Biological activity comparative evaluation of the gene-Activated bone substitutes made of octacalcium phosphate and plasmid DNA carrying VEGF and SDF genes: Part 1 - in vitro

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Abstract

High need for effective bone substitutes and drawbacks of the materials approved for clinical use determine the increasing activity of biomedical research in this area. We have developed gene-Activated bone substitutes consisting of a scaffold based on octacalcium phosphate (OCP) and one of the two variants of plasmid DNA carrying either a gene for vascular endothelial growth factor (VEGF) or two genes encoding VEGF and stromal derived factor- 1α (SDF-1α). The aim of the study was to evaluate the cytotoxicity of the gene-Activated materials and their components, as well as biological activity in vitro. We found that both OCP and gene-Activated bone substitutes did not have any cytotoxicity, but reduced the proliferative activity of human bone marrow-derived multipotent mesenchymal stromal cells: material with doublegene construct decreased cell culture doubling rate of 24.3% more compared with the material carrying plasmid DNA encoding only VEGF. Both gene-Activated materials led to an increase in therapeutic genes mRNA levels, but the material with double-gene system enhanced VEGF protein production greater. Thus, the gene-Activated bone substitutes characterized by the absence of cytotoxic properties and possessed a specific activity increasing expression of the therapeutic genes. However, further studies are needed to detail the identified characteristics and assess the feasibility of the defined biological action in vivo.

Keywords

Gene-Activated bone substitute, Octacalcium phosphate, Plasmid DNA, Stromal derived factor-1α, Vascular endothelial growth factor