Mechanical Properties, Biocompatibility and Controlled Release of Transforming Growth Factor from Composite Bone Grafts Consisting of Calcium Phosphate Cement and Biodegradable Particulates

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We have developed novel bone grafts based on calcium phosphate cement (CPC). The powder component of CPC is an equimolar mixture of tetracalcium phosphate and dicalcium phosphate anhydrous. The cement powder is mixed with water to form a paste that can be shaped to fit the contours of a wound. The paste sets within 30 min to yield microcrystalline hydroxyapatite, which is the predominant mineral component of bones. To enhance the ingrowth of bone into the CPC bone graft and the resorption of the graft, we have developed composite bone grafts made of CPC and biodegradable polymer microspheres or water-soluble crystals, which serve as macropore-forming particulates. The composite bone grafts can further be made osteoinductive by adding growth factors to the grafts, such as transforming growth factor- β1 (TGF- β1).

A paste was made from 0.1 g of poly(d,l-lactide-co-glycolide) [PLGA] or poly(d,l -lactide) [PLA] microspheres [0.17 to 0.36 mm in diameter; 0.6 volume fraction], 0.15 g of the CPC powder, and 0.062 g of water. Disks (6.4 mm in diameter, 4.4 mm in height) of the CPC/PLGA composite for diametral tensile strength (DTS) and mass loss measurements were made by applying a 22 N load on the paste in a mold at 37 ^{o}C. The mass of CPC/PLGA disks decreased very little during the first four weeks when placed in saliva-like solution, but the DTS of the CPC/PLGA disks steadily decreased during this period. There was little decrease in the mass probably because the degradation was not sufficient to produce PLGA molecules that were low enough in molecular mass to diffuse from the disks. However, the reduction in the average molecular mass of PLGA, together with the hydration-induced softening of PLGA microspheres, caused the decrease in DTS. For controlled release, fluorescein-labeled Protein A or TGF-β1 was added to the liquid component of CPC. Although half the extractable Protein A was released in 140 h from CPC/PLA disks to phosphate buffered saline solution, the release of Protein A persisted after 640 h, after which it was no longer tested. The release of Protein A from CPC/mannitol disks increased with the volume fraction of mannitol crystals (0.12 to 0.25 mm in length). Thus, the release of proteins from composite grafts can be modulated by the volume fraction and the dissolution rate of porogens. Osteoblast-like cells, when seeded on the grafts, were able to adhere, attain a normal morphology, proliferate and remain viable, suggesting the composite bone grafts to be biocompatible. Thus, we have prepared biocompatible, CPC-containing composites that can release growth factors at a controlled rate.