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Electrospray Preparation of Propranolol-Loaded Alginate Beads: Effect of Matrix Reinforcement on Loading and Release Profile

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ABSTRACT: In the present study, propranolol loaded-calcium alginate beads were prepared from concentrated solutions of sodium alginate, using combined method of electrospray and ionotropic gelation. The objectives of the study were to increase the propranolol-HCl loading and to decrease its initial burst release. However, the effects of voltage, nozzle diameter, flow rate, and concentration of sodium alginate on size of the beads and drug entrapment efficiency (DEE) were also investigated. The matrix of alginate beads was reinforced with dextran sulfate and/or coated with chitosan. The mean particle size of the beads, their swelling behavior, and drug entrapment efficiency were characterized. Furthermore, the drug release profiles from the prepared beads in simulated gastric fluid and intestinal fluid were evaluated and compared. Among the parameters that affected the electrospray of alginate, voltage had a pronounced effect on the size of beads. The size of beads was reduced to a minimum value on increasing the voltage. Furthermore, increasing the flow rate, alginate concentration, and nozzle diameter and decreasing the voltage led to improvement in DEE. Enhancing the alginate concentration as well as coating with chitosan and reinforcing with dextran sulfate led to increase of the encapsulation efficiency and therefore decrease of the drug release rate in both pHs. © 2014 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2015**, *132*, 41334.

KEYWORDS: biomaterials; drug delivery systems; swelling

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INTRODUCTION

In developing drug delivery systems, preparation of uniform and spherical drug-loaded beads or particles has a vital importance. Electrospray is a simple, reliable, and facile method for preparing such particles.[1,2] Electrospray of sodium alginate has been studied by several researchers.[3,4] Sodium alginate is an aqueous soluble salt of alginic acid, which is a naturally occurring non-toxic polysaccharide and biopolymer found in all species of brown alga.[5] Its gelation occurs by crosslinking of the uronic acids with divalent cations, such as Ca^{2+}, leading to preparation of calcium alginate. This unique specification in ionotropic gelation process made possible to encapsulate macromolecular bio-active agent such as cell,[6] enzyme,[7] and protein.[8]

The encapsulation of high molecular weight drugs such as proteins and vaccines into polysaccharide carriers have been studied by several researchers.[7–9] However, the investigation on the release of low molecular weight drugs are limited because of low drug entrapment efficiency (DEE) and burst release of the loaded drugs. The low DEE of alginate beads are related to the gel porosity, which is large enough to cause leakage of the loaded drugs and therefore the further drug diffusion from the gel network to the $CaCl_2$ solution.[10] To overcome these disadvantages, alginate beads has been reinforced by blending polymers, such as chitosan,[11] pectin,[12] methylcellulose,[13] and dextran sulfate.[10]

Chitosan, the deacetylated derivative of chitin, is one of the most abundant naturally occurring polysaccharides. It has recently attracted much interest in the biomedical applications because of its excellent biodegradability, biocompatibility, as well as antimicrobial activity and accelerated wound healing properties.[14] Dextran sulfate is a negatively charged polysaccharide that illustrates a high affinity for proteins.[15]

In this research, propranolol-HCl was used as a model drug for loading and releasing in the simulated gastrointestinal tract. It is usually taken orally as one of the most widely prescribed b-blockers in the long-term treatment of hypertension and in psychotherapy.[16]

Additional Supporting Information may be found in the online version of this article.

Figure 1. Experimental apparatus.

The application of low concentration of sodium alginate solution leads to production of weak mechanical stable beads, which are not suitable for drug release device and causes increase of drug release rate. While, production of the high strength and spherical calcium alginate beads with narrow size distributions from high concentration of alginate solutions is impossible by usual methods. In our previous studies,[17–19] the preparation of calcium alginate beads from viscid solutions of sodium alginate using electrospray/ionotropic gelation method was evaluated; the effective parameters on the size distribution of the produced beads were studied.

As noted earlier, the major drawbacks of alginate based drug delivery systems are their low DEE and initial burst release. The main objective of present study was to improve DEE and decrease initial burst release of propranolol-HCl loaded alginate beads prepared by electrospray method. In order to achieve this goal, the alginate matrix was reinforced by dextran sulfate and coated with chitosan where both are suitable for controlled drug release systems. The effects of operational parameters on size of the beads and DEE were studied. Furthermore, the effects of sodium alginate concentration, chitosan coating, and matrix reinforcement by dextran sulfate on DEE and release profile of propranolol-HCl were investigated.

MATERIALS AND METHODS

Materials

Sodium alginate of medium viscosity (3500 cps, 2% wt/vol aqueous solution at 25°C) and propranolol hydrochloride were purchased from Sigma-Aldrich. Calcium chloride, acetic acid, and propylene glycol were obtained from Merck. Chitosan of medium molecular weight ($M_w \approx 400$ kDa) was acquired from Fluka. Dextran sulfate ($M_w \approx 500$ kDa) was obtained from Applichem. All reagents were at least analytical grade, and were used as received.

Experimental Method

The experimental setups of electrospray and gelation system are shown in Figure 1.

The high concentration solution of alginate was pumped into a nozzle using a syringe pump at a certain flow rate. The nozzle was charged to a high DC voltage while the counter electrode disc was earthed. Finally when electric field and gravitational forces prevailed on surface tension of the droplets at the tip of nozzle, the droplet was separated. Droplets dripped into a container of gelling agent that contains calcium chloride solution, wherein the calcium alginate beads were formed by ionotropic gelation.

Electric field was developed using the high DC voltage source where the positive and negative potential polarities were connected to the nozzle and the ground electrode, respectively. Distance between the nozzle and ground electrode was adjusted by two polypropylene insulator plates.

Alginate beads were prepared using electrospray/ionotropic gelation method. An aqueous solution of 25% (vol/vol) propylene glycol (PG) was used as solvent for increasing solubility. Preweighed amounts of sodium alginate and/or dextran sulfate were dissolved in aqueous solution of 25% (vol/vol) PG. The propranolol-HCl was slowly added to this solution under magnetic stirring for 2 h to prepare 2% or 3% (wt/vol) solution of alginate, containing 0.5% (wt/vol) propranolol-HCl and/or 1% of dextran sulfate. The weighed amounts of $CaCl_2$ and/or chitosan were dissolved in deionized water and deionized water/acetic acid using magnetic stirrer to prepare solution of 3% (wt/vol) $CaCl_2$ and/or 0.5% (wt/vol) chitosan, respectively. The prepared solution of alginate and/or alginate/dextran sulfate containing propranolol-HCl was pumped into a nozzle using a syringe pump. The nozzle (2 mm diameter) was charged to a high DC voltage, while the counter electrode disc (3 cm diameter) was earthed. The sodium alginate and/or alginate/dextran sulfate containing propranolol-HCl dripped into a container that contained gelling agent of calcium chloride and/or calcium chloride/chitosan solution, where the calcium alginate beads were formed by gently mixing of the system for about 10 min. The prepared beads were then filtered and kept in an autoclave at 30°C in order to be dried until constant weight. The dried beads were then stored in desiccators.

To investigate the parameters affecting DEE and the size of beads, set of experiments were carried out. Table I shows the different levels of operational parameters for bead production in this set of experiments.

Particle Size Analysis

The size measurement and shape analyses of at least 100 wet and dried beads were carried out by analyzing the digital images captured by a CCD camera installed on a microscope, using Motic Images Advanced software. The average diameter of the beads was reported as the mean particle size.

Scanning Electron Microscopy

The surface morphology of beads was studied using scanning electron microscopy (SEM), model: XL30 Philips (The Netherlands). The prepared beads were mounted on metal stubs, and gold film was coated under vacuum using sputter coater (Bal-Tec Company, Swiss).

Table I. Levels of Operational Parameters in Experiments

	Studied operational parameters	Voltage (kV)	Flow rate (mL/h)	Nozzle diameter (mm)	Alginate concentration (wt/vol %)
Effect of parameters on size beads	Alginate concentration	0, 2, 4, 5, 6, 7, 8, 9	50	2	1, 2, 3
	Applied voltage	0, 2, 4, 5, 6, 7, 8, 9	50	2	2
	Flow rate	0, 2, 4, 5, 6, 7, 8, 9	20, 50, 250	2	2
	Nozzle diameter	0, 2, 4, 5, 6, 7, 8, 9	50	1, 2, 3	2
Effect of parameters on DEE	Alginate concentration	2, 4, 6	150	2	2, 3, 3.7
	Applied voltage	2, 4, 6, 8, 9	150	2	1, 2, 3
	Flow rate	2	20, 50, 75, 150	2	1, 2, 3
	Nozzle diameter	2	150	1, 2, 3	1, 2, 3

Swelling Behavior

The swelling properties of alginate, chitosan-coated alginate, and chitosan-coated alginate/dextran sulfate beads were determined. Amount of 100 mg of weighted dry beads were placed in HCl solution (pH = 1.2) or phosphate buffer solution (0.2*M*, pH = 6.8) at 37°C. At predetermined time interval, the swollen beads were initially removed from solution and blotted by the filter paper to remove the adsorbed water and their wet weight was then determined on an electronic balance. The beads were finally returned to the solution. The percentage of swelling was calculated using eq. (1)

$$S_P = \left(\frac{W_t - W_0}{W_0} \right) \times 100\% \quad (1)$$

where S_P is the swelling percentage of beads, W_t denotes the weight of the beads at time t, and W_0 is the weight of the dry beads.

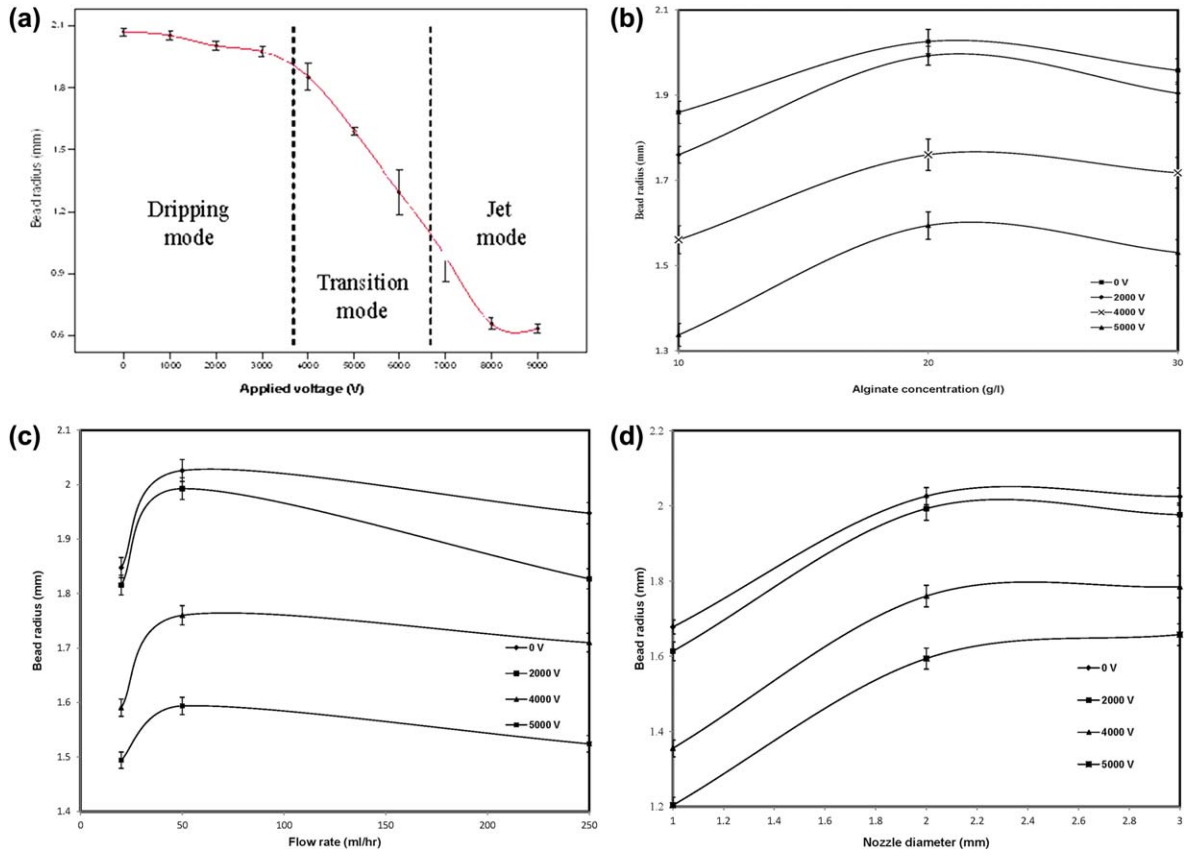

Figure 2. Effects of studied parameters on the beads size. (a) Voltage; (b) alginate concentration; (c) flow rate; (d) nozzle diameter. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

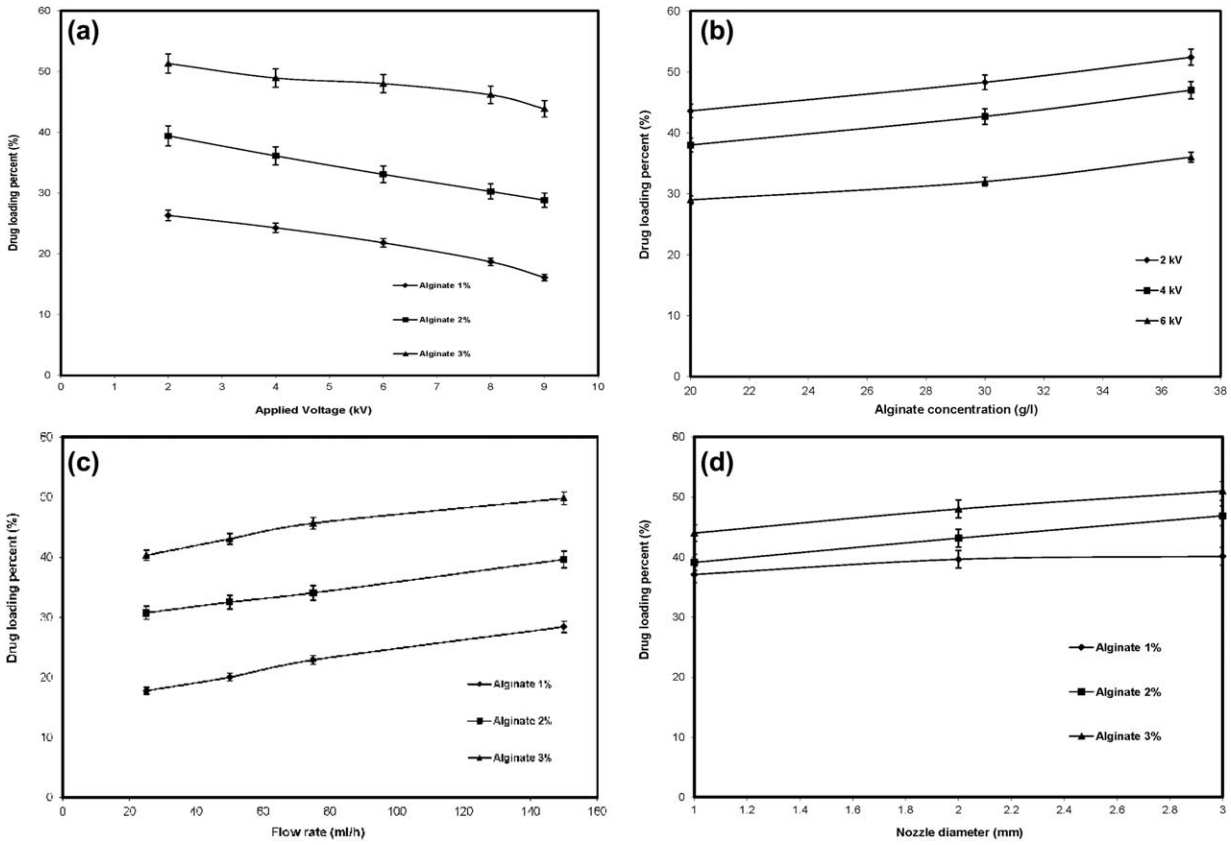

Figure 3. Effect of studied parameters on DEE. (a) Applied voltage; (b) alginate concentration; (c) flow rate; (d) nozzle diameter.

Propranolol-HCl Encapsulation Efficiency

DEE was determined indirectly. The amount of propranolol-HCl loaded in the beads was calculated by the difference between the total amounts of propranolol in pumped solution and the amount of propranolol-HCl that diffused in $CaCl_2$ and/or $CaCl_2$/chitosan solution.

$$\text{DEE} = \frac{\text{total amount of propranolol} - \text{propranolol amount that penetrate throughout}}{\text{total amount of propranolol}} \times 100 \quad (2)$$

Propranolol concentration in $CaCl_2$ and/or $CaCl_2$/chitosan solution was determined spectrophotometrically (Shimadzu-160-Graphicord, Kyoto, Japan), using absorbance measured at 289 nm.

In Vitro Release Study

Dried beads were placed in two different simulated solutions, 100 mL of HCl pH = 1.2 (2 h/120 rpm), and in phosphate buffer pH = 6.8 (6 h/120 rpm) at 37°C. At regular time intervals, sample aliquots were withdrawn and then were analyzed by UV spectrophotometer at 289 nm and the released amount of propranolol-HCl from the beads was calculated.

RESULTS AND DISCUSSION

Effect of Studied Parameters on Beads Size

The effect of voltage on beads size was investigated, as shown in Figure 2(a). It is clear that increasing the applied voltage led to size reduction of the beads to almost a minimum value. At the early stages of increasing voltage (i.e., up to about 4 kV), where the rate of size reduction was relatively low, the dripping mode was dominated. However, within a certain range of voltage (i.e., about 4–7 kV), the size reduction speeded up with voltage. In this range, a transition from the dripping mode to the jet mode occurred and the frequency of droplet formation increased while the size reduced. In the middle part of this range, where none of the spraying modes dominated, an unstable fluctuation between the dripping and the jet modes was observed causing a wide size distribution of the beads. The voltage corresponding to the minimum size of the beads was termed as critical voltage (i.e., about 8 kV). Three regions of dripping, transition and jet modes of spraying are also shown in Figure 2(a).

The effect of alginate concentration on beads size under flow rate (50 mL/h), nozzle diameter (2 mm), and different voltages (0–5 kV) was evaluated, as shown in Figure 2(b).

Table II. Characterization of Propranolol Hydrochloride-Loaded Produced Beads

Sample Code	Polymer solution concentration (wt/vol %)	Gelling medium concentration (wt/vol %)	Diameter of wet beads (mm, ±SD)	Diameter of dried beads (mm, ±SD)	DEE (%, ±SD)
A	Alginate, 2%	$CaCl_2$, 3%	3.7401 ± 0.0290	1.1527 ± 0.0210	38.51 ± 0.12
B	Alginate, 2%	$CaCl_2$, 3%	4.2763 ± 0.0140	1.1738 ± 0.0240	50.49 ± 0.17
		Chitosan, 0.5%			
C	Alginate, 3%	$CaCl_2$, 3%	4.1023 ± 0.0140	1.0911 ± 0.0090	43.15 ± 0.12
D	Alginate, 3%	$CaCl_2$, 3%	4.4213 ± 0.0140	1.3094 ± 0.0270	53.87 ± 0.18
		Chitosan, 0.5%			
E	Alginate, 2%	$CaCl_2$, 3%	4.3357 ± 0.0083	1.2444 ± 0.0390	68.89 ± 0.23
	Dextran sulfate, 1%	Chitosan, 0.5%			
F	Alginate, 3%	$CaCl_2$, 3%	4.6172 ± 0.0138	1.4514 ± 0.0620	70.82 ± 0.38
	Dextran sulfate, 1%	Chitosan, 0.5%			

As seen in the figure, increasing the concentration from 1 to 2% wt/v led to increase of beads size; nevertheless, further increasing of the concentration had reverse effect on the size of the produced beads. Increasing the alginate concentration results in increasing of some properties of the solution such as, viscosity, density, electrical conductivity, and surface tension. Increase of the viscosity and surface tension of the solution have direct effect on the size of the beads, while increasing density and electrical conductivity have reverse effect. Therefore, in a specific limit of operational condition, increasing of concentration may lead to increase of the beads size (i.e., increasing from 1% wt/vol to 2% wt/vol) and in other limits increasing of concentration may lead to decrease of the beads size (i.e., increasing from 2% wt/vol to 3% wt/vol) because of the adverse effects of solution parameters.

The effect of flow rate on beads size prepared from 2% wt/vol sodium alginate solution with 2 mm nozzle diameter and different voltages (0–5 kV) was investigated, as shown in Figure 2(c).

Figure 2(c) reveals that increasing of flow rate in first stages caused to increase of beads size. However after a certain point, increase of flow rate led to gradual decrease of the beads size. This phenomenon has two different reasons. The first reason is that dripping mode is dominate at low flow rate and in this mode increasing of flow rate leads to increase of the bead size. There is a transition from dripping mode to jet mode because of further increasing of flow rate. In this mode of spraying, beads production rate increased with increase of flow rate and consequently, results in decrease of beads size. Shear thinning behavior of alginate solution is the other reason.[20] Shear rate at nozzle tip increases with increase of flow rate and finally non-Newtonian behavior of solution leads to decrease of apparent viscosity that consequently results in decrease of the radius of the beads.

Figure 2(d) reveals the effect of nozzle diameter on beads size. This figure shows the changes of the beads radius as a function of nozzle diameter in different applied voltage and constant concentration of 2% wt/vol and constant flow rate of 50 mL/hr. As it is seen, increasing nozzle diameter generally caused to increasing of mean size of the beads. Increasing of nozzle diameter from 1 to 2 mm led to increase of the radius of the bead, however further increase from 2 to 3 mm has negligible effect on the size of the prepared beads. Effect of increasing nozzle diameter from 1 to 2 mm on the bead size probably counteract by decreasing shear rate and consequently, increasing apparent viscosity. However increasing of nozzle diameter from 2 mm to 3 mm has little effect on the apparent viscosity and hence, on the size of the prepared beads.

Effect of Studied Parameters on DEE

The effect of voltage on DEE was investigated using different concentrations of alginate, while keeping the flow rate (150 mL/h) and the nozzle diameter (2 mm) constant.

As illustrated in Figure 3(a), increasing the applied voltage, in all alginate concentrations, led to the decrease of propranolol-HCl loading percentage. The latter result is attributed to the reduction of particles' diameter and consequently high surface to volume ratio of the prepared beads, causing the propranolol-HCl to diffuse more out of the alginate matrix during ionotropic gelation process.

The effect of alginate concentration on DEE in a constant flow rate (150 mL/h), constant nozzle diameter (2 mm), and in different voltages was studied, as illustrated in Figure 3(b).

According to Figure 3(b), reinforcing the alginate matrix by increasing the polymer concentration led to increase of DEE. Increasing alginate concentration supplies more number of binding sites of alginate for Ca^{+2} ions that results in the formation of a more compact gel membrane, which in turn, decreases diffusion of drug during ionotropic gelation process.

Figure 3(c) reveals the effect of flow rate on DEE in a constant voltage (2 kV), constant nozzle diameter (2 mm) and in different concentrations of polymer.

As shown in Figure 3(c), enhancing flow rate led to increase of propranolol-HCl entrapment efficiency. In these ranges of flow

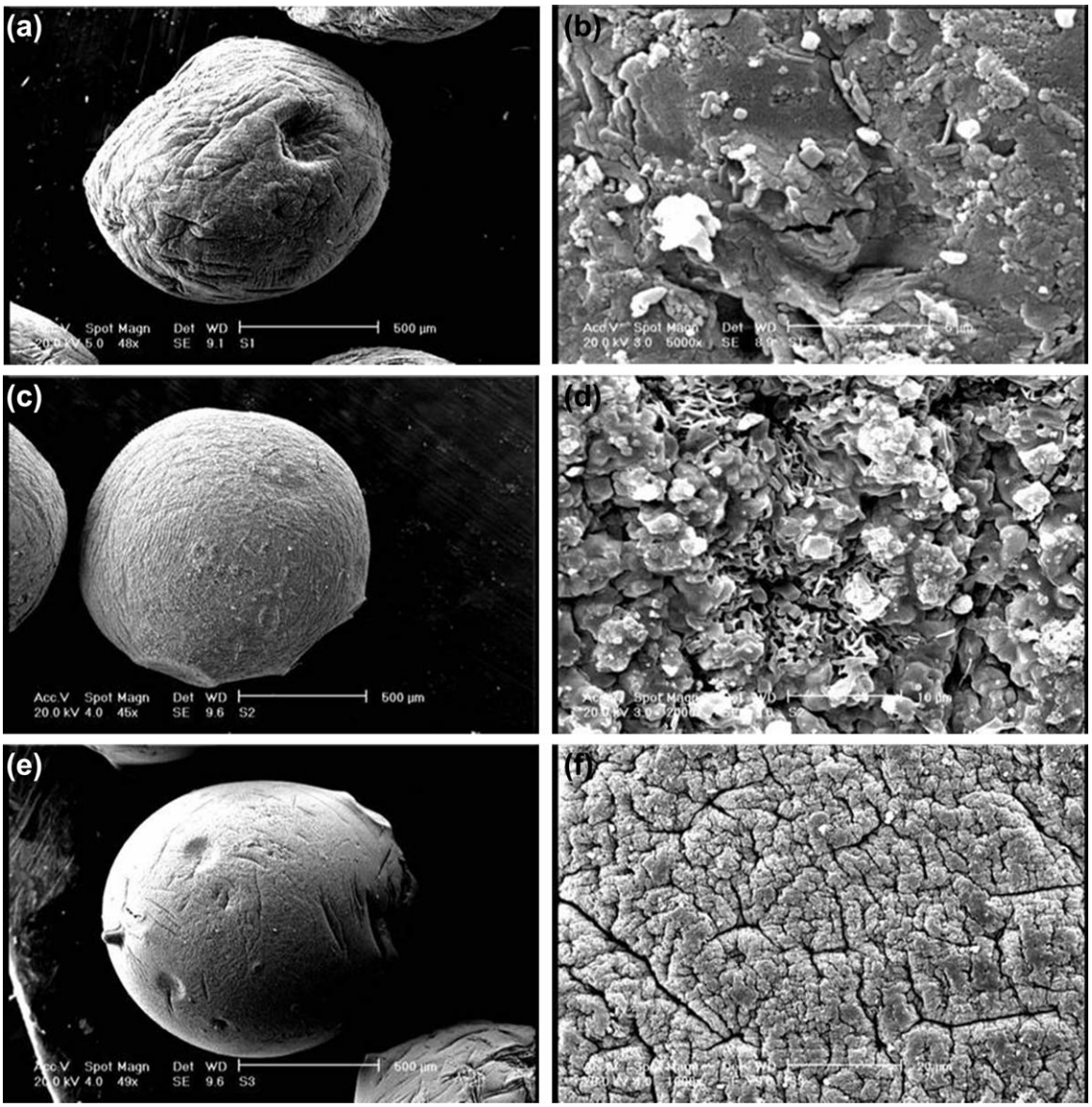

Figure 4. SEM micrographs of different samples of Table II (left) and their surface morphologies (right); (a and b) Sample A; (c and d) Sample B; (e and f) Sample C; (g and h) Sample D; (i and j) Sample E; (k and l) Sample F.

rate, the size of beads was increased with increase of the flow rate. Thus, surface to volume ratio was decreased for beads prepared at higher flow rate. By decreasing surface area-to-volume ratio of the beads, drug diffusion in ionotropic gelation time was decreased hence, DEE was increased.

The effect of nozzle diameter on DEE in a constant voltage (2 kV), constant flow rate (150 mL/h), and in different sodium alginate concentrations is evaluated in Figure 3(d).

Using the higher diameter of nozzle for injection led to slight increase of DEE. As noted previously, increasing the nozzle diameter results in increasing bead size. The larger beads have smaller surface area-to-volume ratio and consequently, smaller surface area for mass transfer. Thus, the amount of released drug from these beads during ionotropic gelation process was lower compared to smaller beads.

Effect of Matrix Reinforcement on Bead Size and DEE

As seen in previous section, DEE was less than 50% in almost all the experiments. In order to enhance DEE in the prepared beads, dextran sulfate was added to the sodium alginate solution and chitosan was added to the gelling medium. It is anticipated that dextran sulfate reinforces matrix of the prepared beads, while chitosan forms a thin layer on the surface of the prepared beads.

Table II shows the different concentration of polymer solutions and gelling medium compositions used to prepare the reinforced beads. Also, the diameter of the wet and dried produced beads and DEE of are presented in Table II.

For the case of chitosan coated beads, the size of the beads was increased from 3.7401 mm to 4.2763 mm (for alginate 2% wt/vol) and from 4.1023 to 4.4213 (for alginate 3% wt/vol) and for the reinforced beads with dextran sulfate, the beads size was

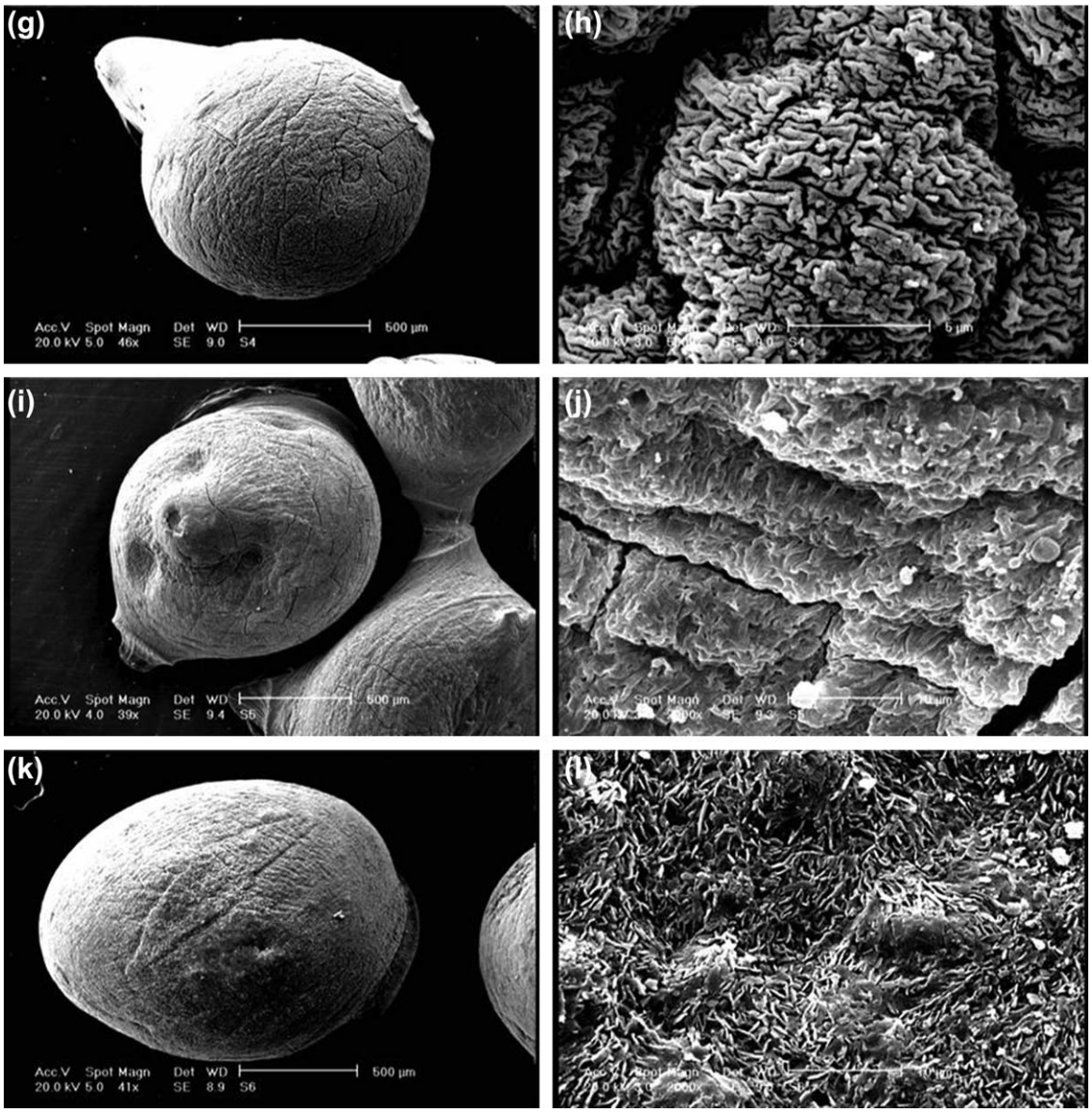

Figure 4. (Continued)

increased from 3.7401 mm to 4.3357 mm (for alginate 2% wt/vol) and from 4.1023 to 4.6172 (for alginate 3% wt/vol). DEE was also increased by coating the alginate with chitosan and reinforcing with dextran sulfate.

Furthermore, the DEE of alginate 3% wt/vol (Sample C), chitosan-coated alginate 3% wt/vol (Sample D), and chitosan-coated alginate 3% wt/vol/dextran sulfate 1% wt/vol (Sample F) were higher than 2% wt/vol ones (Sample A, B, and E). These all represented the alginate matrix reinforcement with increasing the alginate concentration. As compared to the other produced beads, the chitosan-coated alginate/dextran sulfate beads reveal a higher entrapment of propranolol-HCl.

SEM Studies of the Beads

SEM photographs of dried beads and their surface morphology are shown in Figure 4. All the beads showed acceptable spherical shape and relatively smooth surface but with some wrinkles. In pervious studies,[10,21] the change in the shape of dried beads (shrinkage) from sphere was reported for beads that were prepared from low alginate concentration solutions. However, in this research, the prepared beads did not lose their spherical shape after air drying. Detailed investigation of beads' surface structure showed that the cracks were developed by shrinking of the polymer network during air drying. SEM micrographs of propranolol-HCl loaded alginate beads (Sample A) represented the crystalline particles of drug (free drug), attached to the surface beads. This phenomenon is due to the air drying, which causes the movement of the drug to surface.

Comparison of Figure 4(a,b) (Sample A) and 4(e,f) (Sample C) also shows that increasing of alginate solution concentration leads to beads with the denser surface and morphology. In addition, the amount of free drug presented on the beads surface is

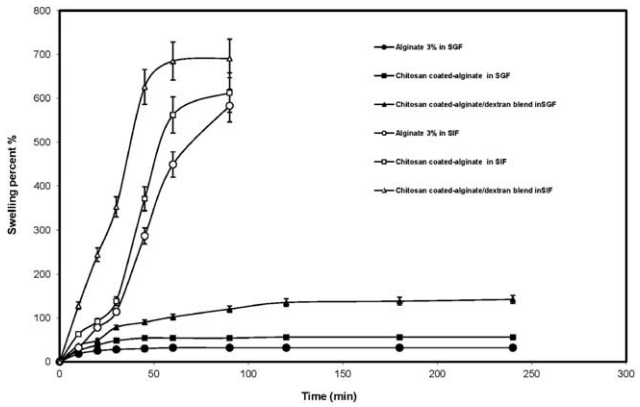

Figure 5. The swelling behavior of alginate, chitosan-coated alginate and chitosan-coated alginate/dextran sulfate beads in SIF and SGF.

reduced. Comparison of Figure 4(d) (surface morphology of Sample B) and 4(h) (surface morphology of Sample D) with Figure 4(b) (surface morphology of Sample A) and 4(f) (surface morphology of Sample C), respectively, shows that calcium alginate beads and chitosan coated calcium alginate beads have different surface morphologies as a result of the formation of composite chitosan/alginate layer on the beads. Furthermore, comparison of Figure 4(d) (Sample B) and 4(h) (Sample D) confirms that the beads that prepared with 3% wt/vol of alginate concentration have a denser surface morphology. As mentioned previously, alginate is an anionic polysaccharide polymer while chitosan is positively charged polymer. Increasing of alginate concentration leads to increase the electrostatic interaction between these two polymers and consequently chitosan coatings on the surface of the alginate beads become denser. Comparison of Figure 4(i,j) (Sample E) and 4(k,l) (Sample F) with Figure 4(a,b) (Sample A) and 4(e,f) (Sample C) and also with Figure 4(c,d) (Sample B) and 4(g,h) (Sample D) represents that prepared beads by dextran sulfate strengthen the network and have a better spherical shape. In addition, comparison of their surface morphology with chitosan coated beads confirms the differences in their surface morphologies. Dextran sulfate also is a negative electric charge polymer. The difference in the surface morphology of the beads could be due to changes in the electrostatic interactions occurring between the coating layer containing chitosan and alginate/dextran beads. Furthermore, comparison of Figure 4(j) (surface morphology of Sample E) and 4(l) (surface morphology of Sample F) shows that the beads prepared from the solution containing 3% wt/vol of alginate [Figure 4(l)] have a needle-shaped surface and its morphology is very different from surface morphology of prepared beads from the solution containing 2% wt/vol of alginate [Figure 4(j)]. This difference could also be due to changes in the electrostatic interactions between the coating layer of chitosan and alginate/dextran sulfate beads due to increasing concentrations of alginate. In addition, as it is seen in Figure 4(b–l), less free drug on the bead surface is observed by increasing of alginate concentration, coating of beads with chitosan and adding dextran sulfate.

In order to verify above mentioned results, ATR-FTIR can be used as presented in Supporting Information material for review.

Swelling Kinetics of Beads in SIF and SGF

The swelling behavior of alginate (Sample C in Table II), chitosan-coated alginate (Sample D in Table II), and chitosan-coated alginate/dextran sulfate beads (Sample F in Table II) are shown in Figure 5. As it is seen, all samples show a high swelling behavior in simulated intestinal fluid (SIF) at pH = 6.8 and have a very lower swelling in simulated gastric fluid (SGF) at pH = 1.2.

Swelling of alginate beads in SGF occurs due to hydration of hydrophilic groups. Alginate beads coated with chitosan show more swelling in SGF because of the hydration of hydrophilic groups and protonization of chitosan amino groups. The latter phenomena create repulsive forces and more swelling of alginate beads coated with chitosan. Alginate/dextran beads coated with chitosan show more swelling, as compared to other beads. Presence of dextran sulfate leads to increase of the water-binding site and consequently increase of swelling of these beads. The same pattern is observed for swelling in SIF. But amount of swelling in the SIF is several times higher than of that in SGF. These results confirm the pH-sensitive swelling behavior of the prepared beads.

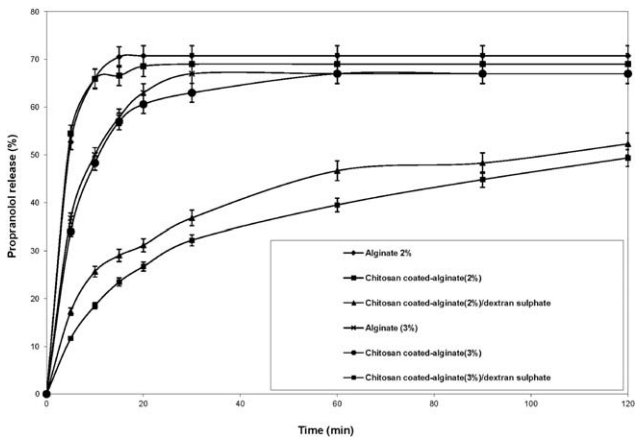

Figure 6. Propranolol release profile at SGF (HCl, pH =1.5) of formulation A, B, C, D, E, and F (Table II).

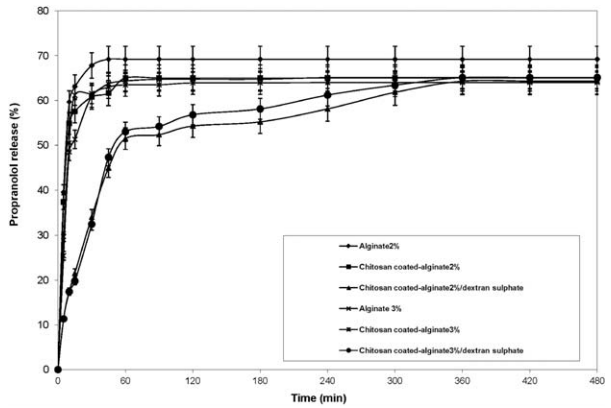

Figure 7. Propranolol release profile at SIF (phosphate buffer, pH = 6.8) of formulation A, B, C, D, E, and F (Table II).

Propranolol-HCl Release Profile

The propranolol release behavior from beads was studied in SGF (at pH = 1.5) and SIF (at pH = 6.8). The release profiles of propranolol-HCl from the prepared beads are presented in Figures 6 and 7.

The burst release observed within 15 min in both solutions was related to matrix stableness of beads and probably drying method (drying in the air) and that some of propranolol-HCl particles placed onto the surface of the beads.

Propranolol is a low molecular weight drug; therefore, its release from the alginate beads is independent of the swelling behavior. Nevertheless, as seen in Figures 6 and 7, coating beads with chitosan and reinforcing their matrix with dextran sulfate led to decreasing the initial burst release and release rate of drug. However, the release rates of coated beads at simulated gastric fluid were not decreased significantly as compared to the un-coated beads. In contrast, using the dextran sulfate partly controlled the release rate and reduced the burst release at primary time.

CONCLUSIONS

The main objectives of this study were to prepare monosized and spherical propranolol-loaded alginate from high viscous alginate solutions using the combined methods of electrospray and ionotropic gelation, decreasing of initial burst release and drug release rate and increasing the propranolol loading percent. The parameters affecting beads size and drug entrapment was of prime interest. The results showed that voltage had a pronounced effect as compared to the other parameters, where, reduction of the beads size occurred by voltage increasing. Increasing the flow rate, alginate concentration, nozzle diameter, and decreasing the voltage improved DEE.

Enhancing of the alginate concentration, matrix reinforcement with dextran sulfate, and alginate coating led to increasing the drug loading percentage more than 70%. Also, adding dextran sulfate to the bead matrix could decrease drug release rate in gastric environment. Propranolol-HCl is a low molecular weight drug and its release rate at both SIF and SGF would be diffusion controlled and independent of swelling behavior of the prepared beads. Therefore, it is anticipated that the developed system in this work would show a better release profile and improved DEE for high molecular weight drugs.

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