Synthesis and Properties of Novel Hydrogel Containing Organic Nanotubes as a Contact Lens

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ABSTRACT SUMMARY

We developed hybrid using of hydrogels and organic nanotubes (ONTs). ONTs were first dispersed in the hydrophilic monomers of the contact lens. The dispersion was polymerized and hydrated to obtain hybrid of ONTs and gel. The hybrids were applicable to materials for contact lenses (CLs) since they were transparent. ONTs in the hybrids should capture several drugs and release them in a controlled manner.

INTRODUCTION

Organic Nanotubes (ONTs) are tubular nanostructures prepared from small organic molecules or macromolecules. These structures have attracted growing attention because cylindrical nanospace of ONTs can encapsulate various guests from small molecule and drugs to DNA and proteins, and can release them. Further, they possess a biocompatible surface covered with sugar, peptide, and phospholipid moieties.

The embedding of ONTs in a polymer should enable us to apply the resultant hybrid to an intelligent therapeutic material with drug release function, such as therapeutic contact lens (CLs), cell cultures, and so on. Previous attempts have been only limited to hybrid of microtubules with diameters of 500 nm, and further most of ONTs, so far, possess same inner and outer surfaces. Thereby, sustained release was limited for proteins and DNA. In addition, their large dimensions should make the hybrids translucent which is unsuitable for application in the CLs.

Recently, we developed novel ONTs in which inner and outer surface of them are coated with a functional groups (Fig. 1). They efficiently encapsulated various materials, drugs, DNA, and protein, and release them in a controlled manner. In addition, they showed excellent dispersibility and stability in water with high optical transparency because the outer diameter (15 nm) and length of them are small enough to avoid scattering of visible light.

Figure 1. ONTs consisted lipids and Monomers for CLs

Here, we studied the embedding of novel ONTs into hydrogels with the aim of development of functional materials for CLs.

EXPERIMENTAL METHODS

The ONTs were prepared by heating and cooling of lipids in DMSO as previously reported. Their dimensions were characterized by transmission electron microscopy (TEM), and the molecular packing within the ONTs by powder X-ray diffraction (XRD) analysis.

The resultant ONTs were dispersed in hydrophilic monomer, hydroxyethyl methacrylate (HEMA), or mixtures of HEMA and following monomers: glycerol methacrylate (GLM), N-vinylpyrrolidone (NVP) and N, N-dimethylacrylamide (DMAA), as described later. Polymerization was demonstrated in a mold of CLs with the presence of cross-linker and radical initiator. The resultant polymers were hydrated to obtain ONT-CLs hybrid gels, and characterized by TEM, confocal laser scan microscopy (CLSM).
RESULTS AND DISCUSSION
ONTs were prepared via self-assembly from carboxylate lipid (ONT-1, in Fig. 1 and Fig. 3(a)) and its methyl ester (ONT-2). For visualization of ONTs under CLSM observation, 0.5mol% ONT-1-Alexa was doped into ONT-1 during self-assembly process to obtain fluorescent Alexa-labeled ONTs.

For preparation of ONTs-CLs hybrid gels, ONT-1 or ONT-2 (1wt%) was, first, dispersed in 40wt% of each monomers of GLM, DMAA, NVP, and HEMA by stirring for 24 h. Secondly, HEMA (59wt%) including cross-linker and initiator were added, filled into the CLs mold, and polymerized. Although all CLs demonstrated were transparent just after polymerization, subsequent hydration makes CLs translucent especially that from NVP / HEMA and DMAA / HEMA (Fig. 2).

We revealed that the stirring time of ONTs with the first monomer, prior to the polymerization, affected dispersibility of ONTs in the CLs as follows: ONT-1 and 2 were dispersed GLM by stirring 6, 24, 100 h, and CLs were prepared as described above. We found that the longer stirring time became, the better transparency of CLs improved. Finally, we achieved to prepare highly transparent CLs with even 5% of ONT-2. Details of the mechanism are under investigation.

Figure 3 shows STEM and CLSM images of ONT-CLs hybrid gels consisted of ONT-1, GLM, and HEMA (Fig. 3(a)), and fluorescence image of slice of CLs consisted of Alexa-labeled ONT-1, GLM, HEMA (Fig. 3(b)). TEM image of ONT-CLs visualized existence of hollow nanospace of ONT-1 in the gel with similar dimensions of native ONTs. CLSM image indicated that the ONTs partially formed bundles. Translucency of the ONT-CLs hybrids were, thus, caused by forming bundle or aggregation in CLs.

Details of these CLs containing ONTs, such as water content, oxygen transmittance, strength, etc. were also analyzed.

CONCLUSION
We synthesized hydrogels conjugated ONTs in which inner and outer surfaces were covered with different function. We optimized process for ONTs-CLs hybrid with high transparency. These results suggested the possibilities to apply the hydrogels conjugated ONTs for the materials of CLs.

REFERENCES

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