Smart ZnO Nanorod Arrays and PLGA Hybrid Coatings – A Biodegradable and Multifunctional Drug Release System on Titanium Implants

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Statement of Purpose: Titanium (Ti)-based implants are used widely in fracture fixation and skeleton reconstruction due to trauma, an infection, cancer, or other causes. Even though the properties of Ti have been improved in many aspects, the biomaterial-associated infection caused by bacteria and inflammation reactions induced by various reasons still could lead to the failure of implants. This study is to design a drug release system to localized deliver anti-inflammation drugs. This drug release system should be biodegradable to ensure the surrounding tissue adheres to the Ti substrate eventually. Meanwhile, the degradation products should be biocompatible and with specific functions such as the antibacterial property.

Method: First, ZnO nanoseeds are prepared by mixing methanol solutions containing zinc acetate and NaOH at 60 ℃ for 2 h. The next step is to drop nanoseeds solution homogeneously onto the surface of pure Ti foils and heat Ti foils in 150 ℃. Repeat the above process 10 – 20 times to acquire the ZnO nanoseeds layer. Subsequently, Ti foils undergo the hydrothermal treatment in an aqueous solution containing zinc nitrate hydrate and hexamethylenetetramine to form the ZnO nanorod arrays. TiO_2 nanotube arrays are studied as the benchmark. Indomethacin, which is a nonsteroidal anti-inflammatory drug, is applied as the model drug. The indomethacin solution (ethanol) is directly dropped onto Ti foils. Poly (D,L-lactic-co-glycolic acid) (PLGA, 50:50) coating is fabricated by the spin coating, while various coating thicknesses are achieved by applying different coating times. The morphology is checked by SEM. Drug release profiles of samples are monitored with UV-vis absorption spectroscopy. The cytocompatibility of samples is evaluated with osteoblasts. Finally, the antibacterial property of all samples has been tested by incubating samples in culture media containing E. coli, and SEM images of surfaces are used to count the adherent bacterial.

Results: ZnO nanorod arrays were fabricated successfully on the foils of Ti. SEM images revealed that the single ZnO rod is with the typical ZnO wurtzite structure, and the whole ZnO nanorod array is more like a grass structure, as shown in Figure 1. After the drug load, the ZnO nanorod arrays are fully coved by the drugs, indicating that drugs can be preserved by the ZnO nanorod arrays. The top surface is covered by the polymer layer after the PLGA coatings, which can protect the drugs from rapid dissolution so that sustainable drug release can be achieved.

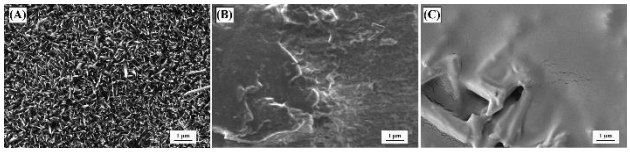

Figure 1. SEM images of (A) ZnO nanorod arrays on Ti foils, (B) ZnO nanorod arrays loaded with indomethacin, and (C) ZnO nanorod arrays coated with PLGA coatings.

As presented in Figure 2, the drug release system composed of ZnO nanorod arrays and PLGA coatings displayed a sustainable drug release behavior last for around 65 days, while the sample with the thin PLGA coating (coated 1 time) release more in the early period and samples with the thick coatings (coated 5 or 10 times) can release more drugs in the late period. On the contrary, the drug release system composed of TiO_2 nanotube arrays and PLGA coatings showed a fast release profile, which can only last for around 45 days, and the majority of drugs released after 10 days.

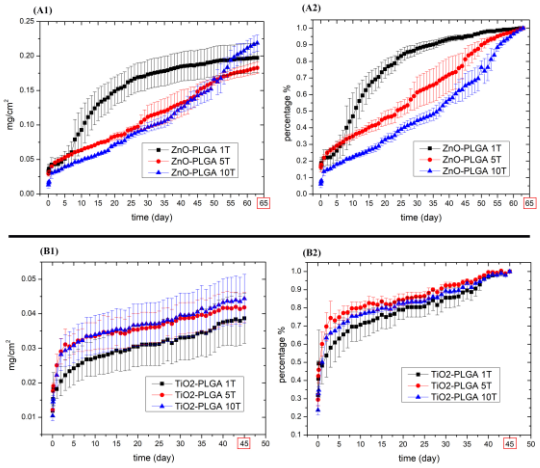

Figure 2. Drug release profiles of ZnO nanorod arrays coated with various PLGA coatings, (A1) mg cm^{-2} as a function of time and (A2) percentage as a function of time; Drug release profiles of TiO_2 nanotube arrays coated with various PLGA coatings, (B1) mg cm^{-2} as a function of time and (B2) percentage as a function of time.

On different samples, osteoblasts present distinct cellular behavior. ZnO nanorod arrays exhibit certain cytotoxicity where osteoblasts maintain in a small and round shape. The cytocompatibility of ZnO nanorod arrays was significantly improved with the PLGA coating on the top surface, which is similar to TiO_2 nanotube arrays with PLGA coatings. On the other hand, ZnO nanorod arrays deliver a stronger antibacterial property compared to TiO_2 nanotube arrays. The antibacterial property of ZnO nanorod arrays was intact with thin PLGA coatings on the top, while thick PLGA coatings can weaken the antibacterial efficiency.

Conclusion: ZnO nanorod arrays coated with PLGA coatings can serve as a biodegradable drug release system with antibacterial property on the surface of Ti-based implants. The drug release behavior, cytocompatibility, and antibacterial property of this system can be modified by the thickness of the PLGA coating.