

Preparation of Magnetic Polyelectrolyte Nanoparticles and Their Application to Magnet-induced Injectable Gels

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Statement of Purpose: With an aim to develop an injectable gel-forming scaffold that can be used to repair tissue injury or regenerate substrates, a pair of magnetic nanoparticle (NPs) coated with alginate (AA) and chitosan derivative polyelectrolytes was developed. The design displayed the advantages over the performed scaffold approach: flowable and dispersible NPs can fill any shape of defect, magnetite particles can be controlled and deposited under magnet induction, all materials can be biodegradable or resorbable, and finally gel-forming process can be accelerated by optimizing the concentrations, particle sizes and magnetic forces.

Methods:

1. Preparation of magnetite particles: The superparamagnetic magnetite was synthesized using a partial reduction and co-precipitation procedure. Briefly, 2 M of FeCl_3 solution was mixed with 1M of Sodium sulfite and then 80 ml of 1.8 % ammonia water were poured into the flask under sonication (20 % of 100 W, Branson) for 30 min. the NPs were collected after rinse and centrifugation.
2. Preparation of methylated chitosan (MCS): the synthesis procedure was modified according to the literature. [1] The MCS was precipitated and separated by using ethanol and then dissolved in deionized water. After repeated precipitation steps for 3 times, the MCS was dried by freeze-drying for further use.
3. Preparation of Fe_3O_4 (core)-AA/MCS(shell) magnetic NPs: The zinc ion doped process was modified from the literature.[2] The positive-charged magnetite was dispersed into 50 ml NaOH aqueous solution (pH 10) and then an aliquot of 50 ml of 0.05%(w/v) AA in NaOH solution was added to form the gel-coated NPs under ultrasound irradiation. After centrifugation, re-dispersion of the NPs in phosphate buffer solution (PBS, pH 7.4) or diluted hydrochloride solution (pH 3.0) by gentle shake was employed and mixed with 50 ml of 0.05% (w/v) MCS in diluted HCl solution to fabricate the AA/MCS-coated NPs. All the nanoparticles were purified by centrifugation and re-dispersed in PBS.
4. In situ gel-forming tests: the AA-coated NPs and the AA/MCS-coated Ns were dispersed in PBS solution. They did not precipitate within 6 hr. To force the particles gelation, the magnet with 3000 gauss was fitted beneath the dish to attract the two kinds of particles. The particles were aggregated to form a thin complex layer covering the dish. After decanting the residual clear solution and freeze-drying the film, SEM was applied to characterize the gel morphology.

Results/Discussion:

By partial reduction of ferric ions to ferrous ions and forming the stable complex, the iron oxide NPs prepared under ultrasonic irradiation displayed well-dispersion in aqueous solution with about 5 nm diameter. X-ray diffrac-

tion analysis verified the particles as iron oxide. And also the SQUID measurement showed the superparamagneticity of NP without any hysteresis in the range of -20000~20000 gauss.

Besides, the particle surfaces were doped with zinc ions under ultrasound irradiation, forming positive-charged surfaces. The surfaces provided a high affinity to alginic acid, giving the well-dispersed AA-coated NPs with 102 nm diameter by adsorption in diluted basic solution. The basic environment assisted the electrical double-layer of surfaces loosely to attach the alginate by ionic interactions. Figure 1 shows the dispersion of NPs in the TEM photograph. The chitosan-coated NPs have been prepared using the layer-by-layer technique to deposit the chitosan on the AA-coated particle surfaces. However, the mass precipitation occurred as soon as mixing the two components. It was suggested that the chitosan is sensitive to the pH value and gel-forms instantly with AA. We replaced the chitosan with methylated chitosan (MCS) by use of the formation of quaternary ammonium ions on the chitosan chains, giving the water-soluble, pH-independent cationic polyelectrolytes. The MCS adsorbed on the AA-coated NPs in diluted acid solution gave the AA/MCS complex shells. The AA/MCS-coated NPs with 108 nm diameter still displayed the well-dispersion and magnetic properties.

In the in situ gel-forming tests, the AA-coated and AA/MCS-coated NPs mixed together in PBS were found no precipitate formation. By applying the magnet to attract the NPs, the thin film was found to deposit on the dish within half an hour and did not re-disperse again due to gelation forming.

Conclusions: The NPs coated with positive and negative charges were successfully prepared and well-dispersed in PBS. By applying magnet field, the NPs were able to aggregate and forma gel film. It displays a promising potential to use as an in situ gel-forming scaffold

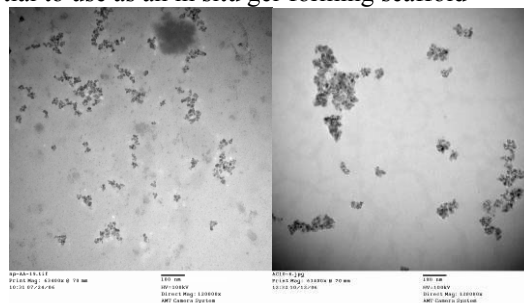


Figure 1. TEM photographs for AA-coated NPs (left) and AA/MCS-coated NPs (right).

References:

1. Curti E, de Britto D, Campana-Filho SP. *Macromol Biosci.* 2003; 3: 571–576.
2. Dhas NA, Zaban A, Gedanken A. *Chem Mater.* 1999; 11: 806.