Absorption Isotherm of Caffeine and Release Kinetics from Swollen NIPAAm Hydrogels: Experiments and Modeling

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A series of NIPAAm-based hydrogels, including nonionic, cationic, and anionic types, was prepared by the free radical polymerization method, and the absorption equilibriums and release kinetics of caffeine in the prepared hydrogels were experimentally measured at 25 °C. The experimental absorption data were successfully correlated by the Langmuir isotherm model that results in the same absorption equilibrium constant for the same type of hydrogels and relative affinity sequence: anionic types > cationic types > nonionic types. The maximum caffeine absorption capacity significantly increases with the swelling ratio of the nonionic and cationic hydrogels, while it slightly decreases with the swelling ratio for the anionic hydrogels. The caffeine release kinetic data were analyzed, and the effective diffusion coefficients in different hydrogels were estimated by the traditional and a modified mass transfer model, respectively. The results show that the traditional model underestimates the effective diffusion coefficients, while the modified model provides more accurate estimation of the effective diffusion coefficients. For the same type of hydrogels, the diffusion coefficients estimated by the modified model increase with the swelling ratio of the hydrogels.

Introduction

Correctly measuring drug diffusion coefficients is very crucial in designing controlled release systems using hydrogels. A great deal of attention has been paid to study the drug release rates in hydrogels, and many techniques have been used to determine the diffusion coefficients in the hydrogels. For example, Degiorgi et al. studied the release kinetics of ampicillin in HEMA hydrogel and found the accumulated amount of release is proportional to the square root of time.[1] Colombo et al. used the inverse sectioning method to determine the drug diffusion coefficients in swollen hydrogels.[2] Brazel and Peppas investigated the transport of water and eight drug compounds in two cross-linked polymer systems.[3] Favre and Girard studied the release kinetics of five model solutes from mixed cellulose ethers hydrogels at a temperature between 20 and 60 °C.[4] Kwak and Lafleur used the NMR Pulsed-Field-Gradient technique to measure the self-diffusion coefficients of water, poly(ethylene glycol)s, and cetylpyridinium chloride micelles in Curdlan gels.[5] Kwak and Lafleur used Raman spectroscopy to measure the solute concentration along hydrogel cylinders.[6] The resulting one-dimensional solute distribution in the hydrogel was analyzed with a model based on Fick's diffusion law, and the mutual-diffusion coefficient was then determined. Almost all of the drug release studies adopted Fick's law to describe the release fraction of drug as a function of time and estimated the diffusion coefficient from the experimental data. Various models[7−10] have been used to fit the drug release kinetic data from which the drug diffusion coefficients can be obtained.

It is well-known that poly(*N*-isopropylacrylamide) (NIPAAm) is a typical thermosensitive hydrogel for its possessing lower critical solution temperature (LCST). The NIPAAm hydrogels suddenly change their shape from swollen form to shrunken form at the transition temperature ($T \approx 32$ °C) by increasing the incubation temperature in water. The NIPAAm hydrogels, therefore, are applied in thermosensitive drug delivery systems[11] and a separation process.[12] In those systems, the substrates in the NIPAAm hydrogel are squeezed out at the target tissue in a body by shrinking the gel in response to temperature.[13] Although a series of NIPAAm hydrogels were synthesized and their properties were characterized,[14−16] the drug release kinetics in the NIPAAm hydrogels was not fully studied. This study was therefore aimed at synthesizing NIPAAm-based porous hydrogels by adding pore-forming agents and comparing the release kinetics of a model drug, caffeine, in the prepared hydrogels. The caffeine release kinetic data were analyzed by various mass transfer models, and the caffeine diffusion coefficients were estimated from fitting the experimental data to the models.

Experimental Section

The experimental work of this study includes the synthesis of thermosensitive copolymeric hydrogels and the measurement of the caffeine absorption equilibrium and release kinetics from the synthesized hydrogels. First, the monomers required to prepare ionic hydrogels were synthesized. Then, various hydrogel disks with 12±1 mm diameter and 1.1±0.1 mm thickness were prepared by free radical polymerization method. The details about the materials used and the procedures of monomer synthesis and hydrogel preparation can be found in the previous publication.[17] Table 1 shows the synthesis recipes of the hydrogels prepared in this study. The letter codes for different hydrogel types are as follows: N, T, and A stand for nonionic, cationic, and anionic, respectively; S stands for superporous, and C stands for CMC. For example SNC stands for the superporous nonionic hydrogel with CMC. The structures of the monomers used in this study are as follows:

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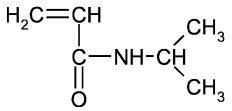
Table 1. The Compositions of NIPAAm-Based Hydrogels[a]

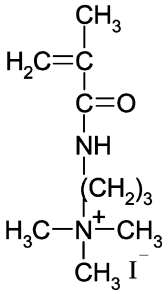
	monomer				cross-linking agent	initiator	co-initiator	pore-forming agent	
gel code	NIPAAm, mol %	TMAAI, mol %	DMAPS, mol %	AA, mol %	NMBA, mol %[b]	APS mol %[b]	TEMED, mol %[b]	CMC, g	$NaHCO_3$, g
N	100	0	0	0	5	1	1	0	0
T	90	5	5	0	5	1	1	0	0
A	90	0	5	5	5	1	1	0	0
SN	100	0	0	0	5	1	1	0	0.5
ST	90	5	5	0	5	1	1	0	0.5
SA	90	0	5	5	5	1	1	0	0.5
SNC	100	0	0	0	5	1	1	0.05	0.5
STC	90	5	5	0	5	1	1	0.05	0.5
SAC	90	0	5	5	5	1	1	0.05	0.5

[a] Legends: NIPAAm: N-isopropylacrylamide; TMAAI: trimethyl methacrylamino propylammonium iodide; DMAPS: 3-dimethyl-(methacryloyloxy ethyl) ammonium propanesulfonate; AA: acrylic acid; NMBA: N,N′-methylenebisacrylamide; APS: ammonium persulfate; TEMED: N,N,N′,N"-tetramethylethylenediamine; CMC: carboxymethylcellulose. [b] Based on total monomer amounts.

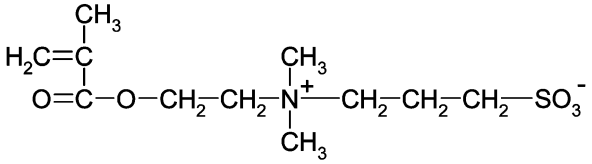
N-isopropylacrylamide (NIPAAm):



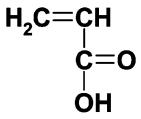
trimethyl methacrylamino propylammonium iodide (TMAAI):



3-dimethyl(methacryloyloxy ethyl) ammonium propanesulfonate (DMAPS):



acrylic acid (AA):



Caffeine Absorption Equilibrium Measurement. The prepared hydrogel disks were first immersed in an excess amount of deionized water at 25 °C for 1 week to reach swelling equilibrium. Then the hydrogel disks were taken out of the water, and the surface water was quickly wiped by filter paper. Different pieces of the swollen hydrogel disks were weighed and put in several flasks that contain caffeine solutions of the same volume. The covered flasks were then put in a shaker (Hotech, Taiwan) operated at 100 rpm and 25 °C for 1 month to ensure that caffeine absorption in the hydrogels reach equilibrium. The concentrations of caffeine before and after absorption equilibrium were measured by a UV/vis spectrophotometer (JASCO, V530). The amount of caffeine absorbed by the hydrogel in each flask was calculated by the following mass balance equation

$$q = \frac{V(C_0 - C)}{W/\rho} \tag{1}$$

where q = the amount of caffeine absorbed in the hydrogel, mg/mL; V = the volume of the caffeine solution, mL; C_0, C = initial and final caffeine concentrations in the solution, respectively; W = swollen hydrogel disk weight, g; ρ = swollen hydrogel density, g/mL. The swollen hydrogel densities of all of the hydrogels used in this study have been measured.[17] Since different pieces of hydrogels were put in the flasks, the final equilibrium caffeine concentrations in gel and solution phases are different.

Drug Release Experiment. The hydrogel disks were again equilibrated in caffeine solution at 25 °C for 1 month to get uniform loading in the hydrogels, and the amounts of caffeine absorbed were calculated by the mass balance relationship. Then the saturated hydrogel disks, supported by a stainless screen, were put in a well-stirred beaker initially filled with 100 mL of deionized water and immersed in a water bath at 25 °C. The preloaded caffeine then released from the hydrogel disks and the caffeine concentrations in the beaker at different time intervals were pumped through and measured by the UV/vis spectrophotometer without replacing the water.

Results and Discussion

Absorption Isotherm Model. The absorption isotherm of caffeine in the hydrogels at 25 °C aqueous solution was experimentally determined by the batch tests, and the results are shown in Figures 1 and 2. Also shown in Figures 1 and 2 are the predicted curves calculated by the Langmuir isotherm model with model parameters K and Q obtained from the nonlinear regression of the experimental data and listed in Table 2

$$q = \frac{KQC}{1 + KC} \tag{2}$$

where K is the absorption equilibrium constant, Q is the maximal absorption capacity, and q and C are equilibrium caffeine concentrations in the gel and solution phases, respectively.

As shown in Figures 1 and 2, the Langmuir model fits the caffeine absorption data satisfactorily with a correlation coefficient greater than 0.99 for each curve.

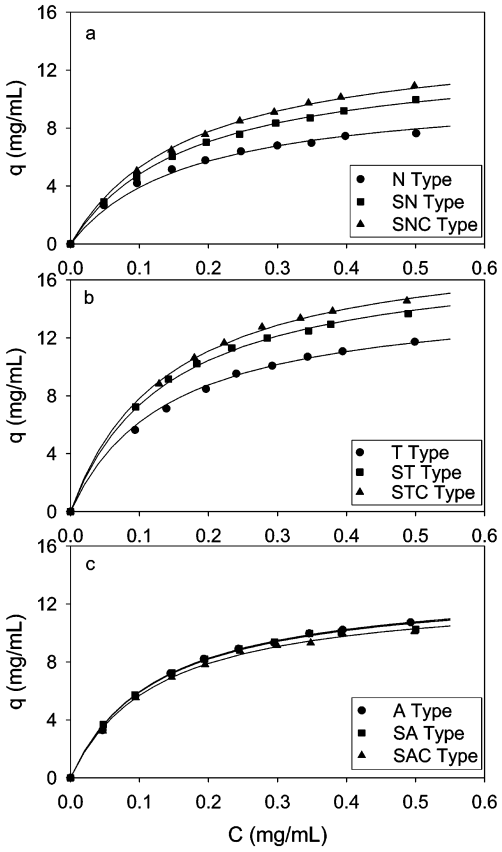


Figure 1. Effect of pore forming agent on the caffeine absorption isotherm at 25 °C. Symbol: — predicted curves by Langmuir model; ● experimental data for N, T, A types; ■ experimental data for SN, ST, SA types; ▲ experimental data for SNC, STC, SAC types.

For low concentration ranges, i.e., $KC \ll 1$, eq 2 becomes

$$q = KQC = K_dC \tag{3}$$

where the partition coefficient K_d is actually the product of the absorption equilibrium constant and the maximal absorption capacity of the Langmuir model. It is important to note that the linear form of absorption equilibrium, expressed by the partition coefficient, is valid at low concentration only. The Langmuir model as shown by eq 2 is more adequate to describe the caffeine absorption equilibrium in wider concentration ranges.

Effects of Pore Forming Agent on Caffeine Absorption. The effect of pore forming agent on the caffeine absorption isotherm at 25 °C is shown in Figure 1. Figure 1a,b shows that the amounts of caffeine absorption increase in the presence of pore forming agents for nonionic hydrogels (SNC > SN > N) and cationic hydrogels (STC > ST > T). However, Figure 1c shows that the amounts of caffeine absorption slightly decrease in the presence of pore forming agents for anionic hydrogels (A > SA > SAC). Table 2 shows that the pore forming agent has no influence on the caffeine absorption equilibrium constant K for the hydrogels with the same charge characteristics (K = 5.75 for nonionic hydrogels, K = 7.00 for cationic hydrogels, K = 7.88 for anionic hydrogels), but it has a marked effect on the maximal absorption capacity Q. Figure 3b clearly shows that the maximal absorption capacities of the nonionic and cationic hydrogels increase with the swelling ratios that are higher in the presence of the pore forming agents. The fine pores in the SN, SNC, ST, and STC hydrogels not only increase the water absorbing capacity but also provide more absorbing sites for the caffeine molecules. Figure 3b however also shows the maximal absorption capacities of the anionic hydrogels slightly decrease in the presence of the pore forming agents. This suggests that the addition of the pore forming agents provide more pores for water absorption, but the caffeine absorption mechanism in these anionic hydrogels may be different from that in the nonionic and cationic hydrogels; the increased number of sites for water may not favor the caffeine absorption.

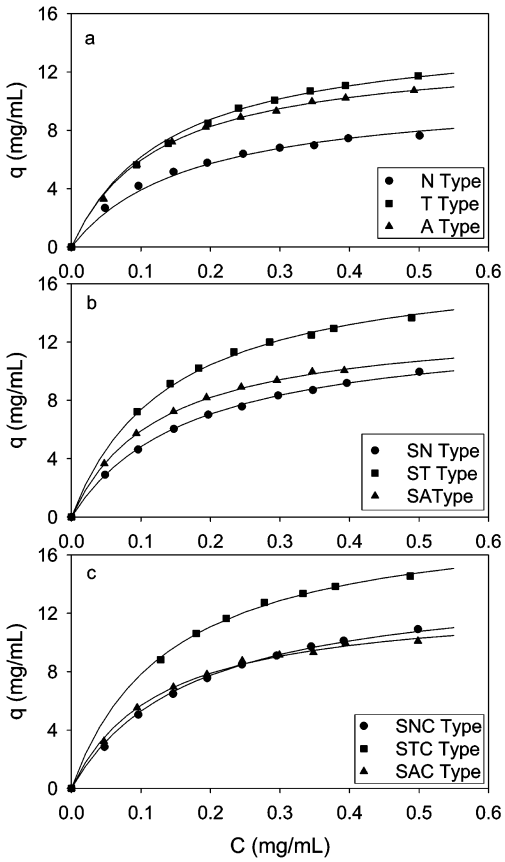


Figure 2. Effect of hydrogel charge on the caffeine absorption isotherm at 25 °C. Symbol: — predicted curves by Langmuir model; ● experimental data for N, SN, SNC types; ■ experimental data for T, ST, STC types; ▲ experimental data for A, SA, SAC types.

Table 2. Langmuir Model Parameters and Effective Diffusion Coefficient of Caffeine in Hydrogels

gel type	SR (−)	K (mL soln/mg)	Q (mg/mL gel)	D × 10^7 (cm^2/s)[a]	D × 10^7 (cm^2/s)[b]	remark
N	7.88	5.75	10.7	5.85	5.66	nonionic hydrogels
SN	10.8	5.75	13.2	7.88	4.89	
SNC	12.2	5.75	14.5	8.52	5.24	
T	22.7	7.00	15.0	4.78	2.08	cationic hydrogels
ST	26.6	7.00	17.9	5.07	1.47	
STC	32.1	7.00	19.0	5.13	1.27	
A	14.8	7.88	13.5	4.58	2.63	anionic hydrogels
SA	17.7	7.88	13.4	4.63	3.15	
SAC	20.4	7.88	12.9	5.01	2.16	

[a] Effective diffusion coefficient obtained from fitting the data shown in Figure 4. [b] Effective diffusion coefficient obtained from linear plot of (M/M_∞) versus $\sqrt{t}$.

Effects of Hydrogel Charge on Caffeine Absorption. The effect of hydrogel charge on the caffeine absorption isotherm at 25 °C is shown in Figure 2.

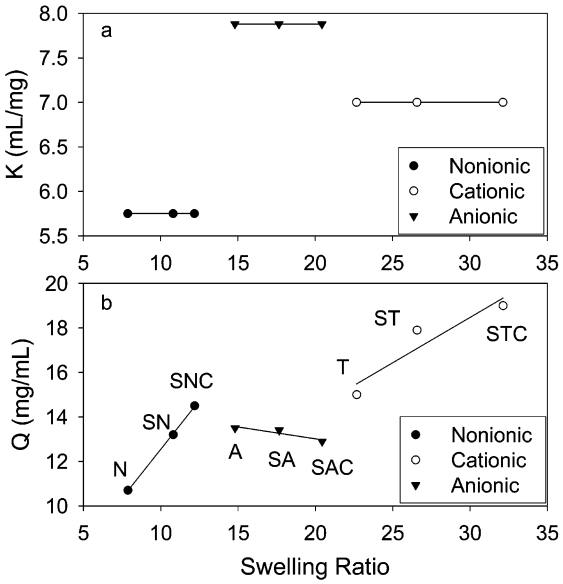


Figure 3. Effect of swelling ratio on caffeine absorption parameters. Symbol: ● nonionic gels; ○ cationic gels; ▲ anionic gels.

Figure 2a shows the amounts of caffeine absorption sequence for the regular hydrogels are T > A > N; Figure 2b shows the amounts of caffeine absorption sequence for the porous hydrogels are ST > SA > SN; Figure 2c shows the amounts of caffeine absorption sequence for the superporous hydrogels are STC > SNC ≈ SAC. These absorption capacity data agree with the SEM observations.[17] Cationic and anionic hydrogels that have more fine pores provide higher absorption capacity for caffeine. In addition to the more fine pores, the affinity of caffeine to the hydrogels with charge may be different according to the following absorption equilibrium

$$A + S \leftrightarrow AS \quad K = \frac{[AS]}{[A][S]} \tag{4}$$

where A stands for the caffeine molecule, and S and AS stand for the unoccupied and absorbed sites, respectively. The absorption equilibrium constant K depends on the functional groups in the hydrogels. Table 2 and Figure 3a show that the anionic hydrogels with the highest K value are the most favorable for the caffeine, while the nonionic hydrogels are the least favorable for the caffeine. The maximum absorption capacities Q of the cationic hydrogels are much higher than those of the anionic and nonionic hydrogels, as shown in Table 2 and Figure 3. Therefore the overall amounts of caffeine absorbed by the cationic hydrogels are greater than those absorbed by the anionic and nonionic hydrogels, as shown in Figure 2.

It is important to note that the caffeine solution pH for each test run was not controlled. At different solution pHs, the fractions of ionized and un-ionized species will be different; this may influence the absorption equilibrium according to eq 4. The effect of solution pH on the caffeine absorption isotherm should be studied in the future to better understand the absorption and release behaviors of caffeine in different solution environments.

Caffeine Release Kinetics. The caffeine release kinetic data were first analyzed by the following empirical equation:[3]

$$\frac{M}{M_\infty} = kt^n \tag{5}$$

The nonlinear curves of $\ln(M/M\infty)$ versus $\ln(t)$ suggest that this empirical equation is not adequate to fit the release kinetic data. Moreover, all the n values are less than 0.5. We can therefore make sure that the caffeine release phenomenon is a Fickian process. The effective caffeine diffusion coefficients in various hydrogels were then determined from the early parts of the fractional release versus $\sqrt{t}$ curves according to the following expression:

$$\frac{M}{M_\infty} = \frac{4}{L}\sqrt{\frac{Dt}{\pi}} \text{ for } M/M_\infty \le 0.5 \tag{6}$$

Although eq 6 has been widely used to determine drug diffusion coefficients in hydrogels, a careful examination of its presumed model reveals that it is probably not adequate to describe drug release kinetics by the presumed model.

The widely used model recognizes the drug release kinetics as a diffusion process that is described mathematically by the following mass transfer model

$$\frac{\partial q}{\partial t} = D\frac{\partial^2 q}{\partial x^2} \text{ for } -L/2 < x < L/2 \tag{7}$$

where q and D are the drug concentration and effective drug diffusion coefficient in the hydrogel disk, respectively.

The initial and boundary conditions for the above equation are as follows:

$$\text{IC: At } t = 0 \quad q = q_0 \quad \text{for } -L/2 < x < L/2 \tag{8}$$

$$\text{BC1: At } t > 0 \quad x = 0 \quad \frac{\partial C}{\partial x} = 0 \tag{9}$$

$$\text{BC2: At } t > 0 \quad x = \pm L/2 \quad q = 0 \tag{10}$$

The initial condition just states that the initial drug loading in the hydrogel is q_0. This initial drug loading can be determined by eq 1. The first boundary condition results from symmetry, and the second boundary condition assumes that the drug concentration in the bulk solution is so dilute that the equilibrium drug concentration in the hydrogel boundary is zero. With such initial and boundary conditions eq 7 can be solved analytically:[18]

$$q = q_0 - q_0\sum_{n=0}^{\infty}(-1)^n \left[erfc\frac{(n+(1/2))L - x}{2\sqrt{Dt}} + erfc\frac{(n+(1/2))L + x}{2\sqrt{Dt}}\right] \tag{11}$$

The amounts of drug remaining in the hydrogel are obtained by the volume-average integration:

$$\bar{q} = \frac{1}{L}\int_{-L/2}^{L/2} q\,dx = q_0 - q_0\frac{4}{L}\sqrt{Dt}\left[\frac{1}{\sqrt{\pi}} + 2\sum_{n=1}^{\infty}(-1)^n ierfc\frac{nL}{2\sqrt{Dt}}\right] \tag{12}$$

The fractional release can then be calculated by the mass balance relationship:

$$\frac{M}{M_\infty} = 1 - \frac{\bar{q}}{q_0} = \frac{4}{L}\sqrt{Dt}\left[\frac{1}{\sqrt{\pi}} + 2\sum_{n=1}^{\infty}(-1)^n ierfc\frac{nL}{2\sqrt{Dt}}\right] \quad (13)$$

For the early release stage, eq 13 can be reduced to eq 6 and widely used to determine the drug diffusion coefficients. If this model is correct, eq 13 should be able to predict the release kinetic curves correctly. Unfortunately Figure 4b shows that the predicted curve does not agree with the experimental data. This suggests that the caffeine diffusion coefficient determined by the early part of the fractional release versus $\sqrt{t}$ curve may not be correct. The caffeine diffusion coefficients in the other 8 hydrogels were also calculated by the same method, and all the predicted release curves do not fit the experimental data well.

Modified Drug Release Kinetic Model. As the hydrogel disks preswollen in the caffeine solution are placed in a well-stirred beaker filled with deionized water, the absorbed caffeine will be released into the water. The release of the caffeine from the hydrogels probably involves the following steps:

- The solution-phase caffeine near the hydrogel surface will diffuse through a liquid film to the bulk liquid. Because of uniform mixing, this external mass-transfer resistance is assumed to be negligible. The caffeine concentration near the hydrogel surface therefore equals that in the bulk solution.
- The solid-phase caffeine concentration is in equilibrium with the solution-phase concentration.
- Due to the concentration gradient as the driving force, the absorbed caffeine inside the hydrogels will diffuse through hydrogel networks toward the hydrogel surface.

Since the traditional model cannot be used to determine accurate diffusion coefficients, it must be modified to allow a more accurate estimation of the diffusion coefficients. Based on the above description of the caffeine release steps, the diffusion equation based on Fick's law remains the same; the initial and first boundary conditions are also the same as in the traditional model. However, the second boundary condition must be modified as follows

$$\text{BC2*:}\quad \text{At } t > 0 \quad x = \pm L/2 \quad q = \frac{KQC_b}{1 + KC_b} \quad (14)$$

where C_b is the caffeine concentration in the bulk liquid phase, and K and Q are the predetermined Langmuir isotherm parameters. The modified boundary condition assumes the gel-phase caffeine concentrations at both sides of the gel surfaces are in equilibrium with that in the bulk liquid phase.

The bulk liquid-phase caffeine concentration is not a constant; its accumulation rate can be expressed by the following unsteady-state mass balance equation

$$V_L\frac{dC_b}{dt} = 2A\left(-D\frac{\partial q}{\partial x}\right)_{x=L/2} \quad (15)$$

where V_L is the bulk solution volume and A is the single-side surface area of the hydrogel disk. The initial condition to the above equation is as follows:

$$\text{At } t = 0 \quad C_b = 0 \quad (16)$$

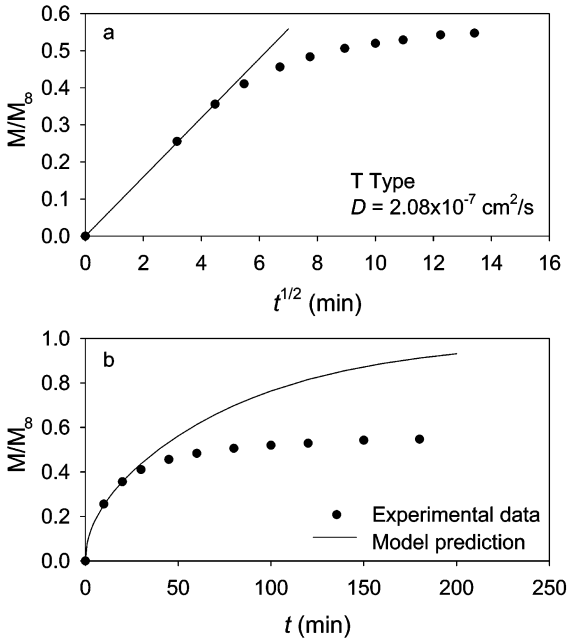


Figure 4. Typical effective caffeine diffusion coefficient determined from linearized plot and the predicted release kinetic curve.

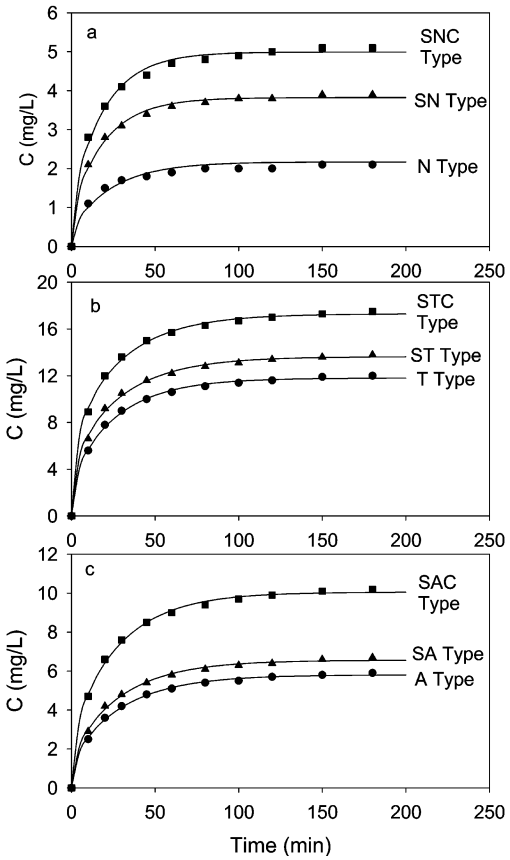


Figure 5. Effect of pore forming agent on the caffeine release kinetics at 25 °C. Symbol: — predicted curves by Langmuir model; ● experimental data for N, T, A types; ■ experimental data for SNC, STC, SAC types; ▲ experimental data for SN, ST, SA types.

Equations 7 to 9 and eqs 14 to 16 constitute the mathematical model for drug release kinetic model. Since eqs 14 and 15 are coupled, it is impossible to solve for the drug concentrations in both phases analytically. Therefore, a finite difference method was used to solve the model equations numerically. In the numerical solution, the hydrogel thickness was divided into 100

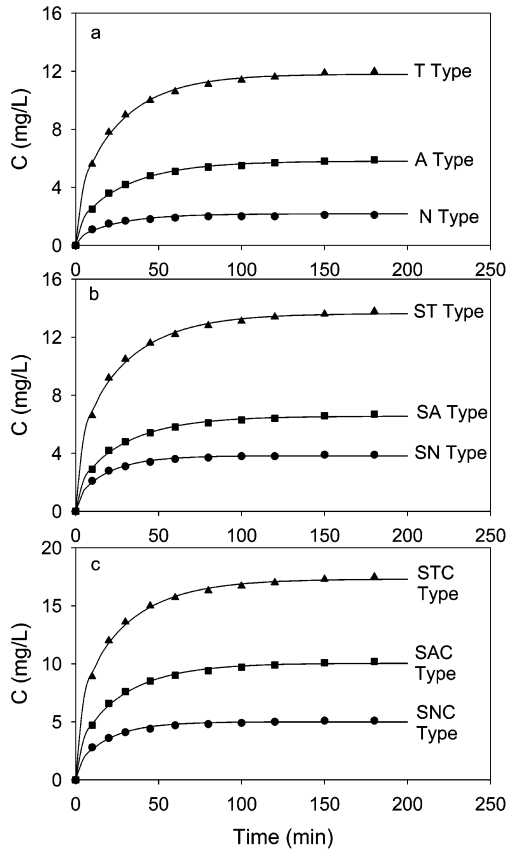


Figure 6. Effect of hydrogel charge on the caffeine release kinetics at 25 °C. Symbol: — predicted curves; ● experimental data for N, SN, SNC types; ■ experimental data for T, ST, STC types; ▲ experimental data for A, SA, SAC types.

slices, and the original partial differential eq 7 and eq 15 was converted to a system of ordinary differential equations. The system of ordinary differential equations was then solved by a numerical integration method using a FORTRAN IMSL subroutine. For a given D value, the drug concentration at any time in the bulk solution C_b was solved and compared with the experimental values. The least-squares method was then used to find the D value that best fit each experimental release kinetic curve. Table 2 summarizes the caffeine diffusion coefficients in all the hydrogels used in this study. Figures 5 and 6 show that the modified model is able to fit the experimental caffeine release curves quite satisfactorily. The effective caffeine diffusion coefficients obtained are therefore more accurate than those obtained from the traditional model that assumes zero caffeine concentration in the bulk liquid solution. The release kinetics of other drugs such as phenol red is being measured, and the preliminary results show the experimental data can also be successfully fitted by the mathematical model developed in this study. Therefore, we expect that the mathematical model may be applicable to other drugs.

Figures 5 and 6 show the experimental and predicted caffeine concentrations in the bulk liquid solutions containing various hydrogel disks that have been saturated with caffeine initially. We can observe from Figure 5 that the caffeine release rate is increased in the presence of the pore forming agents. At first glance, Figure 6 seems to show that the effective caffeine diffusion coefficients in the cationic and anionic hydrogels are greater than those in the nonionic hydrogels. Actually, Table 2 and Figure 7 show that the effective

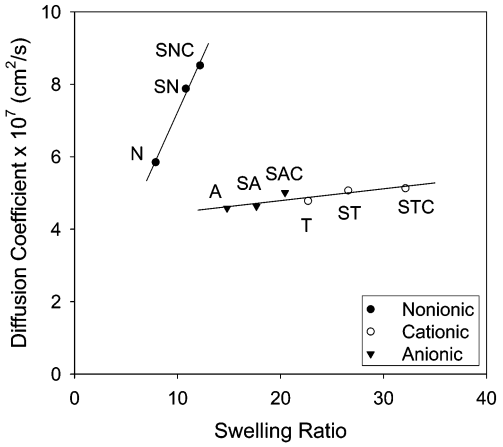


Figure 7. Effect of swelling ratio on caffeine effective diffusion coefficient in the hydrogels. Symbol: ● nonionic gels; ○ cationic gels; ▲ anionic gels.

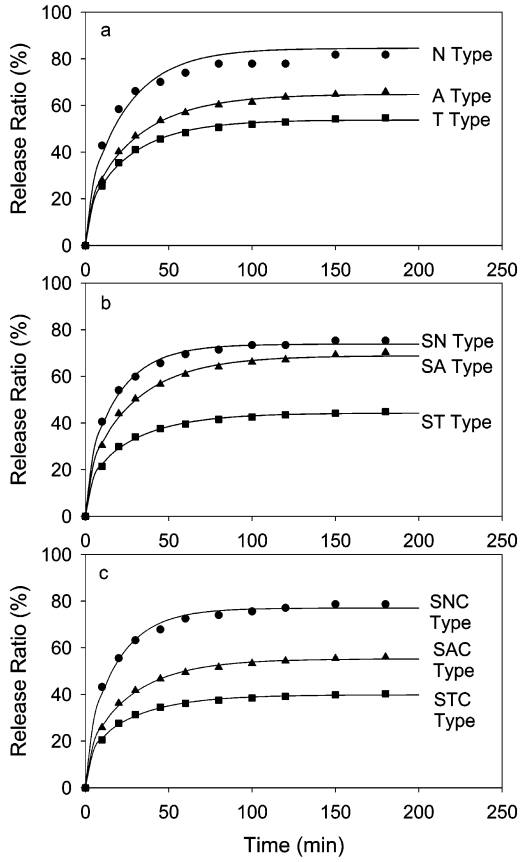


Figure 8. Effect of hydrogel charge on the caffeine release ratio at 25 °C. Symbol: — predicted curves; ● experimental data for N, SN, SNC types; ■ experimental data for T, ST, STC types; ▲ experimental data for A, SA, SAC types.

caffeine diffusion coefficients in the nonionic hydrogels are greater than those in the ionic hydrogels. Since caffeine has a higher affinity to the cationic and anionic hydrogels (greater K values of the Langmuir absorption isotherm as shown in Table 2), the release process may be retarded by caffeine-gel interaction; the effective caffeine diffusion coefficients in the cationic and anionic hydrogels are therefore less than those in the nonionic hydrogels. But because the ionic hydrogels have larger absorption capacities (greater Q values of the Langmuir absorption isotherm as shown in Table 2), more caffeine is present in the hydrogels initially, the apparent release rates from the ionic hydrogels are therefore higher.

Because the water is not replaced during the caffeine release experiments, as more caffeine is released to the water, the mass-transfer driving force decreases and will eventually reach a concentration plateau in the bulk solution. The amounts of caffeine residual in the hydrogel and the release ratios can then be calculated and compared. To make a fair comparison, the release ratios of caffeine from various hydrogels were calculated using the modified model and shown in Figure 8. The sequence of the release rate is in agreement with the relative value of the caffeine diffusion coefficient in the various hydrogels.

The effective caffeine diffusion coefficients of various hydrogels, determined by the modified model, range from 4.58×10^{-7} to 8.52×10^{-7} cm^2/s, while the caffeine diffusion coefficient in 25 °C aqueous solution estimated from the correlation[19] is 7.53×10^{-6} cm^2/s. The effective caffeine diffusion coefficients thus range from 6.1 to 11.3% of the diffusion coefficient in water; this range is reasonable for the hydrogels with swelling ratios from 7.88 to 32.1.

It is important to note that the effective caffeine coefficients estimated from the tradition model using the initial slopes of the fractional release versus $\sqrt{t}$ curves are less than those estimated from the modified model and do not show significant trends with the swelling ratio, as shown in Table 2. The effect of the pore forming agents and the effect of the hydrogel charge on the diffusion coefficient, estimated by the traditional method, cannot be observed clearly, while Figure 7 clearly shows that the effective caffeine coefficients determined by the modified model increase with the swelling ratio. Such a significant difference in the two models suggests that the modified one is better with regards to release kinetic data fitting and diffusion coefficient estimation.

Conclusions

The absorption equilibria of caffeine in 9 different NIPAAm-based hydrogels at 25 °C were experimentally measured, and all the absorption data were successfully correlated by the Langmuir isotherm model. According to the K value that indicates the affinity of caffeine to each hydrogel, the anionic hydrogels have the highest affinity to caffeine, while the nonionic hydrogels have the lowest affinity. For the nonionic and cationic hydrogels the maximum caffeine absorption capacity significantly increases with a swelling ratio that is increased by the pore forming agents; for the anionic hydrogels, the maximum absorption capacity slightly decreases with the swelling ratio.

The caffeine release kinetics from preloaded hydrogels was experimentally measured, and the effective diffusion coefficients of caffeine were determined from the traditional and a modified mass transfer model, respectively. The results show that a traditional model, that cannot correctly fit the whole release kinetic curves, underestimates the effective diffusion coefficients, while the modified model, that can correctly fit the whole curves, provides a more accurate estimation of the effective diffusion coefficients and the estimated diffusion coefficients show reasonable correlation with the swelling ratio of the hydrogels. In the presence of pore forming agents, the effective caffeine diffusion coefficients are higher for all the hydrogels; the effective caffeine diffusion coefficients in the nonionic hydrogels are greater than those in the ionic hydrogels.

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