International Journal of Pharmaceutics 400 (2010) 131–137

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Modeling of dispersed-drug delivery from planar polymeric systems: Optimizing analytical solutions

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ARTICLE INFO

Article history:
Received 16 April 2010
Received in revised form 20 August 2010
Accepted 27 August 2010
Available online 21 September 2010

Keywords:
Mathematical modeling
Dispersed drug
Moving front
Refined Integral Method
Drug release

ABSTRACT

Analytical solutions for the case of controlled dispersed-drug release from planar non-erodible polymeric matrices, based on Refined Integral Method, are presented. A new adjusting equation is used for the dissolved drug concentration profile in the depletion zone. The set of equations match the available exact solution. In order to illustrate the usefulness of this model, comparisons with experimental profiles reported in the literature are presented. The obtained results show that the model can be employed in a broad range of applicability.

1. Introduction

The modeling of the diffusional release of a dispersed or dissolved solute from a polymeric matrix is a problem of special interest in the area of the controlled release of pharmaceuticals or chemicals. The mathematical analysis of the release kinetics is often complicated by the presence of a moving diffusional front separating the undissolved core and the partially extracted region (Cabrera et al., 2006). The mathematical descriptions of such mass transfer problems are known as moving boundary problems or Stefan problems.

In the case of a planar non-erodible polymeric matrix, the first effort to analyze the kinetics of release was made by Higuchi (1961). This author proposed a pseudo-steady state approximation (PSSA) to obtain an analytical solution for the slab under perfect sink condition. Higuchi's results have been applied frequently to the controlled release of drug in where the initial solute loading per unit volume (A) is greater than the solute solubility in the polymeric matrix (C_s) (Higuchi, 1963; Roseman and Higuchi, 1970; Paul and McSpadden, 1976; Paul, 1985; Wu and Zhou, 1999; Siegel, 2000; Zhou and Wu, 2002). However in the limit of $A \to C_s$, the PSSA introduces considerable error giving less precise results (Lee, 1980; Paul, 1985; Zhou et al., 2005; Helbling et al., 2010). One example of a system that represents this limit situation is the commercial transdermal patch Trial SAT® 50mcg manufactured by Laboratorios BETA S.A. (Argentina). In this Transdermal Administration System the A/Cs ratio is 1.15 as was reported by the manufacturer (personal communication). As will be seen later, the Higuchi model fails when trying to predict the cumulative amount of drug released from this system. This drawback was removed by Paul and McSpadden (1976) who achieved an exact solution for slabs under sink condition. Unfortunately, the exact solution involves a transcendental expression which is cumbersome for routine usage. Other authors have also modeled the release of solute from planar matrices using various strategies (Lee, 1980; Paul, 1985; Bechard and McMullen, 1986; Wu and Zhou, 1999; Tongwen and Binglin, 2000; Chen and Lee, 2002). Lee applied the Refined Integral Method (RIM) to develop an approximate explicit analytical solution which is simpler than McSpadden's solution but more accurate than Higuchi's results for small A/C_s ratio (Lee, 1980).

The pseudo-steady state approximation assumes a linear concentration profile in the dissolved solute zone, which is valid only when the solute loading is in great excess of the solute solubility ($A \gg C_s$). In reality, however, the solute solubility, practical dosage level and rate requirements limit the loading to be not in great excess of the solubility (Langer, 1980; Chien, 1992; Ranade and Hollinger, 2004). To obtain a more general analytical solution that can be used in a wide range of A/C_s ratios, Lee replaced the linear concentration distribution by an approximate function. This function was a polynomial of grade two.

The purpose of the present work was to derive an explicit analytical solution for the case of dispersed-drug controlled release from non-erodible planar matrices that fits better the exact solution. In order to achieve the aim, a new adjusting equation for

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doi:10.1016/j.ijpharm.2010.08.043

Nomenclature

A	initial drug loading in matrix (g/cm^3)
C	drug concentration in matrix (g/cm^3)
C_s	maximum drug solubility in matrix (g/cm^3)
D_p	drug diffusion coefficient in matrix (cm^2/s)
f_{DR}	$Q/A\,R$, fraction of drug released (dimensionless)
n	adjusting exponent (dimensionless)
Q	cumulative amount of drug released per unit area (g/cm^2)
r	coordinate along the matrix thickness (cm)
R	matrix thickness (cm)
$S(t)$	position of dissolution–diffusion moving front (cm)
t	time (s)
x	r/R, coordinate along the matrix thickness (dimensionless)

Greek symbols

$\delta(t)$	$S(t)/R$, position of the dissolution–diffusion moving front (dimensionless)
θ	C/C_s, drug concentration in matrix (dimensionless)
ξ	integration variable (dimensionless)

the dissolved drug concentration profile in the depletion zone was used.

2. Model development

The mathematical model is developed for planar single-layer devices containing solid drug particles. The system is schematically illustrated in Fig. 1.

The assumptions of the model to be mathematically formulated are the following: (i) the system is a planar single-layer device; (ii) the device is considered as an isotropic medium; (iii) the device is composed by a polymeric matrix that contain solid drug particles dispersed in its interior; (iv) the initial distribution of the drug in the polymeric matrix is homogeneous; (v) the initial drug loading in the matrix is higher than the maximum drug solubility in the polymer; (vi) for simplicity, all the drug particles have the same size and a spherical form; (vii) the polymeric matrix is inert, unswellable and non-erodible; (viii) the dissolution of the solid drug particles in the polymeric matrix occurs at a high rate and does not constitute a controlling step of the general release process; (ix) the rate controlling step of the release process is the drug diffusion across the polymeric matrix, which is described according to Fick's laws; (x) the mass transport of drug is assumed to be effectively one-dimensional; (xi) the drug diffusion coefficient in the polymeric matrix is considered constant; (xii) resistance to external mass transfer is negligible; (xiii) the volume of the release medium is considered infinite to ensure the "sink" condition; (xiv) there exist a drug depletion zone with a thickness S. This thickness increases with time and as more solid drugs elute out of the device, thus leading to the inward advancement of the interface of the dispersed-drug zone/depleted drug zone, phenomenon commonly referred to as "dissolution–diffusion moving front" (xv) the model formulated is valid till all solid drug particles dissolve in the polymer and no discrete crystals remains in the device. This stage is achieved when the "dissolution–diffusion moving front reaches $r = 0$; (xvi) at the initial time ($t = 0$), the elution medium has not been yet in contact with the device and therefore there is no depletion zone. It is considered that the "dissolution–diffusion moving front" is outside of the device ($S = R$); (xvii) at $r = 0$ there is an impermeable coating; there is no drug release through that surface;

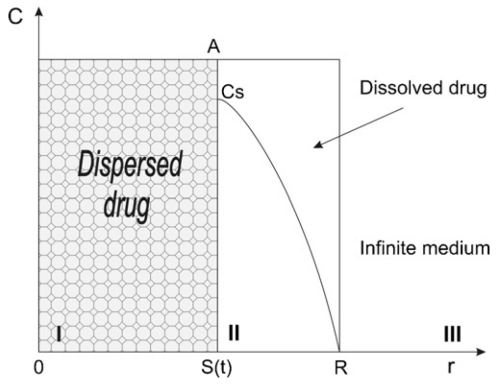

Fig. 1. Schematic illustration of drug concentration profile in a non-erodible polymeric device. I, dispersed drug zone; II, dissolved drug zone; and III, release medium.

The general diffusion equation describing the concentration distribution C in the matrix after exposing it to a well stirred solution is (Crank, 1975):

$$\frac{\partial C}{\partial t} = D_p \frac{\partial}{\partial r}\left(\frac{\partial C}{\partial r}\right) \quad S(t) < r < R \tag{1}$$

where C is the drug concentration in the matrix, t is the time, D_p is the drug diffusion coefficient in matrix, r is the coordinate along the matrix thickness, $S(t)$ is the position of the dissolution–diffusion moving front and R is matrix thickness.

Assuming equilibrium between the surface and the external fluid at all t, the initial and boundary conditions are

$$C(R, t) = 0 \tag{2}$$

$$C(S(t), t) = C_s \tag{3}$$

$$D_p \frac{\partial C}{\partial r} = (A - C_s)\frac{\partial S}{\partial t} \quad r = S(t) \tag{4}$$

$$S(0) = R \tag{5}$$

With reduced dimensionless variables defined as

$$x = \frac{R - r}{R},\ \delta(t) = \frac{R - S(t)}{R},\ \theta = \frac{C_s - C}{C_s}$$

a more general set of equation is obtained:

$$\frac{\partial \theta}{\partial t} = \frac{D_p}{R^2}\frac{\partial}{\partial x}\left(\frac{\partial \theta}{\partial x}\right) \quad 0 < x < \delta(t) \tag{6}$$

$$\theta(0, t) = 1 \tag{7}$$

$$\theta(\delta(t), t) = 0 \tag{8}$$

$$\frac{\partial \theta}{\partial x} = \left(1 - \frac{A}{C_s}\right)\frac{R^2}{D_p}\frac{\partial \delta}{\partial t} \quad x = \delta(t) \tag{9}$$

$$\delta(0) = 0 \tag{10}$$

where x is the dimensionless coordinate along the matrix thickness, $\delta(t)$ is the dimensionless position of the dissolution–diffusion moving front, θ is the dimensionless drug concentration in the matrix. Even though other authors have considered dimensionless time, the present work has excluded the dimensionless time variable since it is considered that otherwise the notion of real-scale applicability of the devices would be lost.

Utilizing Eqs. (6) and (8), Eq. (9) becomes:

$$-\left(\frac{\partial \theta}{\partial x}\right)^2 = \left(1 - \frac{A}{C_s}\right)\frac{\partial}{\partial x}\left(\frac{\partial \theta}{\partial x}\right) \quad x = \delta(t) \tag{11}$$

Eq. (11) is a non-linear differential equation. The approximate solution can be obtained using the Refined Integral Method. Integrating directly twice, combining with Eq. (9), gives (Tan et al., 2001; Sadoun et al., 2006; Myers, 2009):

$$\frac{\partial}{\partial t}\left[\int_{\delta}^{0}\partial\xi\int_{\delta}^{\xi}\theta\partial x-\left(1-\frac{A}{C_s}\right)\frac{\delta^2}{2}\right]=\frac{D_p}{R^2} \tag{12}$$

where ξ is an integration variable. The next step is to assume a functional form which approximates the solute concentration distribution in the partially extracted region. A polynomial concentration profile satisfying the boundary condition (7), (8) and (11) has the form:

$$\theta=a_0+a_1\frac{x}{\delta}+a_2\left(\frac{x}{\delta}\right)^n \tag{13}$$

where n is the adjusting exponent and

$$a_0=1 \tag{14}$$

$$a_1=-1-a_2 \tag{15}$$

$$a_2=\frac{1}{2(n-1)}\times\left[n\left(\frac{A}{C_s}-1\right)+2-\left(n^2\left(1-\frac{A}{C_s}\right)^2+4n\left(\frac{A}{C_s}-1\right)\right)^{1/2}\right] \tag{16}$$

Upon substitution of Eq. (13) into Eq. (12), the position of the dissolution–diffusion moving front is:

$$\delta=\left(\frac{3(n+2)D_pt}{R^2\left[((3A/2C_s)-1)(n+2)-a_2(n-1)\right]}\right)^{1/2} \tag{17}$$

The amount of solute released per unit area (Q) is calculated from a mass balance equation:

$$Q=AR-AS-\int_{S}^{R}C\,\partial r \tag{18}$$

Introducing the reduced dimensionless variables defined previously and with the use of Eq. (13), Eq. (18) results in:

$$Q=R\delta\left[A+C_s\left(a_2\left(\frac{1}{n+1}-\frac{1}{2}\right)-\frac{1}{2}\right)\right] \tag{19}$$

The fraction of drug released (f_{DR}) is defined as:

$$f_{DR}=\frac{Q}{AR} \tag{20}$$

This analysis is valid till all drug dispersed in the device is dissolved ($\delta=1$).

The exact resolution for the position of the dissolution–diffusion moving front was reported by Paul and McSpadden (1976). The expression contains the error function that made complicated their routinary usage. Expanding the integrand using a Taylor series gives:

$$2\left(\frac{A}{C_s}-1\right)\lambda e^{(\lambda)^2}\sum_{i=0}^{\alpha}\frac{(-1)^i\lambda^{2i+1}}{i!(2i+1)}=1 \tag{21}$$

where

$$\lambda=\frac{R\delta}{2(D_pt)^{1/2}} \tag{22}$$

Upon substitution of Eqs. (16) and (17) into Eq. (22), Eq. (21) becomes:

$$\left(\frac{A}{C_s}-1\right)(f_n)^{1/2}e^{(f_n/4)}\sum_{i=0}^{\alpha}\frac{(-1)^i\left((f_n/4)^{1/2}\right)^{2i+1}}{i!(2i+1)}=1 \tag{23}$$

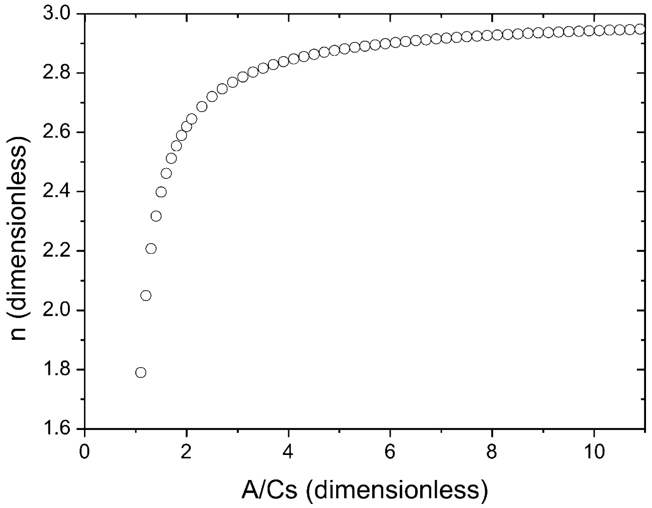

Fig. 2. Values of the exponent n calculated according to Eq. (23) for different A/C_s ratios.

where

$$f_n=\frac{6(n+2)}{((3A/C_s)-2)(n+2)-n((A/C_s)-1)-2+\left(n^2(1-(A/C_s))^2+4n((A/C_s)-1)\right)^{1/2}} \tag{24}$$

From Eq. (23), the values of n that minimize the error in the approximation of the exact solution can be calculated.

3. Results and discussion

In order to use the developed model to predict the drug release profiles, it is convenient to use suitable computational programs to simplify the calculations (for example MATLAB®, FORTRAN® or MAPLE®). These programs allow the creation of a "routine" in programming language to perform the simulations. Once the routine is created, the user only needs to load the values of the parameters that make up the model and then run the program.

The values of n that minimize the error in the approximation of the exact solution were calculated from Eq. (23) using the computational software MATLAB®. The results are presented in Fig. 2. It shows that increasing A/C_s ratios increases the value of n. For $A/C_s\to\infty$, n tends to 3.

With the values of n obtained previously, the position of the dissolution–diffusion moving front was calculated according to Eq. (17). In order to verify that the developed model fits the exact solution, this position of the dissolution–diffusion moving front was compared with the exact solution reported by Paul and McSpadden (1976) for different A/C_s ratios. The results are plotted in Fig. 3a. From the figure it can be seen that the prediction of the model match perfectly well the exact solution reported by Paul and McSpadden. These results confirm that, with the appropriate value of n, both models are indistinguishable with respect to δ and then the error in the prediction of the cumulative amount of drug release is minimized. Fig. 3b presents the variation of the position of the dissolution–diffusion moving front with A/C_s ratios, independently of time. It can be noted that the influence of the relation A/C_s on the parameter δ is greater when this ratio is small. For large A/C_s, this influence decreases.

To extend the analysis, the result obtained through Eq. (19) was compared with the exact solution reported by Paul and McSpadden (1976) and with the solution reported by Lee (1980). The comparison is presented in Table 1. The "percentages of error" for the Lee's solution and for Eq. (19) are plotted in Fig. 4 for different A/C_s ratios.

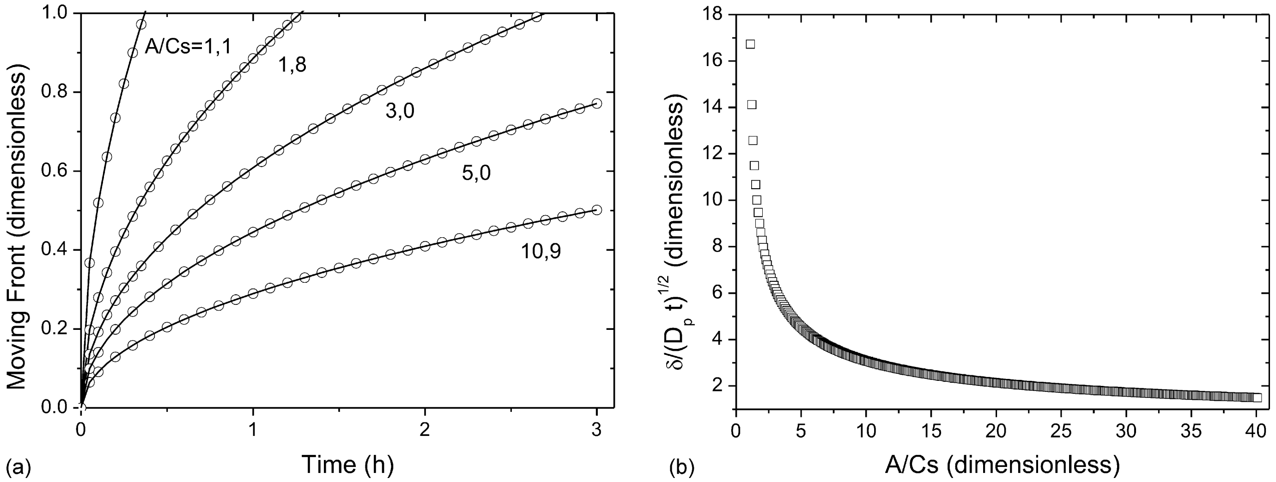

Fig. 3. (a) Comparison of the position of the dissolution–diffusion moving front calculated according to Eq. (17) (—) with the exact solution reported by Paul and McSpadden (1976) (○) for different A/C_s ratios. (b) Variation of the position of the dissolution–diffusion moving front with A/C_s ratios, independently of time. The parameters used are $R = 0.15$ cm; area = 50.265 cm^2; $D_p = 2.68 \times 10^{-6}$ cm^2/s; and $C_s = 2.74 \times 10^{-4}$ g/cm^3.

Table 1
Comparison of the percentage deviation from the exact solution for the solute release from a planar matrix.

A/C_s	$Q/C_s\sqrt{D_p t}$				
	Exact[a]	Lee[b]	% Error	This work	% Error
1.1	1.2102	1.2205	0.85	1.2099	−0.02
1.2	1.3011	1.2960	−0.39	1.2979	−0.25
1.3	1.3789	1.3700	−0.65	1.3766	−0.17
1.4	1.4513	1.4412	−0.70	1.4496	−0.12
1.5	1.5197	1.5094	−0.68	1.5185	−0.08
1.6	1.5849	1.5747	−0.64	1.5840	−0.06
1.7	1.6474	1.6376	−0.59	1.6467	−0.04
2.0	1.8215	1.8130	−0.47	1.8212	−0.02
2.4	2.0301	2.0232	−0.34	2.0299	−0.01
2.8	2.2189	2.2132	−0.26	2.2188	−0.004
3.5	2.5151	2.5109	−0.17	2.5151	0
3.8	2.6318	2.6280	−0.14	2.6318	0
4.5	2.8858	2.8828	−0.10	2.8858	0
10.9	4.5969	4.5960	−0.02	4.5969	0

[a] Paul and McSpadden, 1976.
[b] Lee, 1980.

The "percentage of error" is defined as the subtraction between the values predicted by the tested model and the exact solution, divided by the value predicted by the exact solution and multiplied by hundred. The tested models were the Lee's solution and Eq. (19). It can be observed that Eq. (19) gives better results. For $A/C_s > 1.4$, Eq. (19) is virtually identical to the exact solution (within 0.1%), whereas Lee's equation requires $A/C_s > 4.5$ to have an accuracy within 0.1%. From Fig. 4 it can be seen that the percentage of error for Eq. (19) is always less than the corresponding percentage of Lee's equation. Furthermore, the percentage of error for Eq. (19) is zero for almost the range of A/C_s analyzed.

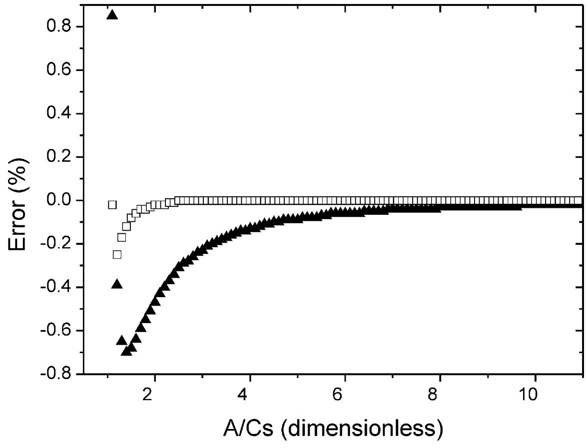

Fig. 4. Comparison of the percentages of error from the exact solution for the cumulative amount of drug released calculated from Eq. (19) (□) and calculated from the solution reported by Lee (1980) (▲) for different A/C_s ratios. The parameters used are $R = 0.15$ cm; area = 50.265 cm^2; $D_p = 2.68 \times 10^{-6}$ cm^2/s; and $C_s = 2.74 \times 10^{-4}$ g/cm^3.

In order to illustrate the previous analysis, the comparison of drug release profiles calculated according to the exact solution (Paul and McSpadden, 1976), Eq. (19), Lee's equation (Lee, 1980) and Higuchi's equation (Higuchi, 1961) are presented in Figs. 5 and 6. Fig. 5 presents the experimental data reported by Paul and McSpadden (1976) and the solute release rates calculated according to the exact solution, Eq. (19), Lee's equation and Higuchi's equation for a red organic dye (Sudan III) from a polymeric matrix of silicone rubber with initial loading higher than solubility. The parameters employed in the simulations were taken from Paul and McSpadden (1976). As expected, the exact solution and Eq. (19) are superimposed and indistinguishable. On the other hand, it can be observed that the solution reported by Higuchi does not fit the experimental release data for low A/C_s ratios. This can be seen clearly in the enlarged figure which shows that for situations where $A \to C_s$, the Higuchi's prediction fails. Also, the Lee's equation approaches the equation reported by Paul and McSpadden but does not match perfectly well with it.

Fig. 6 shows the experimental release data of estradiol from the commercial transdermal patch Trial SAT® 50mcg manufactured by Laboratorios BETA S.A. (Argentina) and the theoretical profiles calculated according to the exact solution, Eq. (19), Lee's equation and Higuchi's equation. The experimental release data were taken from previous studies carried out in our working group (Mengatto et al., internal communication). The parameters employed in the simulations were reported by Laboratorios BETA S.A. Similar to the previous case, the predictions of the exact solution and Eq. (19) are identical. The Lee's equation approaches to the exact solution and the Higuchi's prediction involves certain error. It can be observed in Fig. 6 that the straight line covers approximately the first 50 min of release. From that moment on, only dissolved drug remains in the device; therefore, the developed model is not applicable and the modeling time period ends.

Clearly one can see from the previous examples that with the appropriate value of the n adjusting exponent, the analytical solution is optimized. These results confirm that the error in the

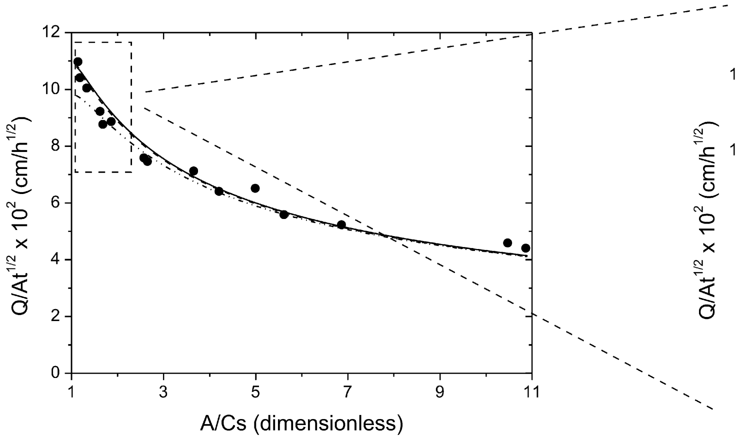

Fig. 5. Comparison of solute release rates calculated according to the exact solution reported by Paul and McSpadden (1976) (· · ·), Eq. (19) (—), the solution reported by Lee (1980) (- - -), the solution reported by Higuchi (1961) (– · · –) and the experimental data reported by Paul and McSpadden (1976) (●) for a red organic dye (Sudan III) release from a matrix of silicone rubber. The parameters used are $R = 0.075$ cm; area = 50.265 cm^2; $D_p = 2.68 \times 10^{-6}$ cm^2/s; and $C_s = 2.74 \times 10^{-4}$ g/cm^3.

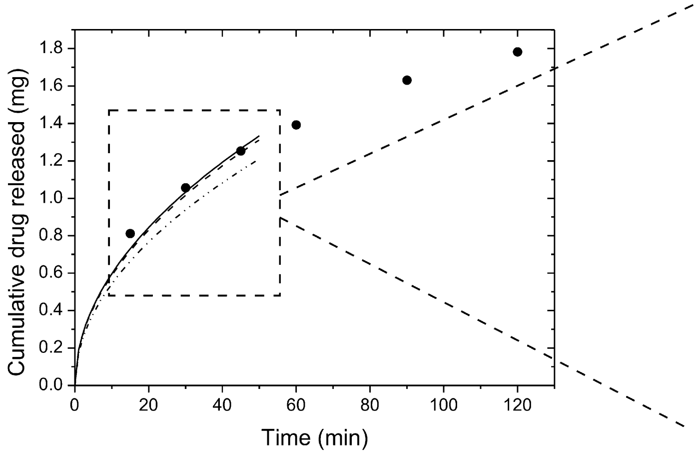

Fig. 6. Comparison of release profile calculated according to the exact solution reported by Paul and McSpadden (1976) (· · ·), Eq. (19) (—), the solution reported by Lee (1980) (—), the solution reported by Higuchi (1961) (– · · –) and the experimental data (●) for estradiol release from the commercial transdermal patch Trial SAT® 50mcg. The parameters used are $R = 0.0085$ cm; area = 15 cm^2; $D_p = 4.63 \times 10^{-9}$ cm^2/s; and $A/C_s = 1.15$.

approximation of the exact solution can be minimized with the new adjusting equation.

In order to illustrate the usefulness of the developed model in the analysis of controlled drug release from planar polymeric matrix-type systems, several examples of simulations are presented and compared with experimental profiles reported in the literature. Fig. 7 shows experimental data reported by Park et al. (2008) and the release profile calculated according to Eq. (19) for estradiol release from a polymeric matrix of EVA 18% with initial loading higher than solubility. The parameters employed were taken from Park et al. (2008). The estradiol diffusion coefficient in EVA copolymer was reported to be in the order of 10^{-9} cm^2/s (Altenburger et al., 1998). The prediction of the model is in good agreement with the experimental data.

Fig. 8 presents the release of 4-aminoazobenzene from a polymeric matrix of cellulose acetate with initial drug loading higher than solubility, calculated according to Eq. (20). The experimental data were reported by Charalambopoulou et al. (2001). The parameters employed in the model were taken from this work. It shows that the prediction of the model is in agreement with the experimental data for the different A/C_s ratios. It can be observed in Fig. 8a that the straight line covers approximately the first 35 h of release. From that moment on, only dissolved drug remains in the device; therefore, the model is not applicable. The same situation can be seem in Fig. 8b for $A/C_s = 4.1$.

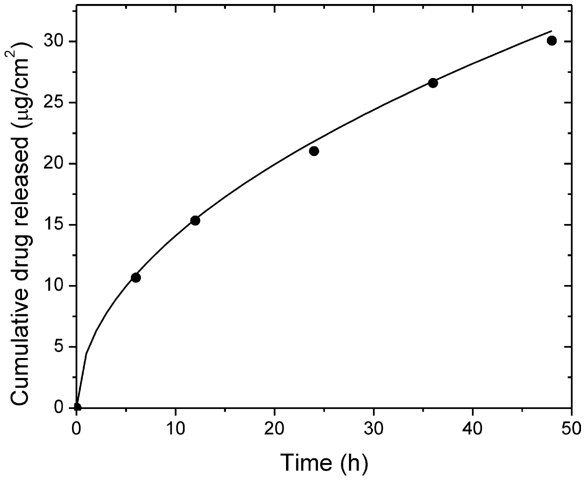

Fig. 7. Comparison of release profile calculated according to Eq. (19) (—) and the experimental data reported by Park et al. (2008) (●) for estradiol release from a matrix of EVA 18% into PBS pH 7.4. The parameters used are $R = 0.0130$ cm; area = 1.77 cm^2; $D_p = 1.1 \times 10^{-9}$ cm^2/s; and $A/C_s = 3.59$.

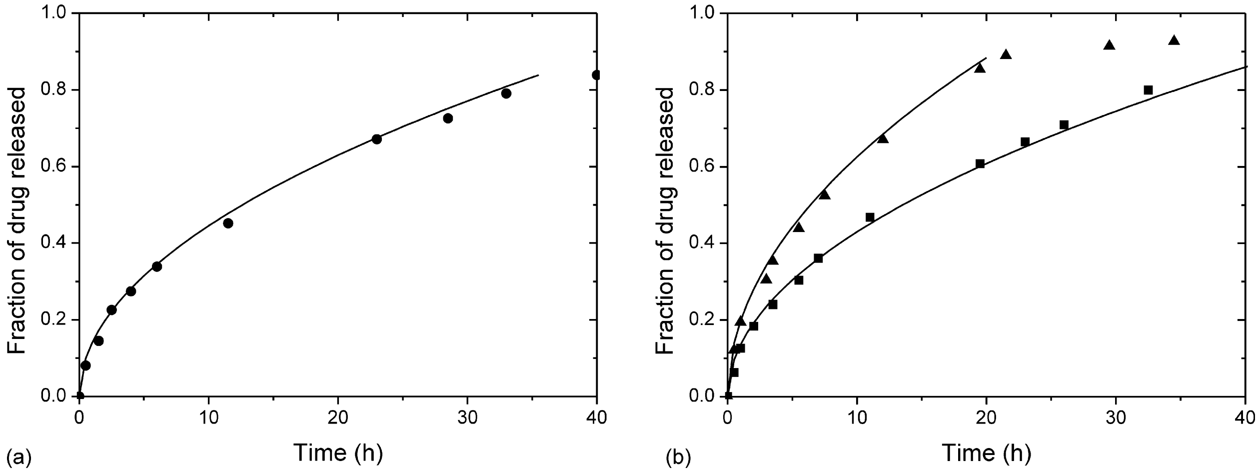

Fig. 8. Comparison of release profiles calculated according to Eq. (20) (solid lines) and the experimental data reported by Charalambopoulou et al. (2001) (symbols), for 4-aminoazobenzene release from a matrix of cellulose acetate: (a) (●) $A/C_s = 3.1$, (b) (▲) $A/C_s = 4.1$, (■) $A/C_s = 7.9$.

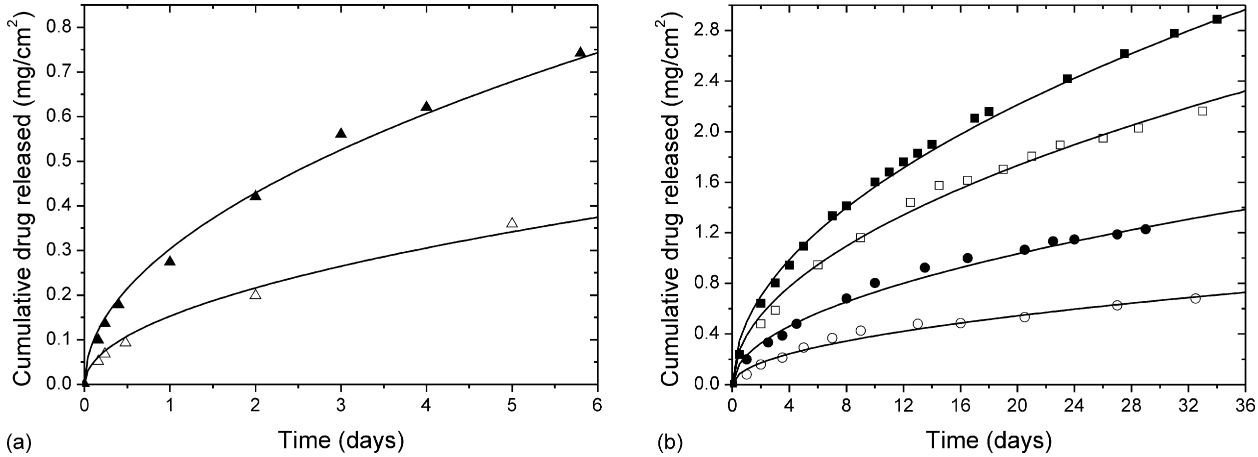

Fig. 9. Comparison of release profiles calculated according to Eq. (19) (solid lines) and the experimental data reported by Roseman et al. (1981) (symbols), for prostaglandins release from a matrix of silicone rubber: (a) dinoprost methyl (△) $A = 2\%$ (▲) $A = 5\%$, (b) carboprost methyl (○) $A = 1\%$ (●) $A = 2\%$ (□) $A = 5\%$ (■) $A = 10\%$.

Fig. 9 shows experimental data reported by Roseman et al. (1981) and the release profile calculated according to Eq. (19), for prostaglandin release from a polymeric matrix of silicone rubber with initial loading higher than solubility. The parameters employed were taken from Roseman et al. (1981). A close match between the model and the experimental data was observed. These examples confirm that the derived equations can be employed in a wide range of initial drug loading.

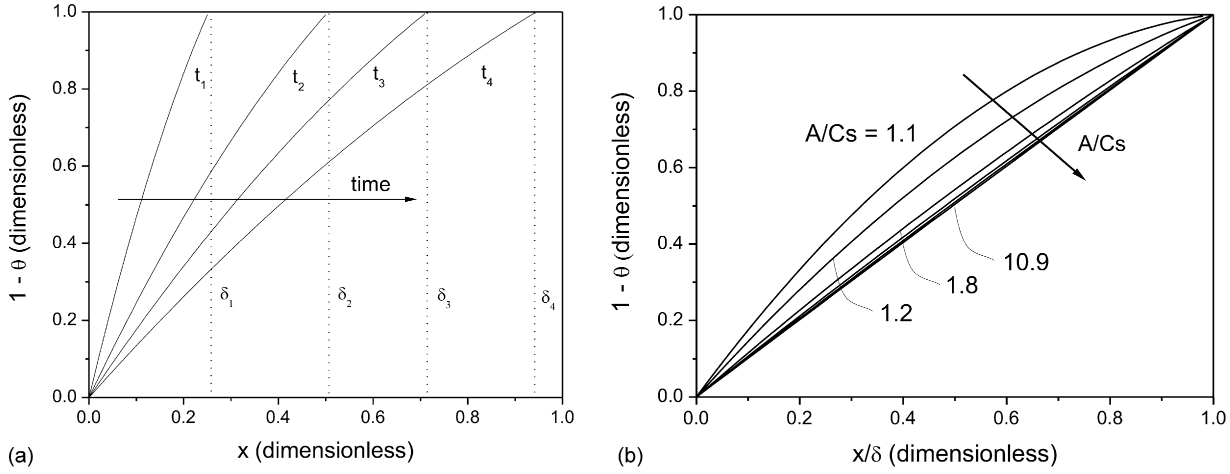

Fig. 10. (a) Concentration distribution profile of dissolved drug in the depletion zone calculated from Eq. (13) for different time: $A/C_s = 1.4$; $t_1 < t_2 < t_3 < t_4$. (b) Concentration distribution profile of dissolved drug calculated from Eq. (13) for different A/C_s ratio: $A/C_s = 1.1$, 1.2, 1.8, 3, 5 and 10.9. The parameters used are $R = 0.15$ cm; area = 50.265 cm^2; $D_p = 2.68 \times 10^{-6}$ cm^2/s; and $C_s = 2.74 \times 10^{-4}$ g/cm^3.

A simulation was carrying out to analyze the variation of the dissolved drug concentration profiles with time and with different A/C_s ratios. This simulation is shown in Fig. 10, which presents examples of concentration distribution profiles of dissolved drug in the depletion zone calculated from Eq. (13). Fig. 10a shows the relative concentration distribution profiles on the position of the dissolution–diffusion moving front corresponding at a given time, for $A/C_s = 1.4$. The $x = 0$ value corresponds to the surface of the slab in which the drug is released. Recalling that $1 - \theta = C/C_s$ (by the conversion to dimensionless), the value $1 - \theta = 1$ in the y-axis represents $C = C_s$. It can be observed from Fig. 10a that the slope of the concentration distribution profile in the drug depletion zone decreases as the thickness of the drug depletion zone increases. This result is consistent with those reported by other authors (Crank, 1975; Paul, 1985; Chang and Himmelstein, 1990). Fig. 10b shows the concentration distribution profile in the depletion zone for different A/C_s ratios. It can be seen that the concentration distribution profiles become linear with increasing A/C_s ratios. This conclusion is consistent with those reported by Paul (1985).

4. Conclusions

Analytical solutions were derived for the case of controlled dispersed-drug release from planar non-erodible polymeric matrices, based on Refined Integral Method. A new adjusting equation for the dissolved drug concentration profile in the depletion zone was used. The value of the exponent n calculated from Eq. (23) increases the precision in the approximation of the exact solution. The set of equations match the available solution reported by Paul and McSpadden (1976). These equations are of practical usefulness and relatively simple to use with the help of an adequate computational software. The utility of the model was corroborated by comparison with experimental profiles reported in the literature. The obtained results show that the model can be employed in a broad range of applicability.

Acknowledgments

The authors wish to express their gratitude to Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), and to Universidad Nacional del Litoral (UNL) of Argentina, for the financial support granted to this contribution.

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