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Dimensionless presentation for drug release from a coated pure drug bead: 1. Analysis

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Abstract

A set of dimensionless equations are presented to describe the release of a drug from a coated pure drug bead in a well stirred elution liquid. Dimensionless presentations for cumulative release and release rate over very wide ranges of dimensionless parameters are discussed. The work is presented in two parts, part 1 describing the analysis and part 2 the experiment.

Keywords: Drug release equations; Drug release parameters; Release curve; Burst release

1. Introduction

Different methods are available to control or to retard the release of an active agent ('drug' for simplicity). One common method is to coat the drug particle with a material that forms a stable coating layer. A coated particle may be in one of three forms in which the core is: (a) a bead of pure drug; (b) a matrix with dissolved drug; or (c) a matrix with dispersed drug. Comparison of these particles shows that form (a), a coated pure drug bead, has the following advantages: (1) the drug content per particle is at its maximum; (2) particle shape and construction are common and simple; (3) the release behavior is describable by a set of simple and directly applicable dimensionless equations; (4) and a constant or nearly constant drug release rate may be achieved under certain conditions. Items (1) and (2) are obvious. For item (1), the risk of overdose due to particle breakage may be reduced by reduction in core size. Items (3) and (4) are the subjects of this paper.

Drug release from a coated pure drug bead in a well stirred elution liquid of a given volume has been analyzed by Lu and Lee (1992) using pseudo-steady state assumptions. Their results are useful as: (a) a complete and exact analytical solution for drug release over the entire duration of release of a coated pure drug bead has not been found in the available literature although exact solutions that are limited to a part of a release lifetime exist; (b) exact or numerical solutions are usually too complex or inconvenient to be used directly; and (c) comparable solutions that will perform similar work have not been found. Their equations, however, are not applicable to drug release during the initial stage.

The equations of Lu and Lee (1992) are with dimensions. They may be transformed into di-

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mensionless equations by using appropriate dimensionless groups. Dimensionless equations can provide an overall view of all possible release behaviors. Experimental data for different systems and sources may also be correlated in dimensionless forms for comparison. Different drug release systems may be considered to be the same system if the dimensionless parameters are completely the same.

The purposes of this paper were as follows: (a) to transform the solutions of Lu and Lee (1992) into dimensionless forms and discuss the implications of the equations obtained; (b) to discuss drug release in the initial stage; (c) to unify release data; (d) to compare the results with the solution of Lu and Chen (1993); and (e) to extend application to the case of burst release.

2. The problem and the dimensionless equations

A pure drug bead of radius b cm is coated with a material so the radius of the coated particle is a cm. The coating forms a firm non-swelling porous shell. When this coated particle is placed in an elution liquid of volume V_e, the liquid diffuses into the core to dissolve the drug which then diffuses through the coating layer and is released into the elution liquid. The release time, t, is divided into two parts – before and after a critical time, t_s, which is the time when the solid drug in the core has just disappeared by dissolution. When $t \leq t_s$, the drug concentration in the core is at saturation concentration, C_s; when $t > t_s$, the concentration falls with time. Drug concentrations in the core, coating layer, and elution liquid are represented by C_c, C and C_e, respectively. K_a and K_b represent, respectively, the ratios C_e/C_a and C_c/C_b. K_a, K_b, and D, the effective diffusivity of the coating layer, are assumed to be constant.

The solutions for the above problem as obtained by Lu and Lee (1992) are now made dimensionless. The results are shown in Table 1. The columns from left to right show: time, the dimensionless equations, the equation numbers of source equations in Lu and Lee (1992), and definitions of the dimensionless groups. In the last column, Eq. 5–10 define, respectively: dimensionless cumulative release, Y; dimensionless time, X; dimensionless parameters, p, s; volume ratio of elution liquid to particle, V_r; and dimensionless critical time X_s. In these equations, a/b is the size ratio of particle to core and K_a/K_b denotes the final concentration ratio $C_{e,\infty}/C_{c,\infty}$ (Eq. 22, Lu and Lee, 1992). As $C_{e,\infty} \leq C_{c,\infty}$, K_a/K_b is unity at most. Eq. 11 shows that X_1 is equivalent to X shifted toward the right-hand side by $1/6$. The reason for the $1/6$ shift will be given later. Eq. 12 is analogous to Eq. 11. X_{1s} represents X_1 at $t = t_s$.

In Table 1, Eq. 1a and 1b represent dimensionless cumulative release before and after t_s; Eq. 2a and 2b represent the dimensionless release rate R, defined by $R \equiv dY/dX = dY/dX_1$, before and after t_s; Eq. 3 is for dimensionless critical time; and Eq. 4 is for total dimensionless cumulative release, Y_∞. These equations contain three dimensionless variables: p, s, and ρ_u/C_s which is the ratio of drug density to saturation concentration.

3. Implications of the dimensionless equations

Eq. 7 and 8 show that p and s are dependent on a/b, K_a/K_b, and V_r. If a/b is given, s represents the effect of K_a/K_b and V_r. If K_a/K_b is also given, s represents the effect of V_r. If $V_r = \infty$, then $s = \infty$, i.e., the case of a perfect sink. If V_r is very small, s is very small, and the situation may be such that the elution liquid may attain C_s before the exhaustion of the solid drug and therefore t_s does not exist; or if V_r is just so small that the elution liquid attains C_s at the exhaustion of solid drug, then the release rate at t_s is zero. The last two cases are special cases that are not encountered under normal testing conditions.

For a release system with the drug and the elution liquid specified, ρ_u, C_s, and therefore ρ_u/C_s, are specified. Drug release then depends on p and s. In the following sections, unless otherwise specified, a release system with $\rho_u/C_s = 2.19$ is used for calculations and discussions.

Table 1
Dimensionless equations for drug release from a coated pure drug bead

Time	Dimensionless equations		Eq. no. Lu and Lee (1992) [a]	Dimensionless groups	
$t \le t_s$, $X \le X_s$	$Y = \frac{s}{p}\left[1-\exp\left(-\frac{p}{s}X_1\right)\right]$	(1a)	(11a)	$Y \equiv \frac{M_t}{4\pi ab(a-b)C_s(K_a/K_b)}$	(5)
	$\frac{dY}{dX} = \exp\left(-\frac{p}{s}X_1\right)$	(2a)	(11b)	$X \equiv \frac{Dt}{K_a(a-b)^2}$	(6)
$t > t_s$,	$Y = \frac{1}{p}\left[\left(\frac{\rho_u}{C_s}-1\right)+\left(1-\frac{\rho_u/C_s}{1+s}\right)\right.$		(19a)	$p \equiv 3\frac{K_a}{K_b}\frac{a}{b}\left(\frac{a}{b}-1\right)$,	(7)
$X > X_s$	$\left.\cdot\left[1-\exp\left(-\left(\left(1+\frac{1}{s}\right)pX_1+(1+s)\ln\left(1-\frac{\rho_u/C_s-1}{s}\right)\right)\right)\right]\right]$	(1b)		$s \equiv \frac{K_a}{K_b}V_r\left(\frac{a}{b}\right)^3$	(8)
	$\frac{dY}{dX} = \left(1-\frac{\rho_u/C_s-1}{s}\right)$		(19b)	$V_r \equiv \frac{V_e}{V_p}$	(9)
	$\cdot\exp\left[-\left[\left(1+\frac{1}{s}\right)pX_1+(1+s)\ln\left(1-\frac{\rho_u/C_s-1}{s}\right)\right]\right]$	(2b)		$X_s \equiv \frac{Dt_s}{K_a(a-b)^2}$	(10)
$t = t_s$, $X = X_s$	$X_{1s} = -\frac{s}{p}\ln\left(1-\frac{\rho_u/C_s-1}{s}\right)$	(3)	(13a)	$X_1 \equiv X - \frac{1}{6}$	(11)
$t = t_\infty$	$Y_\infty = \frac{s}{1+s}\frac{1}{p}\frac{\rho_u}{C_s}$	(4)	(20)	$X_{1s} \equiv X_s - \frac{1}{6}$	(12)
Crank (1975)	$Y = X - \frac{1}{6} - \frac{2}{\pi}\sum_1^\infty \frac{(-1)^n}{n^2}\exp(-n^2\pi^2X)$	(6.52)			
	$t \to \infty$, $Y = X - \frac{1}{6}$	(13)			

[a] See Appendix for equations.

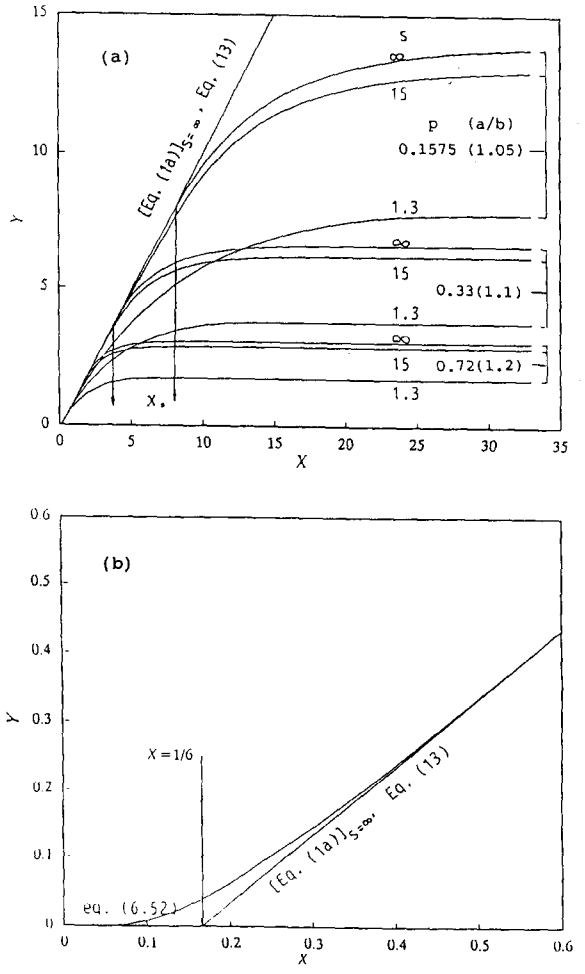

Fig. 1. Dimensionless cumulative release vs dimensionless time. (a) Overall. (b) Small X.

3.1. Dimensionless cumulative release curve Y vs X

The dimensionless cumulative release is calculated as follows: (i) use Eq. 3 to find X_s; (ii) use Eq. 1a to find Y for given X when $X \leq X_s$, and Eq. 1b when $X > X_s$. Fig. 1a shows the results for cases $p = 0.1575$, 0.33, 0.72, each with $s = \infty$, 15, 1.3. The parenthesized a/b after p represents the magnitude of a/b calculated from p assuming $K_a/K_b = 1$. This is shown to indicate the effect of a/b on the curve. The X_s for cases $s = \infty$, $p = 0.1575$ and $s = \infty$, $p = 0.33$ are indicated by arrows. Fig. 1a shows that the effect of s on the curve is significant when p is small. For each p, the effect of s is less significant when $\sim 15 < s \leq \infty$, but becomes significant when $s \ll \sim 15$.

Eq. 1a, however, does not apply to drug release during the initial stage. In this stage, the amount of drug that has been released is still very small and the condition of a perfect sink ($s = \infty$) may be assumed. Therefore, drug concentrations on both sides of a coating layer are $C_b = C_s$, $C_a = 0$, implying that $K_b = K_a = 1$. This initial stage problem has been solved by Crank (1975) and the solution is listed as Eq. 6.52 in Table 1. Eq. 6.52 reduces to Eq. 13 when $t \to \infty$. Inspection of Eq. 1a shows that for $s = \infty$, Eq. 1a reduces to $Y = X_1$. This equation will be identical to Eq. 13 if $X_1 = X - 1/6$. This is why X_1 is defined as Eq. 11. The plots of $[\text{Eq. 1a}]_{s\to\infty}$, Eq. 13, and Eq. 6.52 for very small X are shown in Fig. 1b. Fig. 1a and b together represent the complete Y vs X curves.

3.2. Fractional cumulative release curve Y/Y_∞ vs X

Fractional cumulative release curves for cases $p = 0.1575$ 0.33, 0.72, each with $s = \infty$, 15, 1.3, are shown in Fig. 2. For a given particle, as $Y/Y_\infty = M_t/M_{t\infty}$, the curves are equivalent to the conventional fractional cumulative release curves. Fig. 2 shows that at large p, the effect of s decreases.

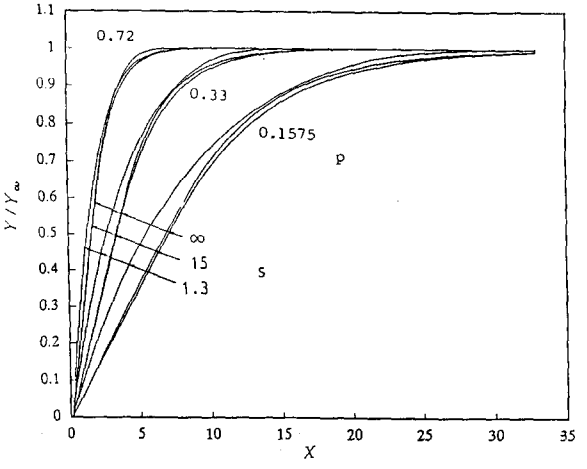

Fig. 2. Fractional cumulative release vs dimensionless time.

The effect of s is negligible for $15 \leq s < \infty$ but not for $s \ll 15$, especially at small p for which, with the decrease in s, there is a significant increase in Y/Y_∞. This is due to the fact that, although both Y and Y_∞ decrease with decreasing s, the decrease in Y_∞ is greater than that in Y, and therefore Y/Y_∞ increases.

Fig. 2 also shows that with the increase in p, the curves shift toward the left-hand side. This may be explained by considering two cases where the only difference is in the ratio a/b. The relation among a/b, b, and $a-b$ is shown in Fig. 3. It shows that for particles with the same coating thickness, the greater the ratio a/b, the smaller the bead radius b, and therefore the lower the drug content. Thus, the release life shortens as a/b (and therefore p) increases. The curve therefore shifts toward the left-hand side.

3.3. Fractional cumulative release curve Y/Y_∞ vs X/X_s

When the abscissa in Fig. 2 is changed to X/X_s, Fig. 4a results. It shows that for a given s, the effect of p is small and that the effect of p decreases with decreasing s. For each s, as p decreases, there is a limiting curve. As $K_a/K_b \leq 1$ and $p \propto K_a/K_b$, thus, with $K_a/K_b \ll 1$, the effect of p quickly disappears and Fig. 4a will be replaced by Fig. 4b where the curves are the limiting curves that appear in Fig. 4a. Fig. 4b shows that cumulative release curves are unified with respect to p.

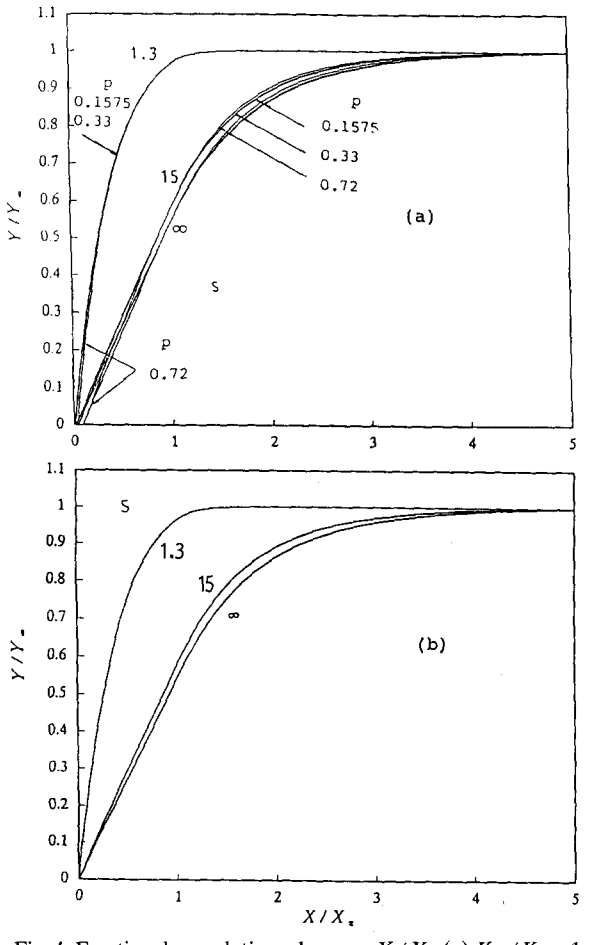

Fig. 4. Fractional cumulative release vs X/X_s. (a) $K_a/K_b \leq 1$. (b) $K_a/K_b \ll 1$.

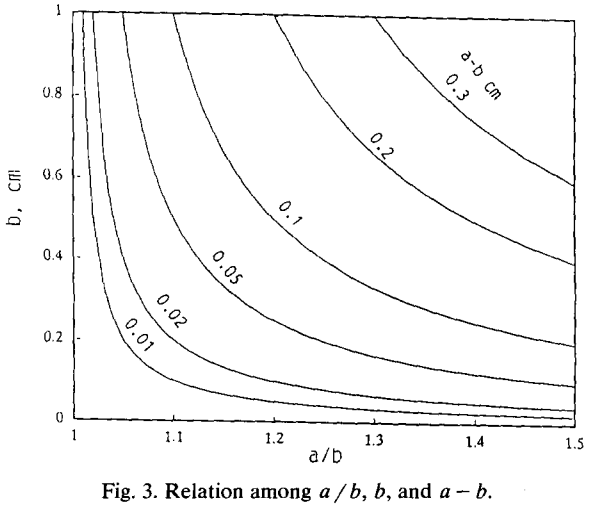

Fig. 3. Relation among a/b, b, and $a-b$.

3.4. Dimensionless release rate dY/dX vs X

Fig. 5a–c shows rate R as calculated by Eq. 2a when $X \leq X_s$ and by Eq. 2b when $X > X_s$. The release rate in the initial stage is calculated by differentiating Crank's Eq. 6.52. Critical times X_s are indicated for few of the cases in Fig. 5.

Fig. 5a is for cases with perfect sink. It shows that for $X \leq X_s$, R is unified to 1, and for $X > X_s$, R falls continuously to zero. The rate calculated from Crank's equation shows that R increases

from 0 to 1 and then remains at 1 for the rest of the time. The real rate curve is: R increases from 0 to 1, remains at 1 until $X = X_s$, and decreases to zero when $X > X_s$. Fig. 5a shows that the smaller the magnitude of p, the longer the dimensionless time over which the rate is constant. When p is about 0.72 or greater, the time for constant R is very short or does not exist. In the following sections, the initial release rate is not calculated unless otherwise noted.

Fig. 5b is for cases with $s = 15$. Two cases of perfect sink are included for comparison. For $s = 15$, R at critical time is around 0.9. This is a relatively small change in R for the large change in s of infinity to 15. Thus, for particles with small p, a period of nearly constant rate exists when $\sim 15 < s < \infty$.

Fig. 5c shows the effect of very small s on R for the case $p = 0.1575$. One perfect sink case is shown for comparison. The effect of s on R is significant when s is very small. Very small s may result from very small V_r and or K_a/K_b.

3.5. Dimensionless release rate dY/dX vs X/X_s

When the abscissa in Fig. 5 is changed to X/X_s, a compact presentation of rate curves for each s results. This is shown in Fig. 6a–c for $s = \infty$, 15, 1.3. Each plot shows that the effect of p on the curve is small and that as p decreases, a limiting curve exists. Since $K_a/K_b \leq 1$ and since $p \propto K_a/K_b$, thus, for each s, when $K_a/K_b \ll 1$, the rate curves will be represented by the limiting curve of that s, i.e., the rate curves are unified with respect to p. Fig. 6d shows such a result for $s = 15$.

4. The effect of parameter ρ_u/C_s

Parameter ρ_u/C_s relates the drug and the environmental liquid. For a given drug, small ρ_u/C_s represents an elution liquid of high drug solubility, and large ρ_u/C_s, an elution liquid of low drug solubility. For the former, rate control is important, for the latter, coating may be for protection of a drug from its environment rather than for rate control.

Fig. 7a and b shows the respective plots of Y/Y_∞ vs X/X_s and R vs X/X_s for $\rho_u/C_s = 8$. The parameters are $s = \infty$, 15, each with $p = 0.1575, 0.33, 0.72$. Fig. 7 shows that the curves are unified with respect to p. The effects of ρ_u/C_s

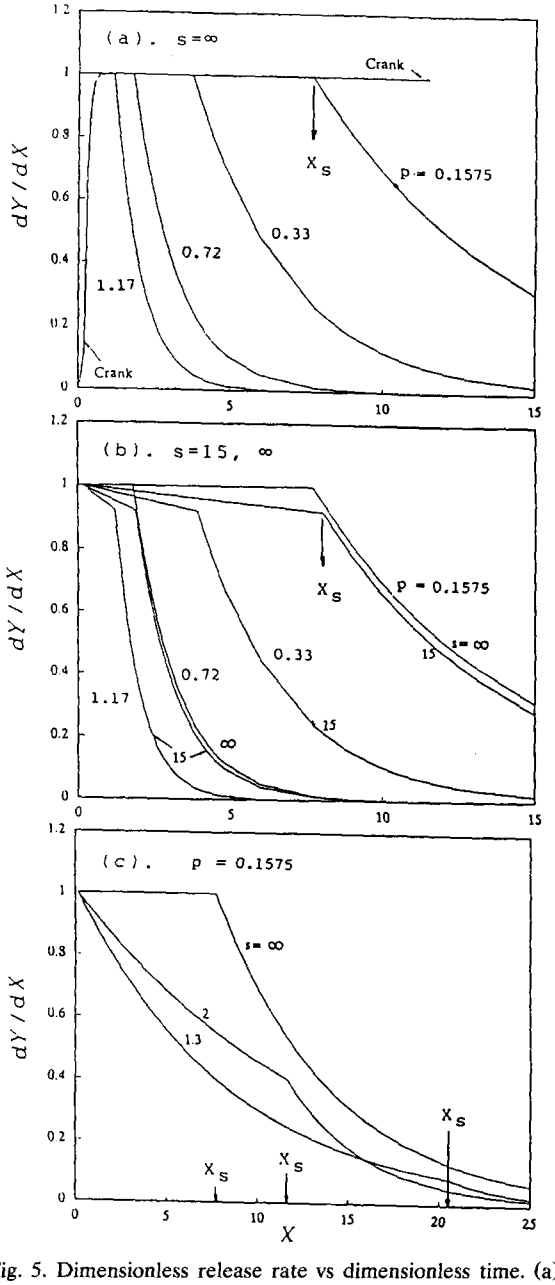

Fig. 5. Dimensionless release rate vs dimensionless time. (a) $s = \infty$. (b) $s < 15, \infty$. (c) $p = 0.1575$.

on the curves are clear on comparing Fig. 7a with Fig. 4a and b, and Fig. 7b with Fig. 6a and b. As ρ_u/C_s increases, p becomes not important, and the time after X_s becomes comparable or shorter than that before X_s.

The effects of ρ_u/C_s on X_s at various s and p are shown by plotting Eq. 3 in the form of Fig. 8. The effect of s on the curve becomes apparent as ρ_u/C_s increases. This is because when ρ_u/C_s is large or when C_s is small, the release rate and the amount of drug that can be released are both decreased. Increase in s or V_r is therefore beneficial to drug release and X_s therefore decreases. When ρ_u/C_s is small, or when C_s is large, the release rate is high and although the amount that can be released decreases with the decrease in s or V_r, the amount that is released is still substantial because of the high saturation concentration. Thus, the effect of s or V_r on X_s becomes less significant.

5. Comparison of Eq. 1b and 2b with the solutions of Lu and Chen (1993)

Eq. 1b and 2b are for $t > t_s$. They are compared with the exact solution of Lu and Chen (1993) which is for drug release from a coated particle into an elution liquid of a given volume, with the coating layer initially free of drug, the core containing dissolved drug, and the initial drug concentration in the core at C_s. It is clear

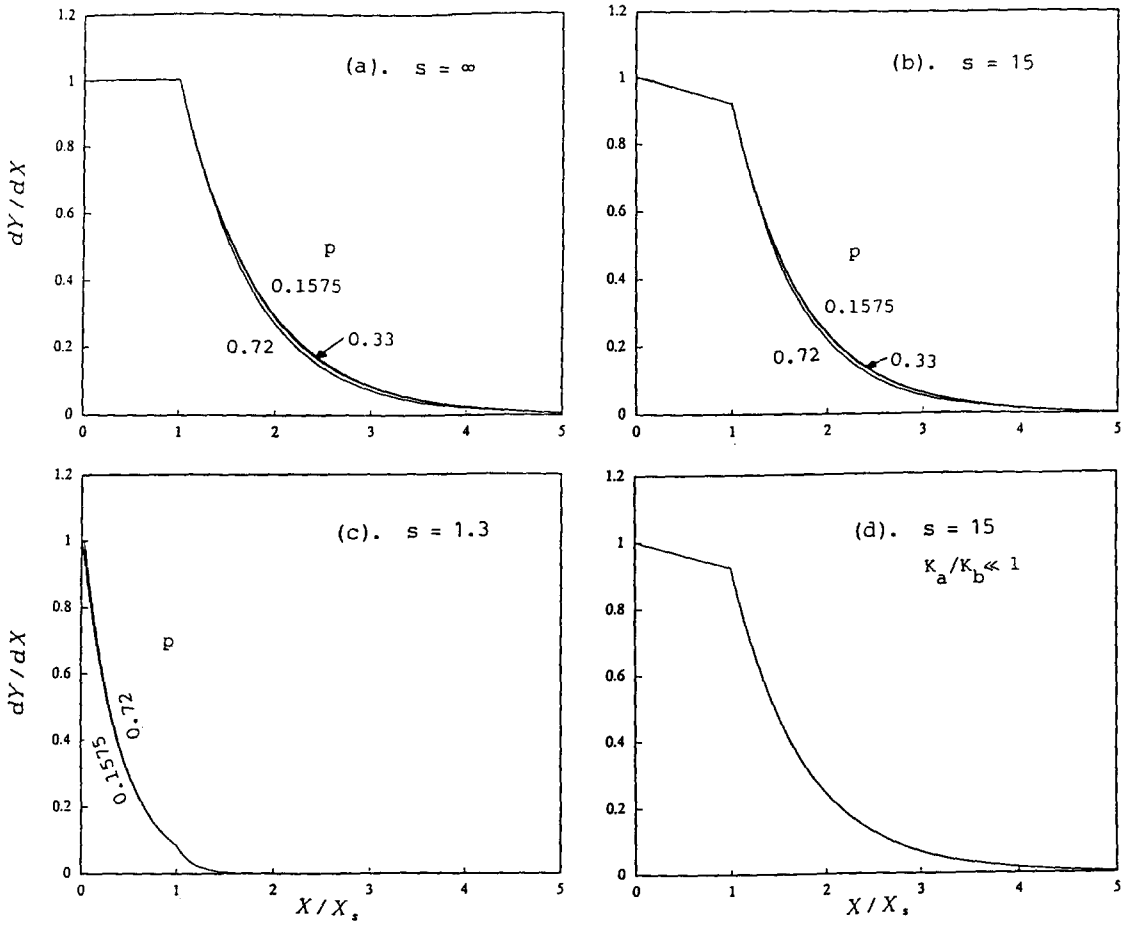

Fig. 6. Dimensionless release rate vs X/X_s. (a–c) for $K_a/K_b \leq 1$, (d) for $K_a/K_b \ll 1$.

that the initial conditions of the above two problems are different and therefore the solutions should be different. However, as time increases, the effect of the initial conditions should fade away. Thus, for particles with coatings that are not thick, the two solutions should approach each other at large time. For comparison purposes, Eq. 1b and 2b have to be modified to the conditions that $t_s = 0$ and $(C_e)_{t_s=0} = 0$. The results are shown by Eq. 14 and 15 of Table 2. The solution of Christensen et al. (1980) may also be reduced to these equations.

The comparison of Eq. 14 and 15 with the exact solution is shown in Fig. 9. The plots in rows a–c represent, respectively, the cases of $s = \infty$, 15, and 1.5. The plots columnwise show, respectively, Y vs X, Y/Y_∞ vs X and dY/dX vs X. In each plot, the cases of $p = 0.1575$, 0.33, 0.72, 1.17, 2.25 are shown. The curves calculated by Eq. 14 and 15 are marked $\tilde{p}$ for pseudo-steady state solution, and the curves calculated by the exact solution are designated by E.

The plots in the first column show that: (1) $\tilde{p}$ curves lie above the E curves; (2) the difference between $\tilde{p}$ and E curves are dependent on s; (3) for $s = \infty$, $\tilde{p}$ and E curves for Y coincide with each other at large time; (4) for small s, the difference between $\tilde{p}$ and E curves persists to large time and this difference increases as s decreases; and (5) $\tilde{p}$ curves generally follow E curves. The plots in the second column show that all Y/Y_∞ curves eventually attain 1 at large time, a result that is due to the nature of the plot. These plots are more informative about the dif-

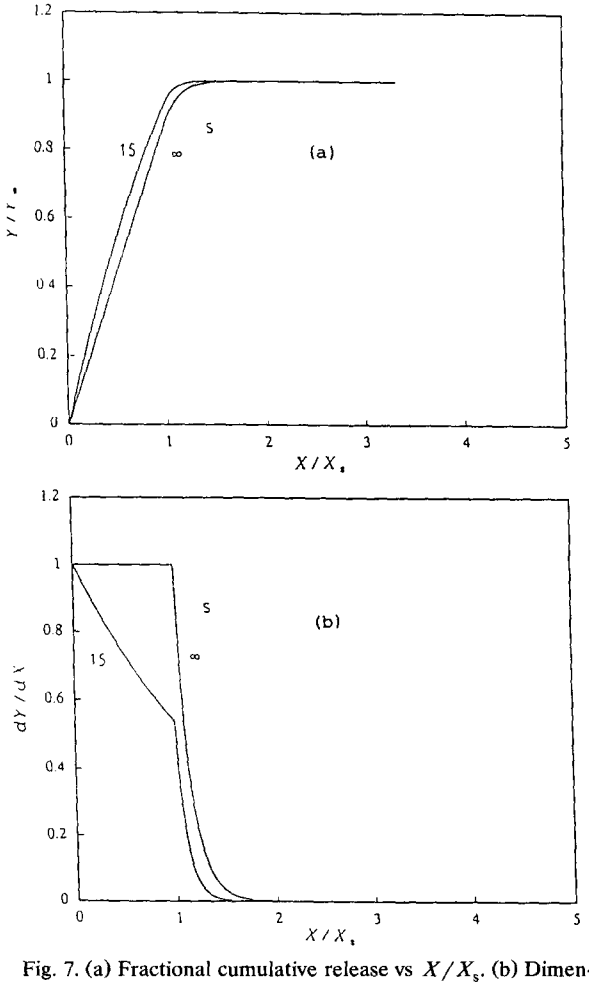

Fig. 7. (a) Fractional cumulative release vs X/X_s. (b) Dimensionless release rate vs X/X_s. For $\rho_u / C_s = 8$; $s = \infty$, 15; and $p = 0.1575$, 0.33, 0.72.

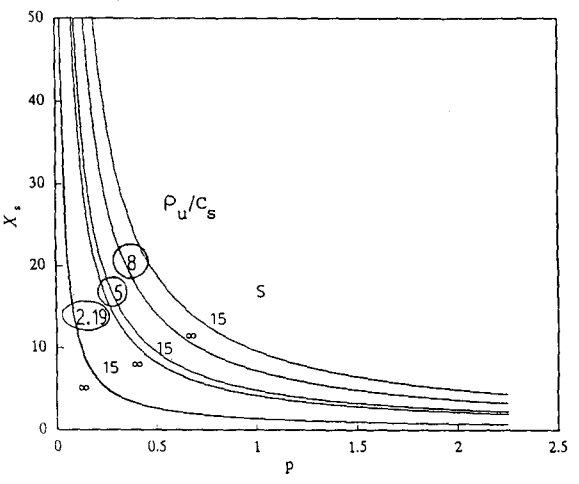

Fig. 8. The effect of ρ_u / C_s on dimensionless critical time.

Table 2
Equations for the case $t_s = 0$, $(C_e)_{t_s=0} = 0$

Time	Dimensionless equations	
$X > X_s$	$Y = \frac{s}{p(s+1)}\left[1 - \exp\left(-\frac{s+1}{s} pX_1\right)\right]$	(14)
	$\frac{dY}{dX} = \exp\left[-\frac{s+1}{s} pX_1\right]$	(15)

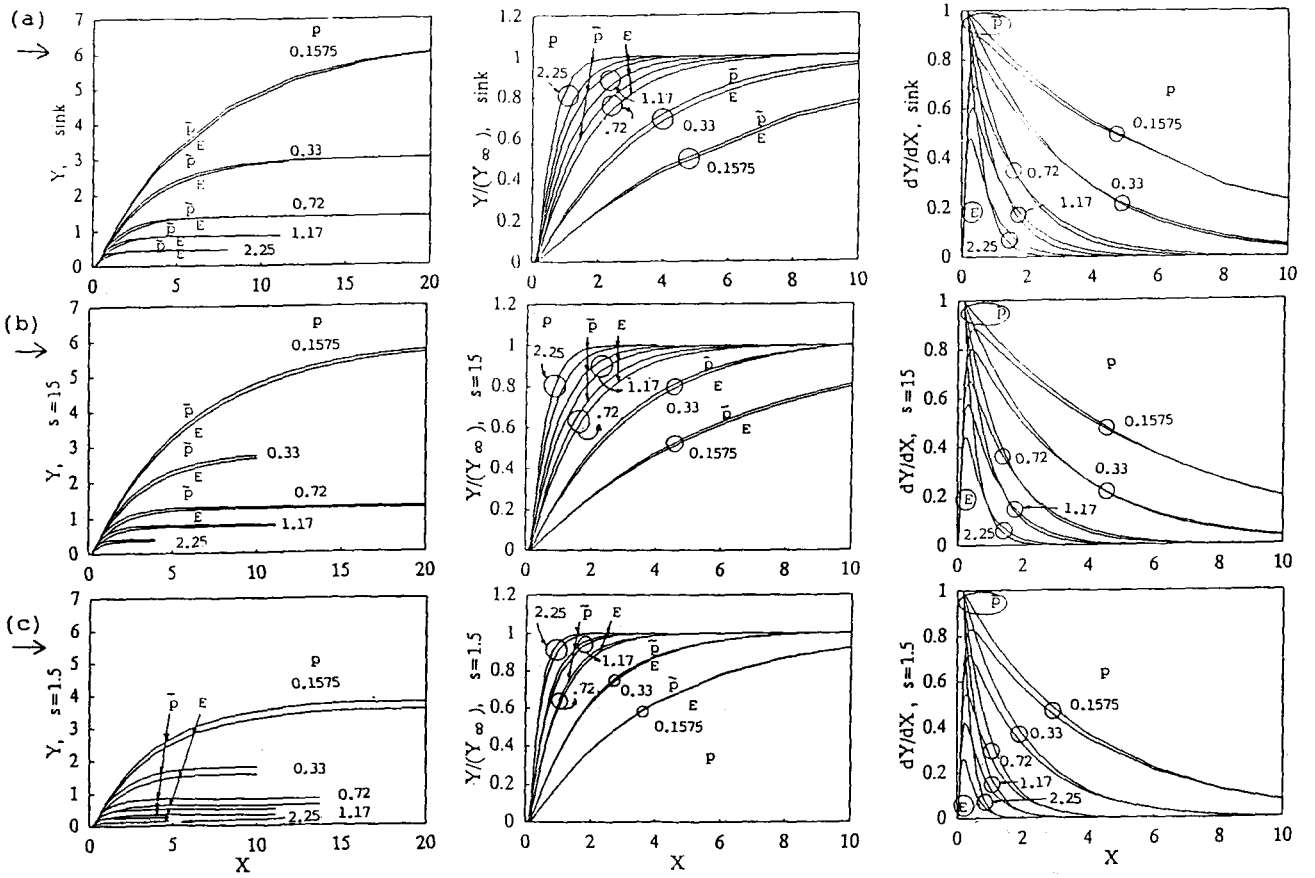

Fig. 9. Comparison of the pseudo-steady state solution, $\bar{p}$, with the exact solution of Lu and Chen (1993), E.

ferences between the two curves in the region where the curves bend to approach $Y/Y_\infty = 1$.

The plots in the third column are for release rate R. They show that: (1) $\tilde{p}$ curves start with $dY/dX = 1$ and decreases monotonically with increasing X, while E curves start with $dY/dX = 0$ and pass maxima before decreasing with increasing X; (2) if p is small, $\tilde{p}$ and E curves will eventually coincide with each other at large X, and this agreement occurs early when s is large; (3) if p is not small, $\tilde{p}$ curves fall below E curves at large X, with decreasing difference between the two curves for decreasing s; and (4) at large time, $\tilde{p}$ curves in general follow E curves.

6. Burst release

For particles that have been in storage for some time, the coating layer may become saturated with the drug and therefore drug release will be instant and initial release rate infinitely large. This is the case of burst release.

In the initial stage of drug release, the conditions $C_b = C_s$ and $C_a = 0$ may be assumed to exist at the surfaces of the coating layer. For this problem, Crank's Eq. 6.50 which is shown in Table 3 applies. This equation, in dimensionless form, is Eq. 16. As $t \to \infty$, Eq. 16 reduces to Eq. 17 which, unlike Eq. 13, is dependent on a/b. Thus, by replacing Eq. 11 and 12 of Table 1 with Eq. 18 and 19 of Table 3, the dimensionless equations listed in Table 1 become applicable to the burst release case.

Fig. 10a shows Y vs X in the case of burst release. Fig. 10b is a magnified plot of Fig. 10a for the range of very small X. To match the Y curves in Fig. 10a with those in Fig. 10b, a/b, rather than p, has to be specified. In Fig. 10a, when X decreases, curves of the same a/b, like curves 1 and 2, or curves 3 and 4, converge,

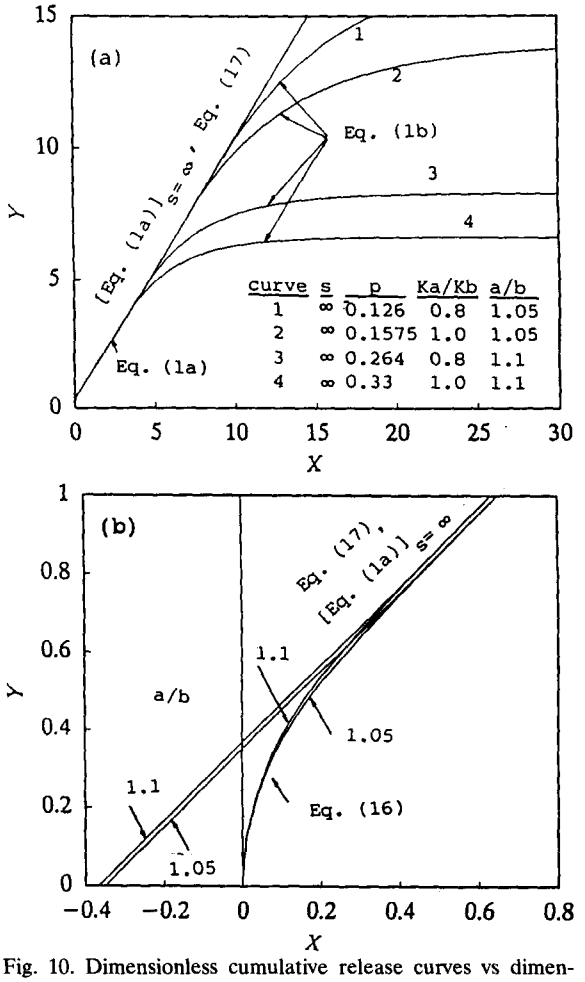

Fig. 10. Dimensionless cumulative release curves vs dimensionless time for burst case. (a) Overall. (b) Small X_s.

Table 3
Equations for burst release

Crank's (1975) equation:

$$C = \frac{C_1 b}{r} - \frac{C_1 b(r-b)}{r(a-b)} + \frac{2}{r\pi}\sum_{n=1}^{\infty}\frac{1}{n^2}\exp(-n^2\pi^2 X) \quad (6.50)$$

Dimensionless cumulative release derived from Eq. 6.50:

$$Y = X + \frac{a}{3b} - \frac{2}{\pi^2}\frac{a}{b}\sum_{n=1}^{\infty}\frac{1}{n^2}\exp(-n^2\pi^2 X) \quad (16)$$

As $t \to \infty$;

$$Y = X + \frac{a}{3b} \quad (17)$$

Dimensionless equations listed in Table 1 apply to burst release. However, Eq. 11 and 12 should be modified as follows:

$$X_1 \equiv X + \frac{a}{3b_a} \quad (18)$$

$$X_{1s} \equiv X_s + \frac{a}{3b} \quad (19)$$

respectively, to a curve specific to that a/b. In Fig. 10, however, the four curves appear to converge to one curve. This is due to the large range of X covered by the abscissa. In Fig. 10b, curves for each a/b are apparent. Fig. 10a and b together represent complete Y curves for the entire release lives of particles.

7. Conclusions

Drug release from a coated pure drug bead into a given volume of well stirred elution liquid was investigated in dimensionless form over wide ranges of variables. Release systems that have the same dimensionless parameters ρ_u/C_s, p, and s may be treated as the same system. For practical cases, fractional cumulative release and dimensionless release rate, plotted in the forms Y/Y_∞ vs X/X_s and dY/dX vs X/X_s, are respectively unified with respect to p for each s. Release rate R for $t \le t_s$ is unified to 1 or near one when s is large. For small s, R for $t \le t_s$ shows different degrees of declines with time.

By simple modifications, the dimensionless equations are made applicable to the burst release case.

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Appendix

The following equations and equation numbers are from Lu and Lee (1992):

$$M_t = \frac{V_c C_s}{\alpha}[1 - \exp(-N_1 t)] \tag{11a}$$

$$\frac{dM_t}{dt} = \frac{V_c C_s}{\alpha} N_1 \exp(-N_1 t) \tag{11b}$$

$$M_t = V_c C_s \left\{ (\beta - 1) + \frac{1 - \alpha(\beta - 1)}{1 + \alpha} \times [1 - \exp[-N_2(t - t_s)]] \right\} \tag{19a}$$

$$\frac{dM_t}{dt} = V_c C_s \frac{1 - \alpha(\beta - 1)}{(1 + \alpha)} N_2 \exp[-N_2(t - t_s)] \tag{19b}$$

$$t_s = -\frac{1}{N_1}\ln[1 - \alpha(\beta - 1)] \tag{13a}$$

$$M_{t,\infty} = \frac{W_u}{1 + \alpha} \tag{20}$$

where

$$N_1 \equiv \frac{4\pi D}{K_a V_e}\frac{ab}{a - b} \tag{6c}$$

$$N_2 \equiv \frac{1 + \alpha}{\alpha} N_1 \tag{17b}$$

$$\alpha \equiv \frac{K_b V_c}{K_a V_e} \tag{9a}$$

$$\beta \equiv \frac{W_u}{V_c C_s} \tag{13b}$$

Nomenclature

- a radius of particle, cm
- b radius of pure drug bead, cm
- C concentration of drug in coating layer; C_a, C at $r = a$; C_b, at $r = b$, g/cm^3
- C_c concentration of drug in core; $C_{c,\infty}$ is C_c at the end of drug release, g/cm^3
- C_e concentration of drug in elution liquid; $C_{e,\infty}$ is C_e at the end of drug release, g/cm^3
- C_s saturation concentration of drug in elution liquid, g/cm^3
- D effective diffusivity, cm^2/s
- K_a, K_b $K_a = C_e/C_a, K_b = C_c/C_b$, –
- M_t cumulative release per particle at $t = t$; M_{t_s}, at t_s; $M_{t\infty}$, at t_∞, g
- n index, –
- p dimensionless parameter, defined by Eq. 7, –
- s dimensionless parameter, defined by Eq. 8, –
- t time; t_∞, infinite time; t_s, time at which

solid drug bead has just disappeared by dissolution, s

V volume; V_e, volume of elution liquid; V_p, volume of coated particle, cm^3

V_r volume ratio of elution liquid to coated particle, –

W_u initial mass of urea, g

X dimensionless time defined by Eq. 6; X_1, by Eq. 11; X_{1s}, by Eq. 12, –

Y dimensionless cumulative release defined by Eq. 5; Y_∞, Y at the end of release test, –

ρ_u density of drug, g/cm^3

References

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