Hydroxyapatite-Titanium Composites with Outstanding Fracture Toughness and Cytocompatibility Properties for the Bone Tissue Engineering Applications

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Statement of Purpose: The stability of bone implant materials depends on the binding of bone with biomaterial surface as well as mechanical properties of the implant to withstand the applied load under physiological conditions. Hydroxyapatite (HA)-based materials are attractive for structural bio-medical applications due to compatible elastic properties with bones and due to the excellent bio-chemical properties. However, an outstanding limitation in the development of these materials has been unacceptably low fracture toughness. Improving the fracture toughness has been an area of intense research for many years and the present work is an important contribution in this area. We will present here a comprehensive study to demonstrate how the fracture toughness can be significantly enhanced by tailoring the morphology as well as distribution of metallic titanium (Ti) and spark plasma sintering (SPS) conditions without compromising with the cytocompatibility of HA.

Methods: Commercially pure Ti was mixed with pure HA powders to obtain different compositions (HA-5wt%Ti, HA-10wt%Ti and HA-20wt%Ti) using ball mill. The powder compacts were spark plasma sintered for 17 minutes at 950 ºC and 30 MPa pressure under agron atmosphere. In order to obtain information on shrinkage behavior real time dilatometry data was collected during SPS. XRD and FT-IR of the as-sintered composites was carried out to identify the phases present before and after the sintering. The EPMA was used to identify any reaction product between HA and Ti. The SEM and TEM were used for detailed microstructural characterization of the as-sintered samples. In order to characterize the designed biomaterials for bone application, relative density, hardness, flexural strength, and fracture toughness (K_{IC}) were measured using Archimedes principle, nanoindentation, 3-point flexural, and 4-point flexural (SEVNB: Single edge V-notched beam) test, respectively. Further, the sintered samples were tested for cytocompatibility using osteoblast cells.

Results: In particular, the novelty of this work lies in the designing of HA-Ti composites with reliable and higher fracture toughness (~ 5 $MPa.m^{1/2}$). Our work illustrates the use to SEVNB technique to obtain reliable toughness values. An effective correlation with the existing theoretical models of crack bridging also support the fact that various toughening mechanisms can be adopted to obtain even higher toughness to match with the upper bound of the cortical bone. In subsequent efforts to further refine the microstructure and enhance the properties, Ti powders are cryo-milled to obtain fine dispersion in HA-matrix. Another important highlight of the present work is to illustrate that Ti addition (upto 10 wt.%) does not significantly alter the osteoblast cell fate processes in terms of cell apoptosis, proliferation index and division index as determined using flow cytometry.

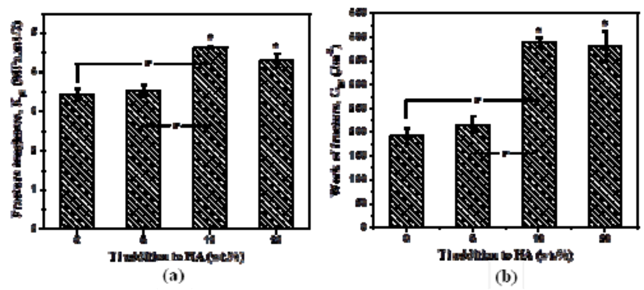

Figure 1. Variation in fracture toughness (a) and work of fracture with wt. % Ti in HA (b). Data in (a) and (b) has been represented as mean ± standard error. Dunnett's t (2 side) were used to compare the HA with HA-Ti samples (marked with *); while Dunnett's C test used to know the significant difference among all samples (marked with #). Statistical analysis shows the significant difference at 0.05 level for n= 5.

Conclusions: For the first time, the present work reports that spark plasma sintered HA-10Ti composite can exhibit high long crack toughness of ~4.6 $MPa.m^{1/2}$ and large work of fracture of upto 400 J/m^2, measured using SEVNB method, which is superior to earlier developed materials (max. toughness available with the existing HA-based biomaterials ~ 3$MPa.m^{1/2}$). High fracture toughness is rationalized on the basis of the bridging of the crack faces by lath shaped elongated Ti particles as well as by weak crack wake debonding at HA/Ti interface. A critical analysis using classical crack bridging models reveals a close correlation between the theoretically estimated toughness enhancements with the experimentally measured toughness values.
The flow cytometry results of the cultured osteoblast cells after incubating on various HA-Ti substrates importantly revealed that all the investigated HA-Ti biocomposites support increased proliferation and division of cells in a comparable manner to that on HA.

References:

1. Alok Kumar, Krishanu Biswas and Bikramjit Basu; Acta Materialia, 61(2013) 5198-5215.
2. Alok Kumar, Thomas J. Webster, Krishanu Biswas and Bikramjit Basu; JBMRA, 101 (2013) 2925-2938.