

CHEMICAL MODIFICATION OF THE SURFACE OF CALCIUM ALGinate GEL BEADS*

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Abstract The chemical modification of the surface of calcium alginate gel beads (CAGB) via grafting copolymerization with vinyl acetate (VAc) was studied. The optimum reaction conditions with activation and graft copolymerization two steps were explored. First, 5 grams CAGB with 2.5 mm initial diameter was initiated with 0.0493 mol/L $K_2S_2O_8$ at 51 °C for 30 min in 15 mL 1% PVA/H₂O. Then 4.34 mol/L VAc was added dropwise and the reaction was allowed to proceed at 48 °C for 3 h. The grafting efficiency could come up to 30%. It was found the stability of modified CAGB in the air and in electrolyte solutions was greatly improved.

Keywords Calcium alginate gel bead, Vinyl acetate, Graft copolymerization, Chemical modification

INTRODUCTION

Sodium alginate, a kind of polysaccharide derived from natural algae, contained numerous hydroxyl and carboxyl groups. Alginate could form gel beads with divalent ion Ca^{2+} . Due to their biocompatibility, calcium alginate gel beads (CAGB) had been widely utilized as matrix for drug controlled release^[1–5]. However, the stability of CAGB was quite poor. Thus, modification of the surface of CAGB would enhance its stability and might make it useful in other area.

To our knowledge, no work has been reported about chemical modification of the surface of CAGB. It was reported that sodium alginate could be modified via grafting copolymerization with vinyl monomers^[6–8]. In this paper, potassium persulphate was used to initiate the graft copolymerization of vinyl acetate onto the surface of CAGB and its stability was evidently improved.

EXPERIMENT

Materials

Sodium alginate (SA, Wenzhou Chemical Agent Factory, Zhejiang, China) was dried before use. Vinyl acetate (VAc, Qidong 2nd Fine Chemical Agent Factory, Jiangsu, China) was distilled before use. Potassium persulphate ($K_2S_2O_8$), anhydrous calcium chloride (Lanxi Chemical Agent Factory, Zhejiang, China) and poly(vinyl alcohol) (PVA, average degree of polymerization = 2400–2500, Tianshan Chemical Agent Factory, Shanghai, China) were used as received.

Graft Copolymerization on the Surface of CAGB

Droplets of sodium alginate solution were fed into 3% calcium chloride with a 50 mL syringe to prepare CAGB of different diameters. CAGB were immersed in distilled water for 24 h at ambient temperature, and blotted with

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soft paper to remove surface water. 5 g CAGB, a suitable amount of potassium persulphate and 15 mL 1% PVA/H₂O solution were placed in a three-neck bottle and kept at a given temperature for some time to initiate CAGB. Vinyl acetate was fed dropwise with stirring. The reaction was continued until the designate time even if the monomer was completely added in a shorter time. The reaction mixture was filtered, washed with distilled water 5 times and dried in air and at 60°C. Then the modified CAGB (MCAGB), was obtained as hard beads.

Measurements

MCAGB was extracted with ethyl acetate and dried at 60°C. Then the grafting efficiency (*GE*) was calculated as followed:

$$GE = (W_3 - W_1)/(W_2 - W_1) \times 100\%$$

where W_1 , W_2 and W_3 were the weight of dried CAGB, MCAGB and extracted MCAGB, respectively.

FTIR spectra of CAGB, extracted MCAGB and poly(vinyl acetate) (PVAc) were obtained on a Nexus 470 FTIR spectrophotometer.

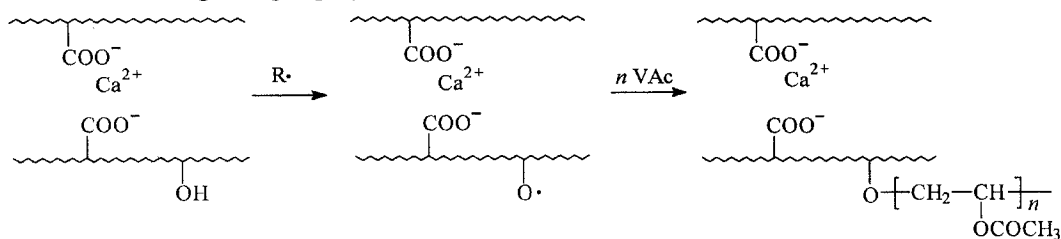
Stability Test

Some CAGB and MCAGB were placed on a glass utensil exposed to air at the ambient temperature and the appearance of the beads was recorded. Some CAGB and MCAGB were placed in Na₂CO₃, Na₂SO₄, and NaCl solutions of different concentrations and the disintegration rate was recorded.

RESULTS AND DISCUSSION

Graft Copolymerization

In a heterogeneous system, CAGB could not be initiated immediately when the primary radicals were formed. Therefore, an activation period was necessary. The reaction mixture should be kept at a given temperature for some time so as to ensure that enough radicals were produced on the surface of the beads. Then the active center formed could initiate the grafting copolymerization of VAc monomer onto CAGB^[9].



Scheme 1 The graft copolymerization of vinyl acetate onto alginate calcium gel beads

The number of active sites formed on the beads depended on the concentration of initiator, the initiation temperature and initiation time, which would affect the grafting copolymerization. For a mixture of 5 g CAGB with initial diameter of 2.5 mm and 15 mL 1% PVA/H₂O solution, it was found that the optimum initiation condition was 0.0493 mol/L K₂S₂O₈, 51–52°C and 30–35 min.

Several factors affecting the grafting copolymerization of VAc onto CAGB were examined under the initiation conditions described above. As the values of variables such as the concentration of monomer, the reaction temperature, the reaction time and the average initial diameter of beads increased, GE came up to a maximum value and then decreased (Figs. 1–4), which was consistent with the general radical reaction principle^[10]. In the heterogeneous system, increasing the value of the variables was beneficial to the graft copolymerization of VAc onto CAGB. Meanwhile, the homopolymerization of VAc was also enhanced. As a result, GE first increased and then decreased. The maximum GE could be obtained when 4.34 mol/L VAc reacted with CAGB at 48°C for 3 h.

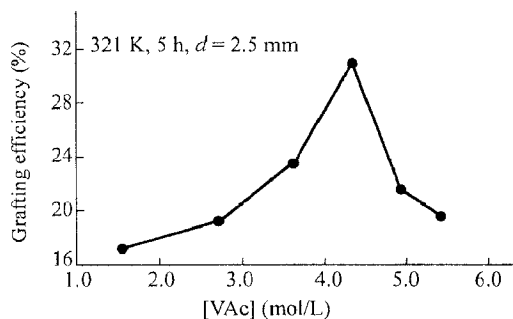


Fig. 1 The effect of monomer concentration on the modification

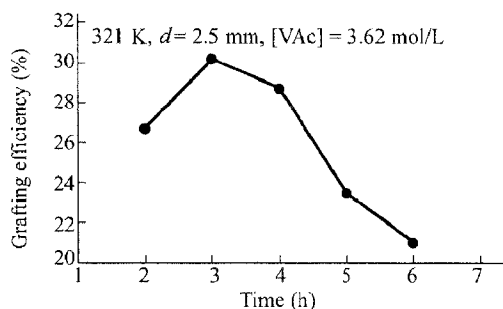


Fig. 2 The effect of reaction time on the modification

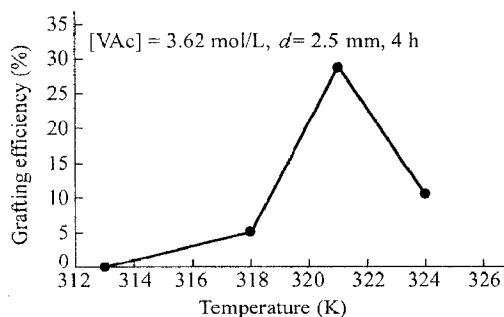


Fig. 3 The effect of reaction temperature on the modification

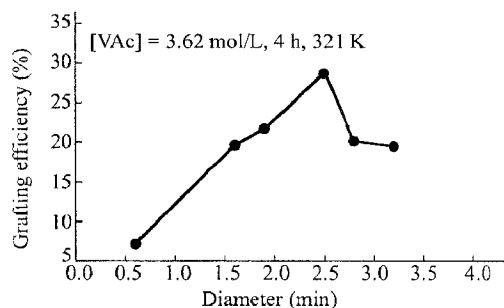


Fig. 4 The effect of initial diameter of CAGB on the modification

Characterization

The FTIR spectra of both PVAc and extracted MCAGB showed their characteristic absorption bands at 1740 and 1240 cm^{-1} , while no corresponding peaks were seen for CAGB, which suggested that MCAGB was the graft copolymer of CAGB and PVAc.

Stability of Gel Beads

There was an evident difference between the appearance of CAGB and MCAGB after exposure to air (Fig. 5), which indicated that the stability of MCAGB was better than that of CAGB.

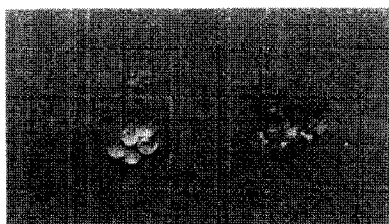


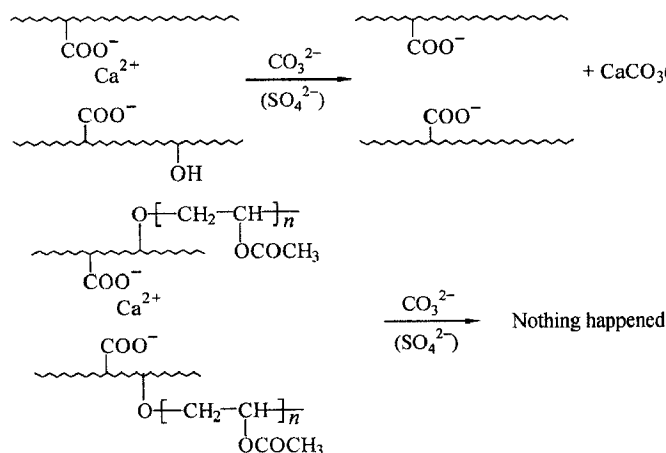
Fig. 5 The appearance of calcium alginate gel beads (CAGB) and modified calcium alginate gel beads (MCAGB) (magnification: $2\times$)
Initial CAGB (right) and CAGB exposed to air for 8 h (upper left)
MCAGB exposed to air for more than 8 days (lower left)

As a kind of polyelectrolyte, the stability of CAGB in solution depends on the anions (Table 1). The formation of calcium sulphate or calcium carbonate precipitate would lead to disintegration of CAGB. In contrast, MCAGB kept its integrity in different electrolyte solutions (Scheme 2). The greatly enhanced stability of the gel beads could be attributed to the fact that it was difficult for anions to diffuse into the beads to form

precipitate with Ca^{2+} because the surface of MCAGB was protected by PVAc.

Table 1. The steadiness of calcium alginate gel beads (CAGB) and modified calcium alginate gel beads (MCAGB) in the electrolyte solutions

Electrolyte Time to dissolve completely (min) Beads	Na_2SO_3		Na_2SO_4		NaCl	
	1.0 (mol/L)	0.2 (mol/L)	1.0 (mol/L)	0.2 (mol/L)	1.0 (mol/L)	0.2 (mol/L)
CAGB	20	30	40	110	Swollen	Swollen
MCAGB	Nothing happened					



Scheme 2 The dissociation equilibrium of alginate beads

CONCLUSION

Chemical modification of the surface of CAGB via grafting copolymerization with VAc was presented. The optimum reaction conditions to obtain maximum *GE* were also given. With greatly improved stability, MCAGB might be useful after fine tailoring.

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