1P273 # 芯鞘ナノファイバーからの薬剤放出メカニズム

（福井大院･工）○黄 琬穎，日比野 隼也，末 信一朗，藤田 聡

Introduction

Recently, highly specific drugs such as antibody preparations and molecular target drugs have been developed, and the design of an efficient drug delivery system (DDS) is highly desired. Especially matrix materials which attain long-term controlled drug release are necessary for cancer treatment and wound healing. Electrospun nanofibers are expected as one of the potential DDS materials, which have high processability and biocompatibility with living tissues. However, the development of nanofiber materials carrying hydrophilic drugs including antibody preparations has not yet been achieved, because it is difficult to sustain and control the burst release of hydrophilic drugs from their surface. Fabrication of nanofibers for delivering hydrophilic drugs in the spatially and temporally regulated manners. which should be the greatest challenge. To overcome the problem, we designed core-shell nanofibers, which have two different types of polymers in their core and shell layers. Shell structure is anticipated to prevent the release of the drug incorporated in the core of nanofibers and enable gradual release for a long-term. In this study, berberine, an anti-inflammatory agent, was used as a drug model and collagen and poly-L-lactic acid (PLLA) were chosen as core and shell materials, respectively. Both materials are safe and biodegradable materials. Collagen as a core layer is expected to play a role to retain berberine and the shell of PLLA, a hydrophobic polymer, sustains the long-term release of the incorporated drug while it is degrading. Overall, the fabrication and the characterization of the drug-incorporated nanofibers, and the evaluation of the drug release profile can be explained by drug release kinetics.

Experimental

Core-shell nanofibers were fabricated using 10% collagen dissolve in trifluoroethanol solution containing 3% berberine as a core layer and 10% PLLA dissolve in hexafluoroisopropanol solution as shell layer by electrospinning. PLLA monolithic nanofibers were prepared as a control. Core-shell and monolithic nanofibers were characterized by SEM, WAXD, DSC and ATR-FTIR. Furthermore, these were incubated in physiological condition (PBS, pH 7.0, 37°C), then the amount of the drug released into the solution was quantified by spectroscopy. To evaluate long-term drug release behavior, the release test was carried out under the alkaline condition (Glycine-NaOH buffer, pH 11.0, 37°C), where hydrolysis of PLLA is accelerated. Bioactivity of released drug was evaluated with MTT assay.

Results and Discussion

From DSC and WAXD results showed that berberine was in amorphous core-shell nanofibers as a result of the interaction with collagen. Furthermore, the results of the cell viability of MDA-MB-231 breast cancer was measured by MTT assay demonstrated neither of the toxicity of core-shell nanofiber nor the possible deterioration of berberine bioactivity caused by the interaction with collagen. The drug was distributed on the fiber surface of the monolithic nanofibers more than core-shell nanofiber. Drug release profile shown as Fig. 1 was analyzed by using Korsmeyer-Peppas equation (Eq. 1), where Qt is a fraction of drug released at time t, K is the release rate constant and n is the release exponent.

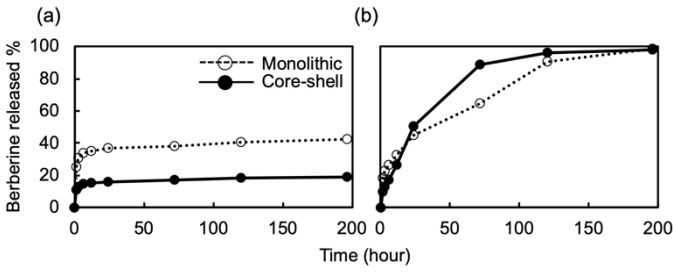

Fig. 1 Drug release behavior under PBS (a) and pH 11.0 (b).

$$\log Q_t = n \log t + \log K \qquad \text{(Eq. 1)}$$

It is an empirical equation can express the drug release mechanism. Base on this model, the value of n characterizes the release mechanism of drug, n of core-shell nanofibers and monolithic nanofiber were 0.81 and 1.49, respectively. Drug released of core-shell nanofiber n <0.89 was diffusion, yet, monolithic nanofiber n>0.89 was probably release by anomalous. In summary of the analysis, monolithic nanofibers drug released along with degradation of PLLA, in contrast, core-shell nanofibers drug released by diffusion. The difference in mechanisms is considered that the drug release controlled by the core-shell structure. It is expected that core-shell nanofibers might achieve long-term drug release.

Mechanism of drug release from electrospun core-shell nanofiber.

Wan-Ying HUANG, Toshiya HIBINO, Shin-ichiro SUYE and Satoshi FUJITA: Graduate School of Engineering, Dept. of Frontier Fiber Technology and Science, University of Fukui, 3-9-1 Bunkyo, Fukui 910-8507, Japan, Tel: 0776-27-9969, Fax: 0776-27-8747, E-mail: fujitas@u-fukui.ac.jp