学 位 論 文 内 容 の 要 旨

博士の専攻分野の名称　博士（工学）　氏名　Naga Vijaya Lakshmi Manchinasetty

学 位 論 文 題 名

Preparation and characterization of calcium phosphate ceramics and polymer composites as potential bone substitutes

（人工骨への応用を目指したリン酸カルシウムセラミックスと高分子の複合体の作製と評価 ）

Abstract

Hydroxyapatite (HAp), β-tricalcium phosphate (β-TCP) and their composites with natural polymers are widely used as filler materials for their biocompatibility and osteoconductivity. A three dimensional interconnection of both macro- and micro-pores (biomodal pores) is important for a porous scaffold, because macropores allow cell, blood vessel and tissue ingrowths and micropores serve as an effective pathway for exchange of fluid in which nutrition and wastes are dissolved. Marine derived biomaterials from corals, cuttlebones, sea urchin spines etc., have shown good potential as bone substitutes due to their interconnected porous structure and ease of conversion to calcium phosphate without any change in their original porous structure. However, corals are considered as reservoir of carbonate gas to decrease greenhouse effect and not recommended to collect from sea, cuttlebones consist of only macropores and sea urchin spines consist of only micropores. Contrarily, gonads of sea urchins are consumed as food in Japan and their skeletons are discarded as waste. Their skeletons consist of bimodal pores and hence utilization of sea urchin skeletons would reduce the waste, encourage Japanese fishery. In this study, calcium phosphate granules were prepared by hydrothermal phosphatization of sea urchin tests in an aqueous phosphate solution. The obtained calcium phosphate (CP1/CP2) was found to be biphasic in nature with 82

Scaffolds, CP1Col/CP2Col (collagen as binder) and CP1Gel_GA/CP2Gel_GA (gelatin as binder) were prepared by mixing the obtained BCP granules with collagen or gelatin solution. The scaffolds obtained exhibited open porous structure and had sufficient strength for good operability during surgery. The in vitro evaluation of scaffolds using human osteoblast-like cell line, MG63 cells under static conditions showed negligible toxicity, higher distribution, proliferation and osteogenic activity in comparison to control collagen or gelatin sponges. From in vitro evaluation of scaffolds under pressure/perfusion cell culture condition, which mimics the biological conditions of bone, significant increase in proliferation (from total DNA analysis) and osteogenic activity from (gene expression analysis) was observed in scaffolds compared to control. The homogeneous, bimodal porous structure enhanced the cell distribution and the Mg2+ containing BCP granules promoted effective osteogenic activity in the scaffolds in both static and dynamic cell culture conditions. The scaffolds prepared by sea urchin-derived calcium phosphates with collagen or gelatin as binder could be a potential candidate for artificial bone filler in non-load bearing defects.

The supplementation of calcium carbonate and calcium citrate to an injectable hydroxyapatite/collagen (HAp/Col) paste prepared with sodium alginate increased its anti-washout property and pH controllability. This is due to coordinate effects of initial washout inhibition by weak but rapid formation of long-range network by citric acid followed by long term anti-washout inhibition by strong but slow network formation by Ca2+ ions. The paste also showed good cytocompatibilty, MG63 cells proliferated with the culture time without any significant difference with the HAp/Col dense bodies. The HAp/Col paste is expected to be utilized in minimally invasive surgery of bone defect to fit irregular bone defects.

The calcium phosphate and natural polymers composites investigated in this study are expected to be utilised as filler materials for replacement and reconstruction of bone defects.