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A Comparative Study of the Biodegradability of Calcium-Alkali-Orthophosphate Ceramics in vitro and in vivo

R. Gildenhaar[1], G. Berger[1,a], E. Lehmann[1], M. Stiller[2], Ch. Koch[3], P. Ducheyne[4], A. Rack[5], H. Seligmann[3], S. Jonscher[3], C. Knabe[3,b]

[1]Federal Institute for Material Research and Testing, Laboratory of Biomaterials, Unter den Eichen 87, 12200 Berlin; [2]Department of Plastic and Maxillofacial Surgery, [3]Department of Experimental Dentistry, Campus Benjamin Franklin, Charité – University Medical Center Berlin; Aßmannshauser Str. 4-6, 14197 Berlin, Germany, [4]Center for Bioactive Materials and Tissue Engineering, University of Pennsylvania, Philadelphia, U.S.A., [5]Hahn Meitner Institut & Helmholtz Research Center Karlsruhe, Germany
[a]georg.berger@bam.de, [b]christine.knabe@charite.de

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Introduction

Bioactive calcium phosphate ceramics have been widely used for bone regeneration. However, depending on the clinical application, these materials need to exhibit varying degrees of biodegradability. For example, in clinical applications in which implants are to be inserted into the regenerated site, rapid biodegradability is more important compared to applications in which this is not the case. Therefore, there have been numerous efforts to develop novel materials with a higher solubility compared to tricalcium phosphate (TCP). Among the various calcium phosphate materials which are currently clinically available, TCP possesses the highest solubility and biodegradability. The most reliable method for evaluating a bone substitute material's capability to degrade and promote bone formation and osseous regeneration is by performing histomorphometric measurements on ex vivo specimens from animal experiments. Animal studies, however, are very cost-intensive. Furthermore, due to an increasing focus on animal ethics, there has been an ongoing search for alternative in vitro methods which can contribute to reducing the number of animal experiments.

Consequently, this study compares an in vitro method for evaluating the biodegradability of novel calcium-alkali-orthophosphate ceramic particulates - by using solubility measurements - to histomorphometric evaluation of the biodegradability of these materials by determining the decrease of particle size in histological sections which were obtained subsequent to implantation in vivo using a sheep model.

Material and Methods

Three novel calcium-alkali-orthophosphate ceramic bone substitute materials were studied. These materials are glassy-crystalline materials with a higher solubility than β-tricalcium phosphate [1-3]. The composition of these materials is rather similar, since their main crystalline phase is the new phase $Ca_2KNa(PO_4)_2$ [4]. In addition to the crystalline phase $Ca_2KNa(PO_4)_2$ these three bone substitute materials contain small amorphous portions with differing quality and quantity. These amorphous portions result from small additions of MgO (material denominated GB14), MgO and SiO_2 (material denominated GB9) or both components as well as P_2O_5 (material denominated GB9/25). GB9/25 [3] also contains a small portion of crystalline and amorphous diphosphates ($Ca_2P_2O_7$), unlike GB9, which does not [1-2]. GB14, GB9 and GB9/25 particulates were made using reagent grade $CaHPO_4$, Na_2CO_3, K_2CO_3, $MgCO_3$, SiO_2 and H_3PO_4. These compounds were mixed and a melt was formed in a platinum crucible at about 1550°C for 2 hours. The material was cast, crushed and sieved to produce granules with a narrow range grain size of 355-400µm.

The solubility of the GB14, GB9 and GB9/25 particulates was determined by immersion in TRIS buffer solution 0.1M (pH7.4, 37°C) according DIN ISO EN10993-14. Immersion experiments of GB14, GB9 and GB9/25 particulates (grain size of 355-400µm) were performed for periods up to 15 weeks in order to extend the in vitro study over a time period which would be comparable to the