Mineralization of Hyaluronic Acid Nanoparticles and Their Potential as the Robust Carrier of Doxorubicin

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Introduction

Organic-inorganic hybrid nanoparticles are unique class of nanomaterials that are widely exploited for various biomedical applications. In particular, calcium phosphate-based hybrid nanoparticles are promising candidates for drug delivery because of their excellent biocompatibility. Self-assembled polymeric nanoparticles that can sequester hydrophobic guest molecules have widely investigated as carriers for cancer therapeutics. However, poor stability of such particles limited their use in clinical applications. To improve the stability of the self-assembled nanoparticular system, we have prepared mineralized nanoparticles based on amphiphilic hyaluronic acid (HA), which could encapsulate a quantity of poorly water-soluble anticancer drugs. The physicochemical characteristics of the mineralized nanoparticles were investigated using transmission electron microscope (TEM), dynamic light scattering (DLS), and FT-IR spectroscopy.

Methods

Amphiphilic hyaluronic acid-5β-cholanic acid conjugate (HACA) was synthesized according to the procedure reported [1]. To prepare mineralized HA nanoparticles (MHA), calcium nitrate solution was added to the HACA solution and stirred for 10 min before the addition of ammonium phosphate solution. The solution was additionally stirred for 10 min. The free ions were removed by dialysis against deionized water. In order to investigate the potential of mineralized nanoparticles as the drug carrier, doxorubicin (DOX) was physically encapsulated into HACA nanoparticles using oil-in-water emulsion method before mineralization. The morphology of HACA and MHA nanoparticles were observed using a TEM. Their particle sizes were obtained using a DLS. The stability of MHA and DOX-MHA was studied in the presence of sodium dodecyl sulfate (SDS).

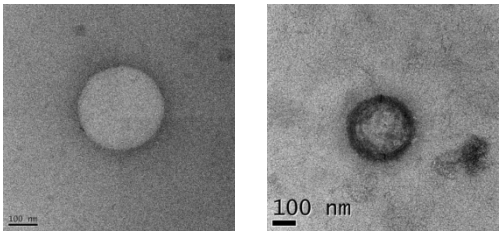
Results

The physicochemical characteristics of the HACA, MHA, DOX-HACA, and DOX-MHA nanoparticles are summarized in the Table 1. The hydrodynamic size of the HACA, MHA, and DOX-MHA nanoparticles was found to be 187, 213 and 230 nm, respectively (Table 1). This indicates that particle size of HACA nanoparticles can increase by physical encapsulation of DOX and mineralization. The zeta potential of HACA nanoparticles significantly decreased after mineralization. Since DOX is the positively charged drug, DOX-MHA had the lowest zeta potential because DOX neutralized carboxyl ions of HA.

Table 1. Physicochemical characteristics of HACA, MHA, DOX-HA, and DOX-MHA nanoparticles

Samples	size[a] (nm)	Zeta potential[a] (mV)	Loading content[b] (%)	Loading efficiency[b] (%)
HACA	187.5	-49.93	-	-
MHA	213.6	-18.91	-	-
10% DOX-HACA	216	-3.16	8	79.9
10%DOX-MHA	230.9	-1.03	8.16	81.6

The morphology of the nanoparticles was observed using a TEM before and after mineralization, as shown in Figure 1. Both of neat and mineralized nanoparticles were spherical in shape. It was of interest to note that MHA had a thin shell due to formation of inorganic calcium phosphate. The mineralization was also supported by the presence of Ca and P in the EDX analysis.



(a) (b)

Figure 1. TEM images of (a) HACA and (b) MHA nanoparticles.

The mineralized particles showed enhanced *in vitro* stability, which was evaluated by monitoring the size of the nanoparticles in the presence of detergents, sodium dodecyl sulfate (SDS).

Conclusion

We have prepared a novel DOX-encapsulated hybrid nanoparticles under ambient temperature. The hybrid nanoparticles exhibited enhanced *in vitro* stability. The results suggested that these hybrid nanoparticles could be useful as robust carriers for drug delivery.

References:

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