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The Release Rate of Curcumin from Calcium Alginate Beads Regulated by Food Emulsifiers

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ABSTRACT: Curcumin-loaded alginate beads, which contain different food emulsifiers, have been prepared using $CaCl_2$ as the cross-linking agent. The controlled release of the curcumin from the beads was investigated at room temperature. For calcium alginate/Span-80/Tween-80 (A/S/T) formulations, almost all of the curcumin loaded in the beads was released into the medium within about 20 h, and the release rates could be regulated by changing the concentration of both Tween-80 and Span-80. However, for the systems of calcium alginate/Q-12A/F-18A (A/Q/F), about 60% of the curcumin loaded in the beads was released at the end of experiments. The studies of scanning electron microscopy indicated that the microstructure of the walls of beads could significantly vary with the concentration or type of emulsifiers. The Fourier transform infrared spectral measurements confirmed that the interactions between calcium alginate and polyglycerol fatty acid esters were stronger than that between calcium alginate and Tween-80/Span-80. The results of swelling studies demonstrated that the initial rates of water uptake for A/Q/F beads were higher than that for A/S/T beads. Moreover, the data of release rates were fitted by an empirical equation, which showed that the release mechanism of curcumin from the alginate gels varied with the composition of emulsifiers for the A/S/T systems. This work provides an important insight into the effect of food emulsifiers on the release rates of the curcumin from calcium alginate beads and will be helpful for the application of the systems in controlled release of other hydrophobic drug.

KEYWORDS: *alginate gels, curcumin, food emulsifier, release rate*

INTRODUCTION

The polyphenolic compound curcumin [1,7-bis-(4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3,5-dione, Figure1], extracted from the rhizomes of turmeric, has low intrinsic toxicity and possesses a wide range of pharmacological activity. The potent therapeutic properties of curcumin for a variety of conditions such as respiratory diseases, liver disorders, and diabetic wounds have been documented in ancient Indian literature.[1] Extensive research within the last two decades has revealed that curcumin exhibits a range of pharmacological activities including antioxidant,[2] anti-inflammatory,[3] antiproliferative, and antiangiogenic activities.[4−7] However, low oral bioavailability of curcumin was observed in clinical studies mainly due to its solubility limitation in water, extensive first pass metabolism, and its physicochemical and biological instability.[8−10] Therefore, enhancement of oral bioavailability of curcumin continues to be highlighted as a major challenge in developing formulations for clinical efficacy. Many formulation strategies including micelles, liposomes, microspheres, hydrogels, and solid lipid particles have already been explored to design delivery systems for curcumin to increase the aqueous solubility and oral bioavailability of curcumin.[11−16]

Over the last few decades, controlled release technology has extensively been used in the drugs administration.[17] The advantages of controlled release technology are as follows: more efficient utilization and less consumption of the active agent, reduced frequency of administration, and minimized side effects of drugs.[18] Hydrogels are cross-linked hydrophilic polymers and can swell by absorbing a huge volume of water or aqueous solutions,[19] from synthetic or natural origin, which have attracted a great deal of attention as a matrix for the controlled delivery of biologically active substances. Alginate hydrogels are one of the major scaffold platforms used in drug delivery because of their tunable degradation kinetics and mechanical properties as well as intrinsic biocompatibility.[20,21] Alginate is a natural biopolymer composed of randomly distributed units of 1,4-linked b-mannuronic and a-guluronic acid residues. The in situ gelation properties of alginate were reported as early as 1947 by Major George Blaine.[22] The encapsulation process using alginate hydrogels as a matrix is simple, mild, and nontoxic. However, the successful encapsulation of oil-soluble agents in the alginate hydrogels still presents challenges in high drug loading due to its hydrophilcity.

Micelles are aggregates of amphiphilic molecules that form at or above a concentration referred to as critical micelle concentration. One of the unique and very useful properties of micelles is their capacity to solubilize solute molecules that are otherwise insoluble in aqueous solutions. There are a few literatures that showed that curcumin's poor solubility in water can be improved using a surfactant such as anionic sodium dodecyl sulfate or cationic cetyl trimethylammonium bromide and dodecyl trimethylammonium bromide,[23] caseinate,[12] and block copolymer poly(ethylene oxide)-b-poly(e-caprolactone).[24] These systems have also been used to stabilize

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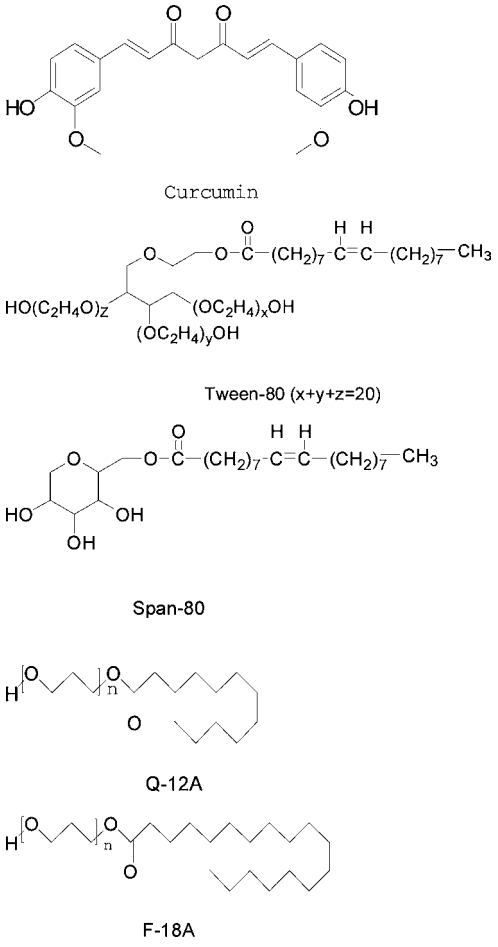

Figure 1. Chemical structure of curcumin and food emulsifiers.

curcumin in solution. Several literatures showed that the addition of surfactants to polymer solutions for encapsulation could alter the resulting microcapsule size and porosity, which are important parameters influencing the controlled release properties of hydrogels.[25−27] That is to say that the mechanical and transport properties of hydrogels may be tuned precisely with an appropriate combination of surfactants and polymers. Our studies showed that the release rate of curcumin from hydrogel beads formed by calcium alginate (Ca-Alg) is very slow, which may limit the application of Ca-Alg beads as controlled release devices for curcumin. Thus, systemic studies about how to manipulate the release rate of curcumin from Ca-Alg beads are still necessary. From the above statements, it is rational to guess that the curcumin solubility and release rate issues for Ca-Alg beads may be successfully overcome by the appropriate combination of some food emulsifiers and Ca-Alg, and the release rate may be tuned by the combination of emulsifier in a wide range as needed.

In this paper, we have prepared curcumin-loaded alginate beads containing different food emulsifiers. The primary goal here was to characterize the composition of food emulsifiers affecting the efficiency of curcumin incorporation in Ca-Alg beads as well as emulsifiers in relation to manipulation of curcumin release. The release mechanism and kinetics of curcumin were also investigated by fitting release data. Additionally, the effect of food emulsifiers on the structure of Ca-Alg beads' wall and the interactions between alginate and curcumin were studied by scanning electron microscopy (SEM) and Fourier transform infrared (FTIR) spectral measurements, respectively.

EXPERIMENTAL SECTION

Materials. Sodium alginate, Span-80 (HLB = 4.3), Tween-80 (HLB = 15), and curcumin were supplied by Aladdin (Aladdin, China), while F-18A (average value of n = 6, HLB = 12.5) and Q-12A (average value of n = 10, HLB = 15.5) were purchased from Shanghai Heyi Food Technology Co. (Shanghai, China). The molecular structure of curcumin and food emulsifiers is shown in Figure 1. The buffer solution was prepared with Tris and HCl (pH 7.2). All of the other chemicals were analytical reagent grade.

Preparation of Ca-Alg Beads. The stock solution was prepared by dispersing 0.5 g of curcumin solution (0.45%,w/w) into appropriate volumes of sodium alginate solution (4%,w/w) containing different amounts of food emulsifiers under continuous mechanical stirring at room temperature. The Ca-Alg beads were prepared by dropwise addition of 10 mL of the stock solution into 20 mL of $CaCl_2$ solution (5%,w/w) through a stainless steel needle with a diameter of 0.7 mm. In this process, the distance between the edge of the needle and the surface of the $CaCl_2$ solution was 5 cm. Finally, the resulting calcium alginate beads were allowed to cure for 10 min in the medium, then separated from the solution by filtration, rinsed with deionized water, and dried in vacuum drying oven at 60 ^{o}C until a constant weight was obtained.

FTIR Measurements. FTIR spectral measurements were performed in a Bio-Rad FTS-40 spectrometer to detect any chemical interactions between the curcumin and Ca-Alg or the emulsifiers. The specimens were crushed and ground with potassium bromide, and pellets were formed under a hydraulic pressure of 500 kg/cm^2. Spectral scanning was done in the range between 4000 and 500 cm^{-1}.

Size and Morphology Examination. Samples of the completely dried beads from different formulations were selected, and their sizes were measured by using a vernier caliper (Chuan Biand, China) with an accuracy of ±0.02 mm, while the morphology characterizations of beads were measured by SEM. The sample was fixed with conducting resin on brass hold and sputtered with gold. SEM photographs were taken with JSM-6390LV Scanning Microscope (Japan) at the required magnification at room temperature. The acceleration voltage used was 25 kV, with the secondary electron image (SEI) as a detector.

Swelling Study of Individual Beads. The dry beads (weight w_1) were soaked in water, and at different time intervals, a few beads were taken out and blotted carefully to remove the surface-adhered water. These beads were weighed (w_2). The measurements were continued until a constant weight was reached for each sample. These studies were performed in triplicate for each of the samples, but average values were considered in data analysis. The standard deviations (SDs) were less than 5%. The percent equilibrium water uptake was calculated as:

$$\left[\frac{\text{mass of swollen beads } (w_2) - \text{mass of dry beads } (w_1)}{\text{mass of dry beads } (w_1)}\right] \times 100 \quad (1)$$

Encapsulation Efficiency (EE) of Curcumin. To determine the EE of curcumin, 10 mg of dried curcumin-loaded beads were accurately weighed and incubated in 100 mL of ethanol, under magnetic stirring, which was continued for several hours to ensure complete extraction of curcumin from the beads. Then, the absorbance of ethanol containing the extracted amount of curcumin was taken at a wavelength of 420 nm with UV−vis spectrophotometer (UV-5100, Shanghai Metash) and pure ethanol as a blank. These studies were performed in triplicate for each of the samples, but average values were considered in data analysis. The EE of curcumin (% EE) was calculated as:

$$\%\ \text{EE} = \frac{\text{the mass of curcumin in beads}}{\text{the mass of the initial curcumin}} \times 100 \quad (2)$$

In Vitro Controlled Release Studies. Release rates for the formulations in buffer solution with different beads were conducted at

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room temperature as follows: Dried beads (100 mg) were placed into a beaker containing 30 mL of an aqueous buffer solution (pH 7.2), which was continuously stirred at a fixed speed of about 100 rpm under magnetic stirring at room temperature. At predetermined intervals of time, certain volumes were collected from the release medium for the analysis of curcumin using UV−vis spectrophotometer at a wavelength of 420 nm. These studies were performed in triplicate for each of the samples, and average values were considered in data analysis.

RESULTS AND DISCUSSION

Effects of Emulsifier on Bead Formation. The size of beads prepared using different formulation parameters is reported in Tables 1 and 2. The beads are spherical with the sizes ranging from 1.02 to 1.24 mm in diameter. The particle size slightly changes with either a change in food emulsifier or an adjustment in the food emulsifier concentration.

Table 1. Effect of Formulation Variables on Size Distribution and EE of Beads for the A/S/T System

sample	Tween-80 (%)	Span-80 (%)	values of HLB	bead diameter (mm)	EE (%)
1	1	0.4	11.9	1.17	85.10
2	2	0.4	13.2	1.12	80.17
3	3	0.4	13.7	1.10	71.99
4	2	0.2	14.0	1.18	74.31
5	2	0.6	12.5	1.24	91.69

Table 2. Effect of Formulation Variables on Size Distribution and EE of Beads for the A/Q/F System

sample	Q-12A (%)	F-18A (%)	values of HLB	bead diameter (mm)	EE (%)
1	2	0.0	15.5	1.02	68.64
2	2	0.1	15.4	1.03	67.25
3	2	0.4	15.0	1.07	66.06
4	1	0.2	15.0	1.02	63.37
5	3	0.2	15.3	1.05	60.45
6	4	0.2	15.4	1.07	51.76

The structure of the capsule walls strongly affects the barrier properties of beads. Therefore, the morphology of beads was studied by SEM as shown in Figure 2. In Figure 2a, panel a gives the whole view of a typical bead, it demonstrated that the beads show similarly acceptable spherical shapes, and the surface of the bead was uneven and dense with the calcium-alginate deposition, while panels b and c, the structure of bead without surfactant, were compact enough to prevent the curcumin release from the bead. For A/S/T systems (Figure 2b), both the surface and the cross-section structure of the beads' wall changed significantly with the composition of the food emulsifiers. At a fixed concentration of Tween-80, the structure of the beads' wall at a higher concentration of Span-80 is more smooth and dense than that at a lower concentration of Span-80. It indicates that the curcumin released from the beads was hard at a higher concentration of Span-80. However, the structure of the beads' wall slightly changed with the composition of the food emulsifiers for A/Q/F systems (Figure 2b). The density of the beads' wall only slightly increased with an increase of the F-18A concentration at a fixed concentration of Q-12A.

FTIR Analysis. FTIR spectra were conducted to characterize the potential interactions between different materials in the beads. Figure 3 shows the FTIR spectra of curcumin and the beads with different compositions. In the spectrum of blank beads, the broad band at 3418 cm^{-1} corresponds to hydroxyl groups; the peaks near 1633 and 1433 cm^{-1} were caused by symmetric and asymmetric stretching vibrations of COO^- groups, respectively. The bands around 1028 cm^{-1} (C−O−C stretching) are attributed to its saccharide structure. After loaded with curcumin, the 1633 and 1433 cm^{-1} peaks shifted to 1615 and 1423 cm^{-1}, respectively. For A/S/T systems (Figure 3d), the wavenumber shifted from 3418 to 3417 cm^{-1}, that is to say, the interaction between food emulsifiers (Tween-80 and Span-80) and Na-Alg was very weak. For A/Q/F systems, the wavenumber shifted from 3418 to 3405 cm^{-1}, which indicates that the interaction between food emulsifiers (Q-12A and F-18A) and Na-Alg was strong. In addition, the strong peaks at 2924 and 2854 cm^{-1} and the weak peak at 1739 cm^{-1} in curcumin-loaded beads with food emulsifiers can be assigned to the stretching of methyl groups and the carbonyl group, respectively. These results may be helpful to deduce the release mechanism of curcumin from our studied systems.

Effects of Emulsifier on EE. The EE of the beads with different compositions is reported in Tables 1 and 2. The EE varied considerably with the composition of the food emulsifiers for a constant concentration of sodium alginate. For the A/T/S systems (Tables 1), the EE decreases with an increase of the Tween-80 concentration at a fixed concentration of Span-80, while the EE increases with an increase of the Span-80 concentration at a fixed concentration of Tween-80. It indicates that the increase of EE is in accord with the decrease of HLB values of the emulsifiers' mixtures. For the A/Q/F systems (Tables 2), although the HLB values of different emulsifiers mixtures hardly change with the compositions of emulsifiers mixtures, the EE decreased with an increase of either the Q-12A concentration or the F-18A concentration at the controlled experimental conditions. Generally, the EE of the A/T/S systems is higher than that of the A/Q/F systems, which may be attributed to the difference of the molecular structure between Tween-80 or Span-80 and Q-12A or F-18A.

Effects of Emulsifier on Swelling. The beads that absorb a large amount of water are prone to swell. As the volume of water inside increases, any significant increase in pressure will probably be compensated for by swelling. Swelling of the dry beads is attributed to the hydration of the hydrophilic groups of alginate[21] as well as the cross-linking density in the polymer matrix. In this case, the addition of hydrophilic or hydrophobic emulsifier to the alginate may significantly influence the hydrophilicities of the groups. To find the effect of emulsifiers on the ability of beads' swelling, swelling was studied in terms of percentage of water uptake by the beads. The percentages of water uptake by different beads with different compositions are presented in Figure 4. For the A/T/S systems, at a constant concentration of Span-80 (Figure 4a), the initial uptake water rate increases with an increase of the Tween-80 concentration and the maximum sorption value, which was reached during the first hour, and also increases with an increase of the Tween-80 concentration. However, at a fixed concentration of Tween-80 (Figure 4b), the initial uptake water rate decreases with an increase of the Span-80 concentration, the maximum sorption value also decreases with an increase of the Span-80 concentration, and the time that reached the equilibrium water content was prolonged with an increase of the Span-80 concentration. FTIR spectra studies indicated that the interaction between Tween-80 or Span-80 and Na-Alg was very weak. Therefore, these observations mainly could be

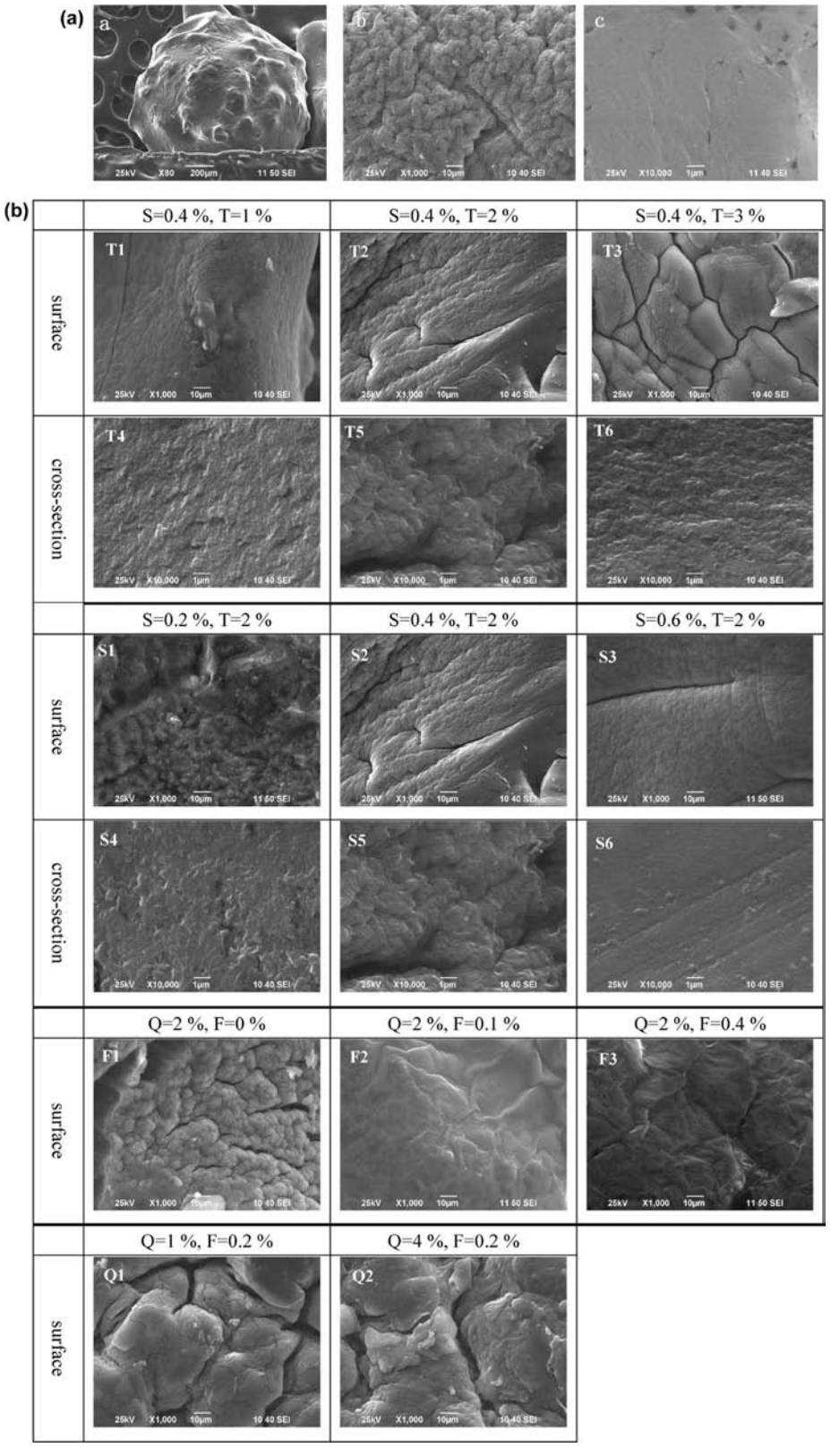

Figure 2. (a) SEM of micrographs of the individual Ca-Alg bead without food emulsifiers (a) and the microstructures: the surface (b) and the cross-section (c). (b) SEM of micrographs of the respective surface microstructures with different food emulsifiers.

attributed to the effect of the composition of Span-80 and Tween-80 on the microstructure of alginate beads. As shown in the Figure 2b, the structures of the beads' wall and cross-section at a higher concentration of Span-80 are smoother and denser than that at a lower concentration of Span-80. It means that the alginate beads for higher Span-80 concentration are more compact than that for a lower Span-80 concentration; hence, the total alginate beads mesh size for a higher Span-80

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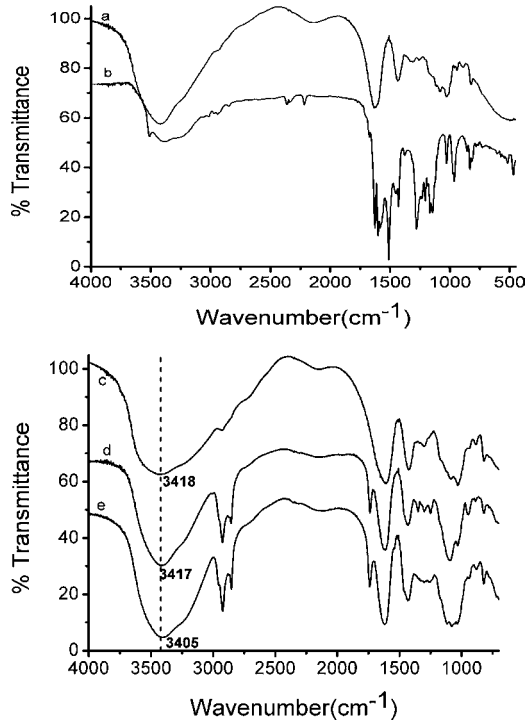

Figure 3. FTIR spectra of blank beads (a), pure curcumin (b), curcumin-loaded beads without food emulsifiers (c), curcumin-loaded beads with Tween-80 and Span-80 (d), and curcumin-loaded beads with Q-12A and F-18A (e).

concentration could be much smaller than that for a lower Span-80 concentration. Consequently, the equilibrium water content at a higher concentration of Span-80 is lower than that at a lower Span-80 concentration for fixed Tween-80 concentration. For the A/Q/F systems, the maximum sorption value increases with an increase of Q-12A concentration at a fixed F-18A concentration (Figure 4c), which could contribute to the increase of hydrophilicity of the alginate beads. Figure 4d shows that the addition of F-18A to the A/Q system can enhance the equilibrium water content; however, the equilibrium water content hardly changes with the concentration of F-18A, which is inconsistent with the results that the microstructures of the alginate beads hardly change with the F-18A concentration for a constant concentration of Q-12A.

Effect of Emulsifiers on in Vitro–Release Studies. The effect of food emulsifiers on the release of curcumin from alginate beads was investigated. When the polymer matrix was placed in a medium, the beads swelled because of absorption of the medium, and then, the curcumin in the swollen part diffused out of the polymer matrix. The in vitro release profiles of alginate beads with different composition are intended to assist in predicting the ultimate behavior of a given alginate bead formulation (Figure 5). For the A/T/S formulations (Figure 5a,b), the initial burst release rate hugely increases with an increase of the Tween-80 concentration at a fixed Span-80 concentration. The amount of initial burst release within 0.5 h increases from 9.5 to 63.9% with an increase of the Tween-80 concentration from 1 to 3%. Additionally, the initial release rate also hugely increases with an increase of the Tween-80 concentration. The time to reach the maximum release amount of curcumin is shortened with an increase of the Tween-80 concentration, and the total release amounts are all close to 100% for the three samples. Meanwhile, it is interesting to note that the release rate is almost constant for the system of A (2%)/T (1%)/S (0.4%). On the contrary, at a fixed Tween-80 concentration, the initial burst release rate slightly decreases

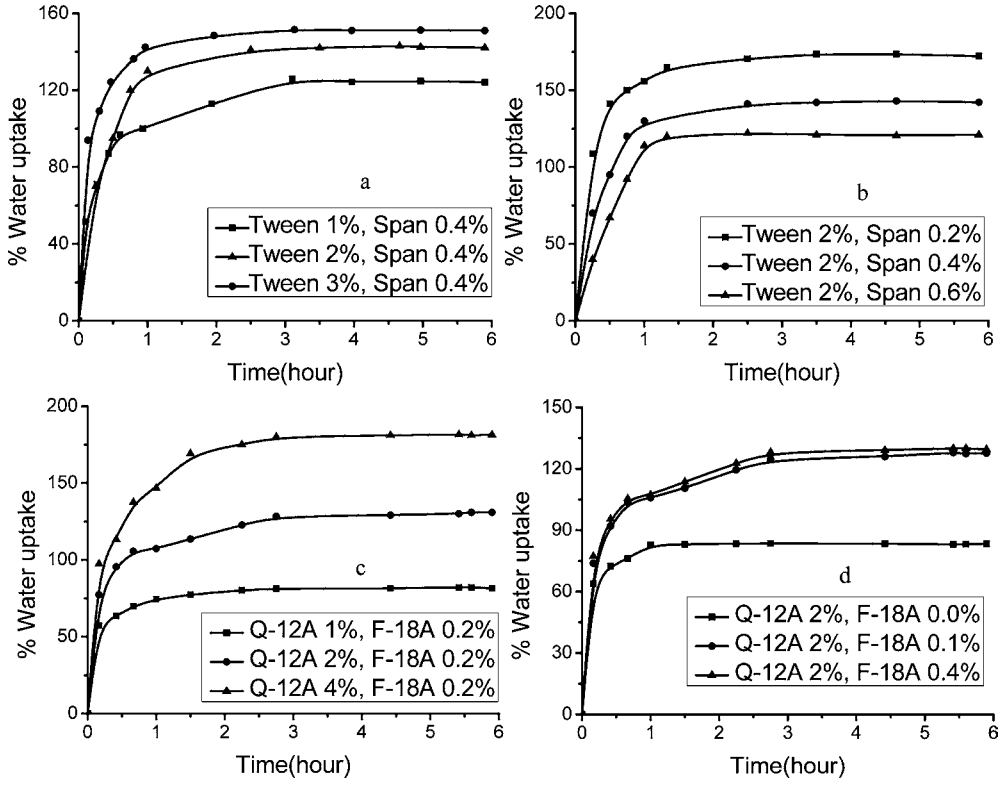

Figure 4. Swelling characteristics of the beads with varied composition.

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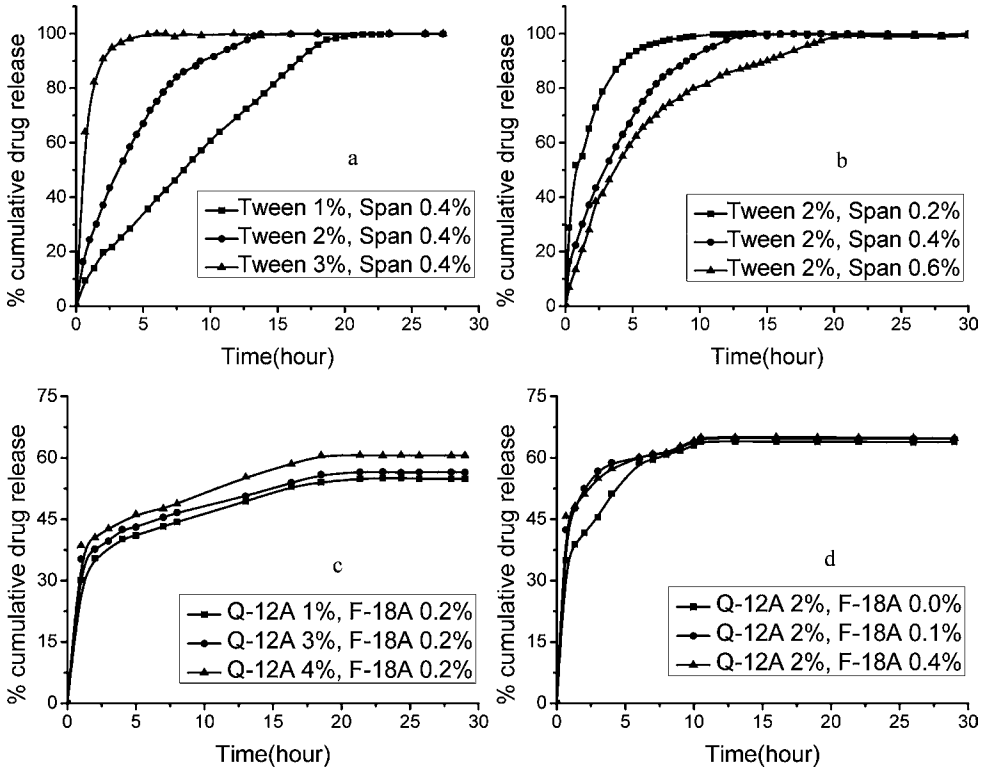

Figure 5. Effect of different composition of emulsifiers on release.

with an increase of the Span-80 concentration. The amount of initial burst release within 0.5 h decreases from 28.8 to 6.9% with an increase of the Span-80 concentration from 0.2 to 0.6%, and the initial release rate also decreases with an increase of the Span-80 concentration. The time to reach the maximum release amount of curcumin is significantly prolonged with an increase of the Span-80 concentration, and the total release amounts are all close to 100% for the three samples. Surprisingly, the above observations confirm that both the release rate and the time to reach the maximum release amount of curcumin can be precisely tuned by selecting an appropriate ratio of Tween-80 and Span-80. However, in regard to the systems of the A/Q/F, the initial release rate, the time to reach the maximum release amount, and the initial burst release rate only slightly change with changing of the composition of Q-12A and F-18A. Moreover, it is obvious that the total release amount for the A/Q/F systems is considerably lower in comparison with the A/T/S systems. This may be attributed to the interaction between Na-Alg and Q-12A or F-18A is stronger than that between Na-Alg and Tween-80 or Span-80 demonstrated in the FTIR studies, which leads to limit the diffusion of Q-12A or F-18A out of the alginate beads; hence, the total release amount of curcumin for the A/Q/F systems is low.

The burst release phenomena have been observed in many controlled release devices.[28] Researchers seek to avoid burst release in controlled release formulations, especially with low molecular weight drugs, which are more likely to have burst release profiles due to their molecular size and osmotic pressures, which accentuate the concentration gradient, because the initial high release rates may lead to drug concentrations near or above the toxic level in vivo.[29,30] This burst release probably represented the release of loosely entrapped and surface-associated active agents. In our studies, an appropriate composition of formulation can significantly diminish the burst effect of alginate beads, which is very important for some drugs administration in clinic application.

On the basis of our experimental observations, we proposed the mechanism of the release behaviors of curcumin in the alginate beads. When the dry beads that have a network structure were soaked in the release medium, every bead underwent significant water uptake, leading to considerable volume expansion. The resulting structure of the alginate beads is the alginate hydrogel containing curcumin-loaded micelles, which can be well distributed in the water phase of the hydrogel due to the hydrophilic shell. Because of the hydrophobicity of curcumin, we speculate that the release of curcumin from the alginate beads may be mainly in the type of the curcumin-loaded micelles. Therefore, the volume of the micelles as well as the microstructure of alginate beads may be the crucial factors to affect the release rate of the alginate beads. As the aforementioned morphology of alginate beads studies, at a fixed Tween-80 concentration, the surface as well as the cross-section of the beads become more smooth and dense with an increase of Span-80 for the A/T/S systems, which may hinder the diffusion of curcumin-loaded micelles out of the beads; consequently, the release rate of the sample is low. For A/Q/F systems, the microstructure of the beads hardly changes with variation of the ratio of Q-12A and F-18A; thus, the release rate slightly changes with the ratio of Q-12A and F-18A. Additionally, we can also observe that for all samples, the variation of the release rate is obviously correlated with the HLB value of the corresponding food emulsifiers' mixture.

Release Kinetics. Extensive research has been conducted to elucidate the mechanisms and models of drug release in the beads. Modeling of a diffusion process in beads can be complicated by nonconstant diffusion coefficients due to large solute loading and solvent/polymer interactions, multidimensional diffusion resulting in complicated solutions, changes in

free volume due to solvent transport (i.e., polymer swelling/deswelling), and multicomponent transport instead of single solute diffusion. These complications partially explain why no universal model has been developed that accurately describes the diffusion mechanism. The generalized model used to explain the nature of the drug release behaviors is an empirical power equation proposed by Peppas et al.[31] The equation is written as:

$$\frac{M_t}{M_\infty} = kt^n, \text{ for } \frac{M_t}{M_\infty} < 0.6 \quad (3)$$

Here, M_t is the cumulative amount of curcumin released at an arbitrary time t, M_∞ is the cumulative amount of the substance released at an infinite time, k is a constant incorporating structural and geometric characteristics of the device, and n is an exponent characterizing the mechanism with which the release kinetics can be described. According to Peppas's equation, there are two distinct physical realistic meanings, as n = 0.45 indicates diffusion-controlled drug release, which is called Fickian diffusion, and n = 0.89 indicates swelling-controlled drug release, which is called case II transport.[32] When n is between 0.45 and 0.89, the drug release behavior can be regarded as the superposition of both phenomena, which is called anomalous transport. In our studies, a nonlinear regression was used to fit the experimental data up to the initial 60% release of the drug with eq 3 to evaluate the release index n and k for each sample tested, and the results are summarized in Table 3. For the A/T/S systems, the value of k increases with an increase of the Tween-80 concentration, while the value of k decreases with an increase of the Span-80 concentration when the concentration of the other emulsifier is constant. For the sample of A/T (2%)/S (0.2%), n = 0.433, which is very close to 0.45, meaning that the curcumin release mechanism from the alginate hydrogel is diffusion controlled. Values of n for other samples are all greater than 0.45 and much smaller than 0.89, indicating that the release of curcumin is anomalous transport. For the A/Q/F systems, the results of n presented in Table 3 are in the range of 0.1300−0.2742, indicating that the release mechanism deviates from Fickian trend. It seems thus very likely that the reason for the effect of food emulsifiers mixtures on the release mechanism of the beads can be explained by its effect on the microstructure of the beads and the interaction between the emulsifiers and the Na-Alg.

Table 3. Results of k, n, and R^2 Calculated from Eq 2

formulation	k	n	R^2
1% Tween, 0.4% Span	0.1038	0.7596	0.9949
2% Tween, 0.2% Span	0.4981	0.4329	0.9971
2% Tween, 0.4% Span	0.2771	0.5589	0.9904
2% Tween, 0.6% Span	0.2086	0.6720	0.9903
2% Q-12A, 0% F-18A	0.1300	0.2507	0.9719
2% Q-12A, 0.1% F-18A	0.2374	0.1626	0.9564
2% Q-12A, 0.4% F-18A	0.2742	0.1332	0.9642
1% Q-12A, 2% F-18A	0.1345	0.1971	0.9769
3% Q-12A, 2% F-18A	0.1889	0.1463	0.9855
4% Q-12A, 2% F-18A	0.2334	0.1185	0.9809

In conclusion, our study has prepared curcumin-loaded alginate beads, which contain different food emulsifiers. The SEM studies showed that both the surface and the cross-section structure of alginate beads varied significantly with the composition of food emulsifiers for the A/T/S systems. However, it changed slightly for the A/Q/F systems. The results also showed that the composition of emulsifiers could effectively affect the other properties of the alginate beads such as swelling, EE, release rate, and release kinetics. We found that the release rate of curcumin and the time to reach the maximum amount of release could be precisely tuned by selecting an appropriate composition of Tween-80 and Span-80, and the curcumin release mechanism varied with the composition of Tween-80 and Span-80 for the A/T/S systems. For the A/Q/F systems, these properties only slightly changed with the composition of Q-12A and F-18A. Moreover, an appropriate combination of food emulsifiers can significantly diminish the burst release of alginate beads, which is very important for some drugs administration in clinic application. This work demonstrated an alternative method of simply designing a sustained release device to improve the solubility of curcumin and regulate the release rate of curcumin from alginate beads. Furthermore, this method also can be extended to encapsulate other hydrophobic drugs to tune the release rate as needed.

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Notes

The authors declare no competing financial interest.

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