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論 文 名 ： Fabrication and histological evaluation of interconnected porous carbonate apatite blocks based on the setting reaction of calcium sulfate hemihydrate granules
（半水石膏顆粒の硬化反応に基づく炭酸アパタイト連通多孔体の創製と組織学的評価）

区 分 ：甲

論 文 内 容 の 要 旨

Carbonate apatite [CO_3Ap: $Ca_{10-a}(PO_4)_{6-b}(CO_3)_c$] has been used as a bone substitute due to its high osteoconductivity and bioresorbability. The architecture of CO_3Ap, particularly the interconnectivity of pores, is also a factor that significantly affects the outcome of bone regeneration. In this study, interconnected porous CO_3Ap blocks were fabricated by the setting reaction of calcium sulfate hemihydrate [CSH: $CaSO_4 \cdot 1/2H_2O$] granules followed by dehydrating heat treatment and two-step dissolution–precipitation reaction.

When CSH granules were immersed in water, calcium sulfate dihydrate [CSD: $CaSO_4 \cdot 2H_2O$] crystals were formed and precipitated on the surface of the granules. The interlocking of CSD crystals from the adjacent granules bridged the granules to each other, resulting in the formation of an interconnected porous block. However, unrestricted growth of CSD crystals clogged significant portions of the pore network, negatively affecting the formation of a highly interconnected porous structure. Controlling the water content, using either filter paper or centrifuge, resulted in successful fabrication of highly interconnected porous CSD blocks. $CaCO_3$ blocks as intermediate precursor were fabricated by immersing CSD blocks in a Na_2CO_3 solution. However, the measured mechanical strength was low. To overcome this issue, the mechanical strength of $CaCO_3$ blocks was greatly improved when calcium sulfate anhydrous [CSA: $CaSO_4$] blocks were prepared by the heat treatment of CSD blocks before carbonation. The $CaCO_3$ blocks were then converted to CO_3Ap via dissolution–precipitation reaction in a Na_2HPO_4 solution.

The effect of pore interconnectivity on bone regeneration was evaluated by reconstructing the rabbit distal femur defect using CO_3Ap blocks with 15% and 30% of interconnected pores. The new bone formation was evaluated histomorphometrically after 4 and 12 weeks of implantation. At 4 weeks, new bone deposition was abundant in the central area of CO_3Ap with 30% interconnected pores. In contrast, CO_3Ap with 15% interconnected pores had limited new bone formation in the central region. At 12 weeks, a large portion (> 90%) of CO_3Ap with 30% interconnected pores was replaced with cancellous-structured bone. In comparison, even after 12 weeks post-operative, CO_3Ap with 15% interconnected pores remained in the defect and the boundary with the host bone was still clear. In conclusion, introducing a highly interconnected pores can significantly elicit rapid bone regeneration by allowing early bone ingrowth, followed by replacement of the material with new bone.