Processing and Hydrothermal Bioactivation of Porous Ti6Al4V towards Accelerated Bone Ingrowth and Osteochondral Healing

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Abstract

Titanium alloys are widely used as implants in orthopaedics and dentistry owing to the properties like high specific strength, superior corrosion resistance and biocompatibility. However, issues associated with modulus mismatch, stress-shielding, osteolysis and aseptic loosening lead to post-implantation failure at the tissue material interface. Macroporosity–guided bone ingrowth for morphological fixation and bioactive material for direct bone bonding were proposed in 1960s to improve interfacial bonding. In this direction, present study makes an effort to bridge the gap between bioactivity and porosity guided bone ingrowth and ongrowth by developing multifunctional Ti6Al4V implants for biological fixation.

Porous Ti6Al4V processing is mostly reported by melt casting and powder metallurgy under regulated environment to minimize oxidation. A facile coagulant assisted foaming technique is developed for macroporous Ti6Al4V through slurry casting followed by sintering. Herein, metal powder dispersed stable slurry was achieved using egg white foam. The samples with 89.3 to 65.2% porosity and 44.6 to 653.8 µm pore size distribution were fabricated by varying powder loading from 8.6 to 13.8 g per ml protein foam. The sintered foam exhibited interconnected porosity with compressive strength ranging from 2.46 to 65.5 MPa owing to variable microstructures.

Porosity, pore size and pore connectivity have significant role in tissue ingrowth. There have been conflicting reports on optimal pore size for osteogenesis and accelerated bone ingrowth. In this study, Ti6Al4V foams with three different porosities (68.3, 75.4 and 83.1%) and average pore sizes (92, 178 and 297 µm) were evaluated for obtaining the highest osteogenic differentiation of mesenchymal stem cells and bone ingrowth in rabbit model. Porous Ti6Al4V with 75.4% porosity and 66.3–507.2 µm pore size distribution (178.4 ±18 µm average) offered significant bone ingrowth.

Osseointegration of titanium implants could be improved by nanostructured bioactive surface. A method for simultaneous nanostructure with *in situ* bioactivation through short-term (≤ 2h) hydrothermal treatment (200 ºC) using aqueous mixture of sodium tripolyphosphate and calcium hydroxide is further reported. Interestingly, wire-like topography similar to that of cicada wings surface exhibited selective osteogenic and bactericidal responses. While implanted in rabbit femoral defects, the treated porous Ti6Al4V with wire-like nanostructure and hydroxyapatite nanodeposit exhibited 7.1% more bone volume (BV) and significantly higher bone penetration than that of the untreated samples as evaluated by Micro-CT image analysis.

Although, treated Ti6Al4V foam has ability to induce rapid bone fracture healing, regeneration of hyaline cartilage is usually impaired owing to its avascular nature. To accelerate the process of cartilage healing especially in osteochondral region, an extracellular matrix mimicking phosphate/sulfate decorated GAGs-agarose hydrogel was developed through functionalization of chitosan. The study revealed that both chitosan phosphate and chitosan sulfate embedded gel was able to promote bone as well as cartilage formation (BV 53.0% and 48.5%, respectively) as compared to agarose gel (BV 31.7%). Therefore, a combined approach involving bioactive porous Ti6Al4V infiltrated with chitosan phosphate/sulfate hydrogel matrix at specific tissue-implant interface could be recommended for accelerated osteochondral healing.

Keywords: Osteochondral defects, Ti6Al4V foam, coagulant assisted foaming, *in situ* hydrothermal bioactivation, bactericidal nanowires, quantitative Micro-CT, bone ingrowth