論文 / 著書情報
Article / Book Information

題目(和文)	骨軟骨治療のための水酸アパタイトとコラーゲンを基材とした二層足場材料の研究
Title(English)	Study on hydroxyapatite and collagen based bilayer scaffolds for osteochondral treatment
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学位種別(和文)	博士論文
Category(English)	Doctoral Thesis
種別(和文)	論文要旨
Type(English)	Summary

（博士課程）
Doctoral Program

論 文 要 旨

THESIS SUMMARY

系・コース： Department of, Graduate major in	材料 系 材料 コース	申請学位（専攻分野）： Academic Degree Requested	博士 Doctor of （ 工学 ）
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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

This thesis is composed of 6 chapters, with a title electrolysis-based fabrication of bilayer scaffolds for tissue engineering of osteochondral injury.

Chapter 1: Introduction

Osteochondral injury affects both of cartilage and bone tissues, which requires simultaneous regeneration of the two tissues for effective treatment. Implantation of autologous osteochondral tissue is a gold standard for regeneration as it delivers new cells, matrix molecules, and bear load at injury site. As the alternative, investigators fabricate artificial tissue by initially growing stem cells inside the porous body (scaffold) and inducing cells to differentiate and secrete matrix components. Physical and chemical characteristics of scaffold have been known to influence the cells fate, thereby selecting scaffold material is crucial for success of tissue-engineering. To address the two-tissues at osteochondral region, two-layers of scaffold is joined in a single structure (bilayer scaffold). Collagen – a natural-based protein – and hydroxyapatite (HAp) – a calcium phosphate material – is used as cartilage and bone layer, respectively. Collagen in the monomeric or fibrillar form is fabricated as porous scaffold; however, a study comparing the capacity of monomeric / fibrillar collagen scaffold in supporting cell proliferation, differentiation, and matrix secretion capacity (cartilage tissue formation) has not yet been conducted. The current methods to fabricate bilayer scaffold is by knitting or gluing collagen sponge and HAp porous body, which pose risk of delamination after implantation. Therefore, a continuous bilayer scaffold: collagen sponge with gradient content of HAp is desired. Electrolysis was previously used to simultaneously deposit fibrillar collagen and HAp; in the current thesis, electrolysis was investigated to fabricate fibrillar collagen sponge with gradient HAp content. Furthermore, a number of studies had reported the combination of HAp with particular type of nanoparticles to promote bone cells proliferation, thereby the possibility to enhance bone layer by addition of iron-oxide nanoparticles (IONP) was also evaluated. This thesis initially aims to elucidate the advantage of fibrillar to monomeric collagen sponges as a cartilage tissue-engineering scaffold; thereafter, the thesis focuses to construct a continuous bilayer scaffold optimized for regenerating osteochondral injury.

Chapter 2: Influence of fibrillar/monomeric collagen on biological properties of Collagen /HAp sponges

The monomeric and fibrillar sponges were fabricated with similar initial conditions (chemical composition, crosslinking degree, HAp/collagen ratio). Fibrillar sponges exhibited slightly higher compressive modulus (~2.3 kPa) and strength (~0.79 kPa) to monomeric sponges (compressive modulus (~1.5 kPa) and strength (~0.4 kPa). Fibroblast attached on fibrillar sponge exhibited elongated (fillopodia) morphology, which in turn was associated with high cell proliferation capacity. In contrast, fibroblast attached on monomeric sponge exhibited flattened morphology, which is associated with low cell proliferation capacity. The results

were explained based on the manner in which cell-binding sites were distributed for monomeric and fibrillar collagens. In conclusion, the fibrillar collagen was beneficial in supporting proliferation capacity of cells.

Chapter 3: Influence of monomeric/fibrillar collagen in Col/Chitosan/HAp sponges to the proliferation, chondrogenic differentiation and matrix secretion capacity of mesenchymal stem cells
Electrolysis was used to fabricate fibrillar collagen sponges. Chitosan addition was investigated to promote the formation of fibrillar collagen by electrolysis. Collagen/chitosan solution 87.5/12.5 (HAp 0.2wt%) was demonstrated as the optimal ratio to enhance fibril formation during electrolysis; the concentration was used for fabrication of monomeric and fibrillar collagen sponges. Fibrillar sponges supported rapid proliferation of MSC, reaching the maximum cell number at 14 days, at the cost of slightly inhibiting chondrogenic differentiation (gene expression analysis). Rapid proliferation of MSC in fibrillar sponges was beneficial for earlier and larger accumulation of matrix molecule (aggrecan - sulfated glycosaminoglycan (sGAG)) compared to monomeric sponges, which in turn contribute to more significant improvement of mechanical properties. In conclusion, fibrillar collagen/chitosan/HAp sponge was deemed suitable as a cartilage tissue-engineering scaffold in comparison to monomeric counterpart.

Chapter 4: Fabrication of a continuous bilayer scaffold of Col /Chitosan/IONP with gradient HAp content
Electrolysis was utilized to fabricate collagen-based sponge with the gradient HAp content; and the influence of IONP addition to the osteoblast-proliferation supporting capacity of fibrillar bilayer structure was conducted. Initial HAp concentration was beneficial to obtain the gradient HAp content in the collagen sponge. Addition of chitosan did not alter the HAp-gradient properties of collagen sponge. IONP (20 mg / ml) was further incorporated into electrolyzed sponge. The presence of IONP was beneficial for enhancing proliferation of osteoblast (bone cells). It was concluded that fibrillar collagen/chitosan/IONP with gradient HAp could act as a scaffold that simultaneously regenerate cartilage and bone tissue (bilayer scaffold).

Chapter 5: Fabrication of a continuous bilayer structure Col sponge and IONP-impregnated HAp sintered body
Simultaneous electrolysis of collagen/HAp solution and HAp-sintered body was used to fabricate a continuous bilayer structure consisting of collagen/HAp sponge and HAp-sintered body.The bilayer structure can be magnetized by incorporating IONP into the HAp-sintered body. It was concluded that electrolysis is a powerful tool to fabricate bilayer structure of collagen and HAp with continuous interface.

Chapter 6: Conclusion
Summary from each chapter was given and general conclusion was given.