches zero throughout the formulation. Equations (19) and (29) describing the cumulative mass of drug released only apply while some drug remains undissolved (*i.e.,* as long as $\tau \le \tau_f$). Drug release after dissolution is complete is described by the solution of the unsteady-state diffusion equation (*e.g.,* by separation of variables) with an initial concentration profile equal to the concentration profile in the dissolved region when $\eta = 1$ (*i.e.,* $\theta = \eta$ at $\tau > \tau_f$) and no flux at $\eta = 1$. When $\tau > \tau_f$,

$$\theta = 2\sum_{m=0}^{\infty} \frac{(-1)^m}{\lambda_m^2} \sin(\lambda_m \eta) e^{-\lambda_m^2(\tau-\tau_f)/\varepsilon} \tag{32}$$

$$\frac{M_R}{ALC_o} = \frac{M_{Rf}}{ALC_o} + 2R\sum_{m=0}^{\infty} \frac{(-1)^m}{\lambda_m^3}\left(1 - e^{-\lambda_m^2(\tau-\tau_f)/\varepsilon}\right) \tag{33}$$

where $\lambda_m = (2m+1)\pi/2$.

An interesting exercise is to ask students to show that $(M_R - M_{Rf})/(ALC_o) = R/2$ in the limit of large τ. Thus, in the limit of large τ, the Higuchi solution correctly predicts $M_R/(ALC_o) = 1 - R/2 + R/2 = 1$, while the pseudosteady-state solution predicts incorrectly that $M_R/(ALC_o) = 1 - R + R/2 = 1 - R/2 \neq 1$. We note that for small values of R, the solubility limit is very low, and consequently little drug will remain in the formulation once the drug has dissolved. That is, for small values of R, $1 - R/2 \cong 1$.

TABLE 1
Summary of Equations for Pseudo Steady-State and Higuchi Solutions

Quantity	*Pseudo Steady-State Solution*	*Higuchi Solution*
θ for $0 \le \eta \le \chi$	η/χ	η/χ
θ for $\chi \le \eta \le 1$	$1/R$	$1/R$
χ	$\sqrt{2\tau}$	$\sqrt{\frac{2(1-R)\tau}{1-R/2}}$
$\frac{M_R}{ALC_o}$	$(1-R)\chi = (1-R)\sqrt{2\tau}$	$(1-R/2)\chi = \sqrt{2(1-R)(1-R/2)\tau}$
τ_f	$1/2$	$\frac{1-R/2}{2(1-R)}$
$\frac{M_{Rf}}{ALC_o}$	$1-R$	$1-R/2$

WHEN THE SOLUBILITY LIMIT OF THE DRUG IS NOT EXCEEDED

What if the drug concentration in the topical formulation is less than its solubility limit (i.e., $C_o < C_s$)? How will the cumulative release rate from the formulation compare with the case when suspended drug is present? For the same drug concentration, will a dissolved or suspended drug give a higher release rate?

An interesting exercise is to compare the release rate from topical formulations containing suspended drug with the rate from formulations containing only dissolved drug. When the drug is entirely dissolved in the formulation, drug release will be described by the solution of the unsteady-state diffusion equation, Eq. (7), with an initial concentration of C_o throughout the formulation (i.e., $\theta = 1/R$ at $\tau = 0$ for $0 \le \eta \le 1$) and no flux at $\eta = 1$. This is easily solved by separation of variables to obtain

$$\theta = \frac{2}{R}\sum_{m=0}^{\infty} \frac{1}{\lambda_m} \sin(\lambda_m \eta) e^{-\lambda_m^2 \tau/\varepsilon} \tag{34}$$

$$\frac{M_R}{ALC_o} = 2\sum_{m=0}^{\infty} \frac{1}{\lambda_m^2}\left(1 - e^{-\lambda_m^2 \tau/\varepsilon}\right) \tag{35}$$

where $\lambda_m = (2m+1)\pi/2$. Although not obvious from Eq. (35), for short times

$$\frac{M_R}{ALC_o} = 2\sqrt{\frac{\tau/\varepsilon}{\pi}} = 2\sqrt{\frac{\tau(1-R)}{\pi R}} \tag{36}$$

which is the solution to Eq. (7) (most easily obtained by Laplace transforms) when the formulation is semi-infinite (*i.e.,* $L \to \infty$ or when τ is short enough that the concentration profile has not penetrated far into the formulation). This is an interesting result, since for both suspended and dissolved drug formulations, the cumulative mass released is proportional to $\sqrt{\tau/\varepsilon}$ until changes in the concentration profile have penetrated almost across the formulation.

ADDITIONAL STUDY QUESTIONS AND ILLUSTRATIVE EXERCISES

In this section, we present additional study questions and exercises that can be assigned. We find that students are usually more proficient at solving a problem than at using the solution they have derived. With the availability of symbolic mathematical tools such as Mathematica or Maple, it is reasonable to ask students to plot and analyze calculations from their solutions. A goal of the questions posed here is to require students to use and think about the physical meaning of their solu-

tion. These exercises can be used in many different ways. For example, we have assigned a series of solution strategies as a take-home exam that students work on for several weeks, submitting solutions to sections as they learn each new solution method (a just-in-time approach). Alternatively, they can be used as a series of homework or in-class problems illustrating many of the analytical mathematical techniques chemical engineers need for solving partial differential equations (*e.g.,* approximate solutions by pseudosteady-state and regular perturbation, separation of variables, Laplace transforms, and similarity transforms).

Plot the concentration profile as a function of dimensionless position, x/L, in the formulation as predicted by the standard pseudosteady-state and Higuchi solutions at a given time for a specified R. Consider formulations in which the drug is initially fully dissolved (i.e., R > 1) as well as initially a suspended solid (i.e., R < 1).

Figure 3 shows C/C_s when R = 0.5, 0.8, 1, and 2 at τ/ε is 0.10. This is the appropriate way to plot concentration if R changes as a result of changes in C_o. An alternative plot of C/C_o is more suitable when the total amount of drug is held constant and R changes by altering the formulation so that C_s changes, an analysis that can be tied to questions about determining which formulation will be more efficacious (*i.e.* more drug is released from the formulation during the same amount of time). This plot is also useful for instructing students about the limitations of approximate solutions. For example, when R = 0.8 (*i.e.,* $C_o/C_s = 1.25$), the pseudosteady-state solution predicts a smaller slope (and thus a smaller release rate into the receptor solution) than when C_o is reduced to C_s (*i.e.,* R = 1). This is physically incorrect and a result of the pseudosteady-state solution being used outside of the appropriate range of R. This same inconsistency is not observed for the Higuchi solution.

Calculate and plot the fraction of the initial drug mass released as a function of $\sqrt{\tau/\varepsilon} = \sqrt{Dt/L^2}$ *for different values of the solubility ratio, R. Compare predictions from the Higuchi and pseudosteady-state solutions while suspended drug remains and then use Eq. (33) to describe drug release after all of the drug has dissolved.*

Figure 4 presents the mass fraction released (*i.e.,* $M_R/(ALC_o)$) as a function of $\sqrt{\tau/\varepsilon} = \sqrt{Dt/L^2}$ for R = 0.2, 0.5, 0.9, >1 as predicted by the pseudosteady-state (S) and Higuchi (H) solutions while undissolved solid remains. The dashed curves represent the solution when drug is completely dissolved (*i.e.,* Eq. 33 when R < 1 and Eq. 35 when R > 1). Significantly, the pseudosteady-state solution has lost mass as indicated by the fact that the total mass fraction of drug released approaches 1 - R/2 instead of the correct value of 1.

The end point of the solid lines, indicated by either an H or an S, represents the mass fraction of drug released during the time required for all of the drug to dissolve (*i.e.,* τ_f/ε). When the total amount of drug provided greatly exceeds its solubility limit (*i.e.,* R is small), undissolved drug remains for a long time. But as R approaches one, the drug excess over the solubility limit decreases with a consequent decrease in time for complete dissolution.

How does the cumulative amount of drug release vary with time (does the rate increase, decrease, or stay constant)? Is there a steady state? Consider formulations in which the drug is initially fully dissolved (i.e., R > 1) as well as initially a suspended solid (i.e., R < 1).

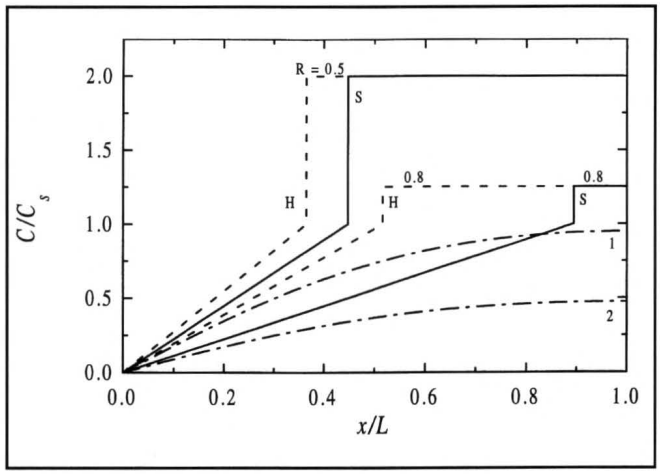

Figure 3. *Normalized concentration (C/C_s) as a function of position (x/L) when R=0.5, 0.8, 1, and 2 at τ/ε is 0.10 as predicted by the pseudosteady-state (S) and Higuchi (H) solutions (while undissolved solid remains) or by the dissolved solid solution when R ≥ 1.*

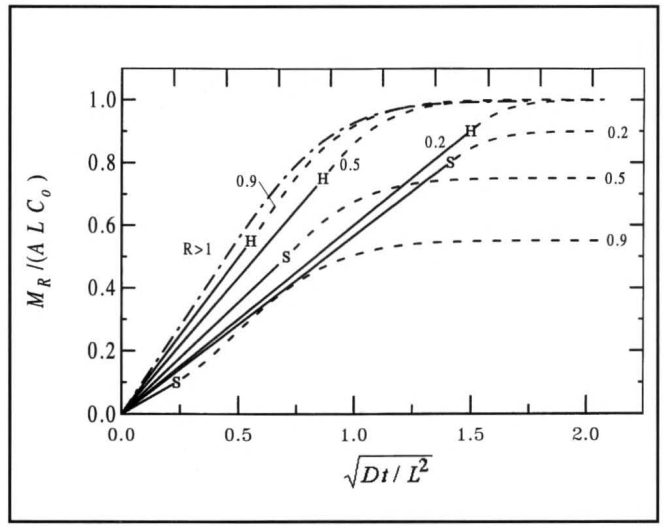

Figure 4. *Mass fraction released (i.e., M_R/ALC_o) as a function of* $\sqrt{\tau/\varepsilon} = \sqrt{Dt/L^2}$ *for R equal to 0.2, 0.5, 0.9, > 1 as predicted by the pseudosteady-state (S) and Higuchi (H) solutions (while undissolved solid remains) or by the dissolved solid solutions (indicated by dashed curves).*

As indicated in Eqs. (19) and (30) and illustrated in Figure 4, the mass fraction released is proportional to the square root of time as long as some drug remains as a suspended solid. When the formulation initially contains only dissolved drug, the mass fraction released is still proportional to the square root of time as long as less than about a third of the original mass is released. This problem does not reach steady state (except when all of the drug has left the formulation).

Federal regulations require that labels indicate the concentration of active ingredient in a topical formulation. If the concentration of a suspended active ingredient is the same, but the solubility in two formulations is different, which formulation will be more effective (i.e., deliver drug at a higher rate)?

The answer to this question is provided in Figure 4, which illustrates the case when the total amount of drug remains constant but the formulation is altered to increase the solubility limit C_s. The formulation with the higher solubility should deliver drug more rapidly. Increasing the solubility limit (increasing R) increases the amount of dissolved drug available for diffusion across the formulation. The Higuchi solution predicts this expected result (*i.e.,* that increasing R should increase the rate of drug release into the receptor solution). By contrast, the pseudosteady-state solution fails when R approaches 1, incorrectly predicting that the release rate is smaller when R = 0.9 than for R = 0.2 or 0.5.

How does increasing the amount of drug affect the cumulative mass released if the solubility limit is fixed? Consider formulations in which the drug is initially fully dissolved (i.e., R > 1) as well as initially a suspended solid (i.e., R < 1).

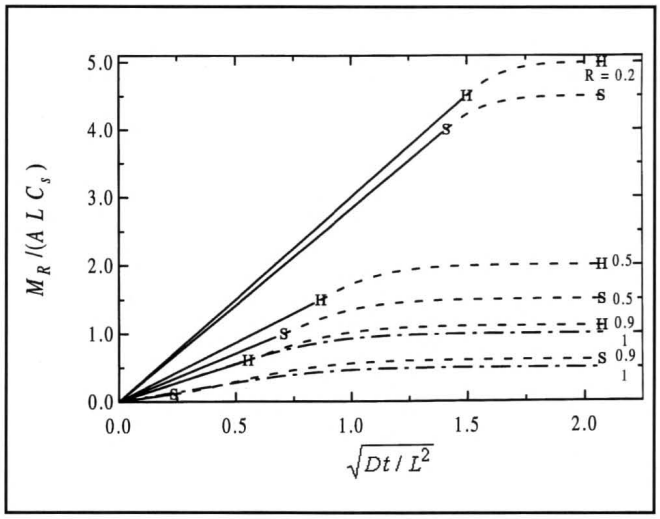

Figure 5. *Mass fraction released divided by R (i.e., $M_R/(ALC_s)$) as a function of $\sqrt{\tau/\varepsilon} = \sqrt{Dt/L^2}$ for R equal to 0.2, 0.5, 0.9, and 1 as predicted by the pseudosteady-state (S) and Higuchi (H) solutions (while undissolved solid remains) or by the dissolved solid solutions (indicated by dashed curves).*

If the solubility limit is fixed, increasing the initial drug concentration will cause R to decrease and will increase the release rate into the receptor solution, as shown in Figure 5. (Again, the pseudosteady-state solution erroneously predicts that decreasing R from 1 to 0.9 causes the release rate to decrease). If R < 1, the release rate is limited by the drug's solubility in the vehicle, and increasing the total drug concentration does not proportionally increase the release rate (*e.g.,* compare R = 1 and 0.5). The pseudosteady-state solution predicts that the rate of release is proportional to $\sqrt{C_o - C_s}$; the Higuchi solution predicts the release rate is proportional to $\sqrt{C_o - C_s/2}$.

A FINAL NOTE

In this paper we have used mass transfer from topical drug formulations to illustrate development of two pseudosteady-state solutions and provided several study questions that can be used to help students become better mathematical modelers.

NOMENCLATURE

A	Area of vehicle application
C	Concentration of drug in the vehicle, mass/volume
C_o	Original concentration of drug in the vehicle, mass/volume
C_s	Solubility concentration of drug in the vehicle, mass/volume
D	Effective diffusivity of drug through the vehicle
L	Thickness of the vehicle
m	Index on summation, Eqs. (32) - (35)
M_o	Mass of drug originally present in the formulation, ALC_o
M_R	Cumulative mass of drug appearing in the receiving chamber
M_{Rf}	Cumulative mass of drug appearing in the receiving chamber during the time required for all of the drug to dissolve
R	Ratio of the solubility concentration to the original drug concentration, C_s/C_o
t	Time since application of the drug suspension
x	Axial position in the vehicle

Greek Letters

δ	Dissolution front position in the vehicle
ε	Ratio of C_s to the difference between C_o and C_s, Eq. (6)
η	Dimensionless axial position in the vehicle, Eq. (6)
λ_m	Eigenvalue in Eqs. (32)-(35), $= (2m+1)\pi/2$
θ	Dimensionless concentration in the vehicle, Eq. (6)
τ	Dimensionless time, Eq. (6)
τ_f	Dimensionless time required for all of the drug to dissolve
χ	Dimensionless dissolution front position in the vehicle, Eq. (6)

REFERENCES

1. Paul, D.R., and S.K. McSpadden, "Diffusional Release of a Solute from a Polymer Matrix," *J. Membrane Sci.,* **1**, 33 (1976)
2. Higuchi, T., "Rate of Release of Medicaments from Ointment Bases Containing Drugs in Suspension," *J. Pharm. Sci.,* **50**, 874 (1961) ❐