Fabrication and Function of Three-Dimensional Device Made of Amino-Group-Modified Titanium Dioxide/Polymer NanoComposite Fibers

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Statement of Purpose: Titanium dioxide (TiO_2) has attracted great interest in medical fields because of its nontoxicity and antibacterial activity by photoreactivity [1]. Recently, we developed a novel inorganic/organic nanocomposite for a percutaneous device: a flexible polymer substrate, the surface of which was coated with amino-group-modified TiO_2 (NH_2-TiO_2) nanoparticles through covalent bonding [2, 3]. When the novel nanocomposite is utilized as a percutaneous device, it is expected to prevent initial bacterial penetration at the insertion site, because the amino groups on the composite improve tissue adhesion of the device. Furthermore, in case of a germ infection after implantation, it is also expected to prevent damage by photoreactivity of TiO_2.

In this presentation, the functionality of the NH_2-TiO_2/polymer nanocomposite was evaluated, and a prototype percutaneous device having three-dimensional structure was developed with the nanocomposite.

Methods: Anatase type TiO_2 (diameter, 200 nm; Ishihara Sangyo Co., Ltd., Japan) were modified with γ-amino-propyltriethoxysilane in toluene at 30˚C. TiO_2/polymer nanocomposite were prepared by adsorption of the NH_2-TiO_2 onto a poly(acrylic acid)-grafted substrate, followed by the coupling reaction of the amino groups on the TiO_2 with the carboxyl groups on the silicone at 120˚C for 2 h under vacuum.

Results: The photoreactivity of the NH_2-TiO_2 composite was evaluated form of the degradation rate constant of CH_3CHO under UV irradiation (λ >300 nm; 2000 μW). The photoreactivity did not change in the case of the amino-group density of less than 2 molecules/nm^2, and drastically decreased with an increase in the amino-group density.

The cell adhesion of the composite was evaluated using L929 fibroblast cells (1 x 10^5 cells; 37˚C; 24 h). In the case of the intact TiO_2 used as a control, cells hardly adhered due to high hydrophilicity. On the other hand, cells dramatically adhered on the NH_2-TiO_2, and the number of cells increased with the increase in the amino-group density.

The antibacterial activity of the NH_2-TiO_2 composite (amino-group density, 3.0 molecules/nm^2) was estimated from survival ratio of *E. coli* bacteria (NBRC 3301 strain, 1 x 10^5 cells) under UV (λ, 360 nm; 800 μW/cm^2) at 37˚C for 2 h. In the case of the control test after 30-min UV irradiation without TiO_2, 10% decrease in the number of bacteria was observed, indicating the direct antibacterial effect of UV rays. On the other hand, in the case of the composite sheet, 45% decrease in the number of bacteria was observed after 30-min UV irradiation, and the number of bacteria decreased significantly after 60-min UV irradiation (79%). It is noteworthy that the mechanical properties of the composite were not observed after the UV irradiation (λ >300 nm; 2000 μW/cm^2; 2 h).

Finally, a prototype percutaneous device having three-dimensional structure was developed with the nanocomposite as shown in Fig.1. The functionality of the device *in vivo* was now evaluating with rats.

Conclusions: In order to incorporate both photoreactivity and cell adhesion into NH_2-TiO_2/silicone composite, it was necessary to optimize the amino-group density on the TiO_2 particles, because the photoreactivity was suppressed and the cell adhesion was improved by covering the intact TiO_2 surface with amino groups. The optimum density of amino groups for both photoreactivity and cell adhesiveness was estimated to be 2.0-4.0 molecules/nm^2. The composite developed here is useful for flexible percutaneous or subcutaneous devices having good tissue adhesion and an antibacterial activity.

References: 1) R. Cai, *Cancer Res* 1992;**52**:2346, 2) T. Furuzono, *J Mater Sci Lett* 2003;**22**:1737, 3) M. Okada, *J Biomed Mater Res A* 2005;**76**:95

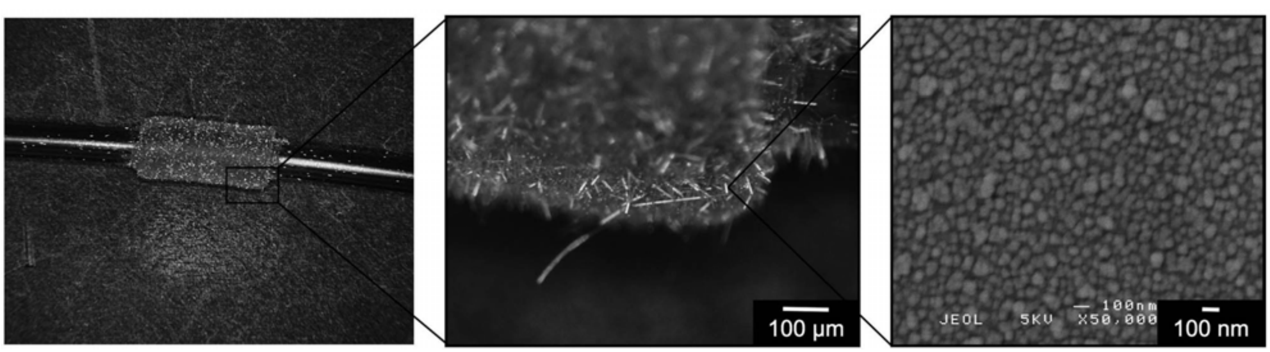

Fig. 1 A catheter installed with the prototype percutaneous device fabricated with NH_2-TiO_2 nanocomposite fibers