Title	Fluoride and carbonate co-incorporated porcine bone derived biological apatite stimulates osteogenesis in vitro via WNT/beta-catenin pathway
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FLUORIDE AND CARBONATE CO-INCORPORATED PORCINE BONE DERIVED BIOLOGICAL APATITE STIMULATES OSTEOGENESIS IN VITRO VIA WNT/BETA-CATENIN PATHWAY

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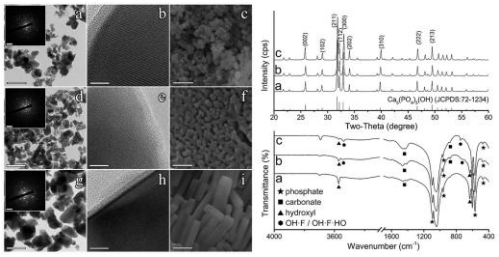
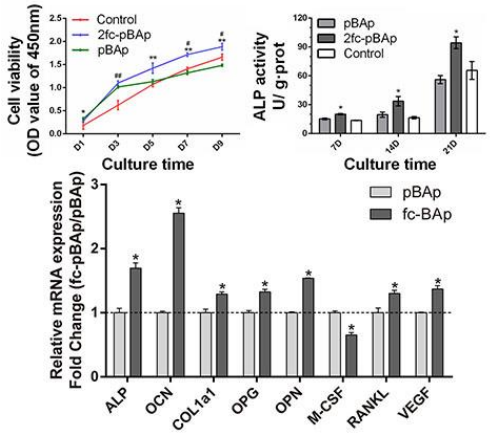
Biological apatite (BAp) is widely recognized as a favorable substitute in bone tissue engineering due to it being biodegradable, biocompatible, and bearing osteoconductive properties. Incorporation of trace ions into BAp was reported to contribute to the physicochemical and biological properties of the substitute.

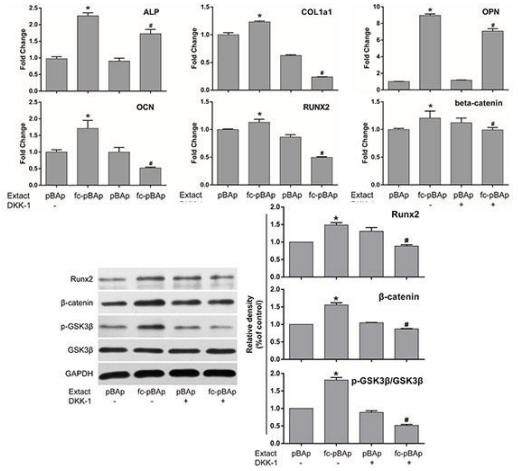
In this study, fluoride and carbonate, two elements that are generally accepted to play vital roles in early osteogenesis were incorporated into porcine bone derived biological apatite (pBAp) through chemical-thermal treatment. The prepared fluoride carbonate co-incorporated porcine bone derived biological apatite (fc-pBAp) exhibited significant changes in crystal shape, size and crystallinity compared with pBAp.



It was also found that fc-pBAp could release fluorine, magnesium etc. into culture medium, thus, significantly stimulated the proliferation and osteogenic differentiation, while inhibited M-CSF and RANKL/RANK system of rat bone mesenchymal stem cells(rBMSCs) in vitro.



This phenomenon was further demonstrated associated with the activation of Wnt/β-catenin signaling pathway, which was recently reported as a major signaling cascade in bone biology. As the extract of fc-pBAp can induce phosphorylation and inhibition of glycogen synthase kinase-3β (GSK-3β), which resulted in nuclear accumulation of the β-catenin. Moreover, the effects of fc-pBAp on ALP activity and osteogenesis-related gene expressions of rBMSCs was abolished by DKK-1, a blocker of Wnt/β-catenin receptor.



These findings suggest that incorporation of fluoride and carbonate into BAp can enhance osteogenesis in vitro by triggering Wnt/β-catenin signaling. Ions incorporation could be a valuable strategy for the development and modification of BAp for applications in bone regeneration.

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