Chitosan–cholesterol 나노파티클의 제조 및 특성
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Preparation and characterization of chitosan–cholesterol nanoparticle
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Abstract

Low molecular weight oligo–chitosans were chemically modified by hydrophobic group of cholesterol. The particle size and critical aggregation concentration (cac) of the hydrophobized chitosan nanoparticles were investigated by using dynamic light scattering and fluorescence spectroscopy, respectively. The MW of chitosan and DS were played a critical roles for the physicochemical characteristics of hydrophobized chitosan nanoparticles.

1. Introduction

Polymeric self–assembly systems have been widely investigated in terms of their micellar behavior as well as their application to the fields of biotechnology and pharmaceutics. Among the numerous synthetic and natural polymers for nanoparticle preparation, chitosan, a natural amino polysaccharide, has been generally considered biocompatible, bio degradable, and of low toxicity[1]. In this study, Chitosan was
hydrophobically modified by introducing cholesterol as a hydrophobic moiety. The hydrophobically modified chitosan nanoparticles according to various ratios of cholesterol were prepared by a self assembly method. And then, we investigated physicochemical properties of the nanoparticles by DLS and fluorescence spectroscopy.

2. Experimental method

2–1. Materials

Chitosan lactate mixture was donated from Kittolife, co. Korea. Cholesteryl Chloroformate and pyrene were purchased from Aldrich. DL–Lactic acid was purchased from Sigma. Various solvent, i.e. dimethyl sulfoxide (DMSO), ethyl acetate, acetone, as a reagent grade were used without further purification.

2–2. Synthesis of Chitosan–cholesterol conjugates

Fractionated Chitosan with molecular weight of 1~3K and 3~5K were coupled with cholesteryl chloroformate (CC). Briefly, Chitosans were pre–dissolved in distilled water and then, DMSO was added to the chitosan aqueous solution. Different amounts of CC solution (in ethyl acetate) were added and stirred for 24h at room temperature. The resulting solution was precipitated into acetone. And dialyzed for a day against the excess amount of water, and lyophilized.

2–3. Preparation and characterization of Chitosan–cholesterol nanoparticles

Chitosan–Cholesterol nanoparticles according to various ratios of cholesterol
were prepared by self assembly method. The particle sizes and size distribution, microscopic physicochemical properties of the aggregates were investigated by Dynamic light scattering (DLS) and fluorescence spectroscopy, respectively.

3. Result and Discussion

Chitosan–cholesterol conjugates formed nano-sized particles in aqueous milieu as shown in Figure 1. Fluorescence excitation spectra of chitosan–cholesterol nanoparticle are shown in Figure 2. When the micelles are formed in an aqueous phase, pyrene molecules locate inside or close to the hydrophobic microdomain of micelles, and their photophysical characteristics are changed[2]. As shown in Figure 3, cac can be determined from the change of intensity ratio of pyrene in the presence of chitosan–cholesterol nanoparticles. As the hydrophobicity by introduction of hydrophobic moiety increases, the cac value decreases.

4. Conclusion

Chitosan, hydrophobically modified by cholesterol, forms self aggregates in water above the critical aggregation concentration. The cac values of the chitosan–cholesterol conjugates depended on cholesterol content.

References

2. Y. Chang et al. Macromolecules. 2001, 34, 269
Table 1. Compositions of Chitosan–cholesterol conjugates

<table>
<thead>
<tr>
<th>Raw material</th>
<th>Sample</th>
<th>Cholesterol</th>
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<tbody>
<tr>
<td>Chitosan 1–3 K</td>
<td>CSN1C2.5</td>
<td>2.5%</td>
</tr>
<tr>
<td></td>
<td>CSN1C5</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>CSN1C7.5</td>
<td>7.5%</td>
</tr>
<tr>
<td></td>
<td>CSN1C10</td>
<td>10%</td>
</tr>
<tr>
<td>Chitosan 3–5 K</td>
<td>CSN3C2.5</td>
<td>2.5%</td>
</tr>
<tr>
<td></td>
<td>CSN3C5</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>CSN3C7.5</td>
<td>7.5%</td>
</tr>
<tr>
<td></td>
<td>CSN3C10</td>
<td>10%</td>
</tr>
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</table>

Figure 2. Excitation spectra of pyrene (6.0x10^{-7}M) as a function of chitosan–cholesterol concentration in water.

Figure 1. Particle size distribution profile of (a) CSN3C2.5, (b) CSN3C5, (c) CSN3C7.5 and (d) CSN3C10.

Figure 3. Plots of \( \lambda_{40}/\lambda_{35} \) (from pyrene excitation spectra) vs log C for CSN3C2.5 (■), CSN3C5 (○), CSN3C7.5 (▼) and CSN3C10 (▼) in water.