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Effect of Sodium Alginate Concentration on Membrane Strength and Permeating Property of Poly-*l*-arginine Group Microcapsule

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Abstract: A novel poly-*l*-arginine microcapsule was prepared due to its nutritional function and pharmacological efficacy. A high-voltage electrostatic droplet generator was used to make uniform microcapsules. The results show that the membrane strength and permeating property are both remarkably affected with the changes of sodium alginate concentration. With the sodium alginate concentration increasing, gel beads sizes increase from 233μm to 350μm, release ratio is also higher at the same time, but the membrane strength decreases.

Keywords: Poly-*l*-arginine, microcapsule, sodium alginate, membrane strength, release.

In recent years, increasing clinical needs promote the development of biomaterials, and synthesizing the degradable polymeric materials has been the hot topic in the study of biomaterials, especially used in drug controlled release system[1]. Now, the most widely used biodegradable polymeric materials include polyortho esters, polyanhydrides, polycaprolactone, polytrimethylene carbonate, polyamino acid, pseudo-polyamino acid, polyglycolic acid, polylactic acid, polyphosphazenes and polysaccharides. Among these materials, polyamino acid has attracted considerable attentions due to its nontoxicity, excellent biocompatibility, nutritional function and pharmacological efficacy. For example, polyarginine and arginine can enhance the drug delivery across biological membranes and tissues[2-3], inhibit tumor growth[4-5], and possess antimicrobial activity[6], besides, that they can cure vascular proliferative responses, asthma, chronic bronchitis, cystic fibrosis, bronchieotasis[7-8] and so on. Mitchell *et al.* [9] also reported that polyarginine can enter cells more efficiently than other polycationic homopolymers.

Furthermore, microencapsulation technique has also been developed quickly after report by Lim and Sun[10]. But sodium alginate has a great influence on the characteristics of microcapsules[11]. In the present work, we attempt to use polyarginine in microcapsule manufacture, to prepare an intervening therapeutic and biodegradable drug carrier, and focused to investigate the effect of the sodium alginate concentration on the membrane strength and permeating property of the alginate-poly-*l*-arginine-alginate microcapsule.

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Experimental

Materials

Poly-*l*-arginine with molecular weight 55300, was kindly provided by Sigma Co. (USA). Sodium alginate was purchased from Dalian Algae Industrial Corp., and its water solution was filtrated through 0.8μm membrane. Bovine erythrocytes hemoglobin (Hb) with molecular weight 64500, was provided by Shanghai Lizhu Dong Feng Biotechnology Co. Ltd. Sodium chloride injection was produced in Shandong Linzi Pharm. Factory (Authorized No. 035003 by Shandong Board of Health). All other compounds were of analytical purity.

Methods

Preparation of alginate- poly-*l*-arginine -alginate microcapsule: Sodium alginate (0.8%, 1.0%, 1.2% and 1.5% respectively, w/v) droplets were produced by syringe pump extrusion (9.90 mL/h) into 0.1 mol/L calcium chloride solution to form the gel beads by means of the high-voltage electrostatic droplet generator (Made in Dalian Institute of Chemical Physics, Chinese Academy of Sciences). 30 minutes later, the gel beads were treated in a 0.05% (w/v) poly-*l*-arginine solution for 10 minutes. The formed poly-*l*-arginine alginate microcapsules were washed two times by 0.9%(w/v) sodium chloride solution, and further treated with 0.15% sodium alginate solution for 5 minutes.

Particle size determination: The particle sizes of 50 microcapsules were measured by the microscope, and their average particle sizes were calculated.

Membrane strength: According to the reference[12], the membrane strength can be characterized by the membrane expansion rate, and was examined by the microscope. Its value was calculated as following equation:

$$\text{Expansion rate}(\%)=\frac{\overline{d}_{microcapsules}}{\overline{d}_{beads}}\times 100\%$$

Where $\overline{d}_{microcapsules}$ and $\overline{d}_{beads}$ are the diameters of the microcapsule and sodium alginate gel beads, respectively. In general, the lower the value of expansion rate is, the stronger membrane strength will be.

Release ratio: Release ratio was determined as follows[13]. 1 mL gel beads were put into 10 mL of 0.5 mg/mL Hb. 2 hours later, the Hb adsorbed gel beads were treated in a poly-*l*-arginine solution under continuous agitation for ten minutes, subsequently, Hb adsorbed microcapsules were prepared. 1 mL Hb adsorbed microcapsules were put into physiological saline solution. The sample solution at different time was collected, and assayed at periodical 405 nm by spectrophotometry.

Results and Discussion

Effect of sodium alginate concentration on the microcapsule membrane strength

The proper sodium alginate concentration to form good spherical beads ranges from 0.8% to 1.5%. When the concentration is too low, the beads can not be obtained, but the

fragments were formed. When the concentration is too high, the beads can be obtained, but the beads are in form of oval. After treating the beads with poly-*l*-arginine with continuous agitation for ten minutes, an ionically bonded semipermeable membrane structure forms. In general, the lower the expansion rate is, the stronger the membrane strength will be. **Figure 1a** shows that the expansion rates are similar when sodium alginate concentration was 0.8% and 1.0%, and when concentration increases from 1.0% to 1.5%, expansion rate increases significantly, which results in the decrease of the membrane strength. This can be explained by **Figure 1b**. If we improve the concentration, it is equal to improve the density of carboxyl groups ($-COO^-$) in the unit area. So the incorporated probability between the imino groups ($=NH_2^+$) in poly-*l*-arginine and the carboxyl groups ($-COO^-$) in calcium alginate is high. But at the same time, beads sizes increase from 233μm to 350μm, which makes the gel pores smaller[14]. Thus it becomes more difficult for polyarginine molecules to enter the calcium alginate network, subsequently the membrane strength decreases. The curve implies a compromise effect of these two factors.

Figure 1a the influence of sodium alginate concentration on swollen degree

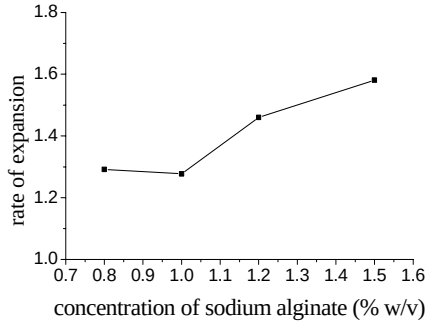
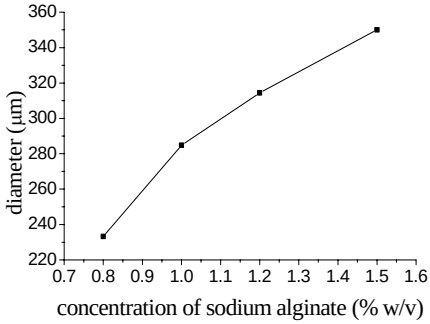


Figure 1b the influence of sodium alginate concentration on particle size

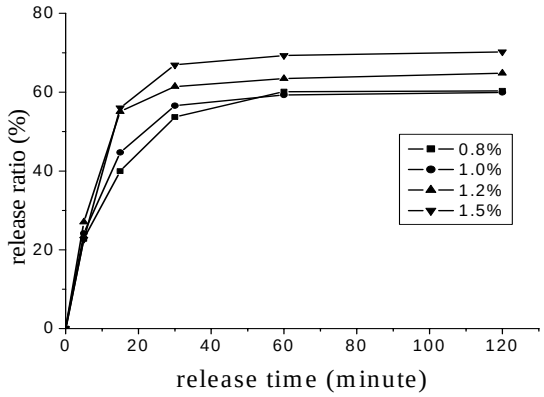


Effect of sodium alginate concentration on microcapsule release ratio

We can see that there is a rapid initial drug release process (39%~57% drug release at 15 min) for these microcapsules with different sodium alginate concentration, followed by slow release of the drug. In the first 30 min, the release rate of the drug for the microcapsules prepared from high concentration is higher than that from medium and low sodium alginate concentration. For example, when sodium alginate concentration is 0.8, 1.0, 1.2, 1.5%, their release ratios respectively are 54, 57, 61, 67% at 30 min. Later, the differences are not obvious when sodium alginate concentration is 0.8% and 1.0%.

It is well-known that the drug release ratio is related to microcapsule expansion rate. **Figure 2** shows the relationship between the microcapsule release ratio and sodium alginate concentration.

Figure 2 The influence of sodium alginate concentration on release ratio



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