Modeling the Crystallization Kinetics of an Injectable Calcium Phosphate Cement from FTIR and XRD Data

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Introduction

Calcium phosphate (CaP) cements have been developed in the last few decades as bone graft substitutes, and are under investigation for delivery of growth and differentiation factors, such as bone morphogenetic proteins (BMPs) [1].

Crystallization kinetics of an injectable, apatitic bone cement were investigated by X-ray diffraction (XRD) and Fourier-Transform Infrared (FTIR) spectroscopy. The cement powder consists of two phases: an amorphous calcium phosphate (ACP) and a crystalline dicalcium phosphate dihydrate (DCPD). The setting reaction is based on the crystallization from a metastable phase (ACP) to a poorly crystalline hydroxyapatite (PCHA) phase, which is similar to bone mineral. Results indicate that the amorphous calcium phosphate based cement converts rapidly, within hours. The **purpose** of this research was to develop kinetic models, based on the changes observed during crystallization in both XRD and FTIR spectra, which elucidate the hardening reaction.

Materials and Methods:

The calcium phosphate paste was generated by mixing cement powder with aqueous solution. Paste samples were injected into saline and incubated at 37^{o}C up to 24 hours. The chemical reaction (conversion) was halted by flash freezing and lyophilization.

XRD analysis was performed on Rigaku Rotaflex and Bruker axs D8advance instruments, scanning from 5-60° (2 Theta). FTIR analysis was performed on a Nicolet Magna 760 FTIR spectrometer in transmission mode, using KBr pellets. Solid standards were generated by physically mixing commercial pure DCPD (Riedel-de Haen) and ETEX pure PCHA powders together over the range 0 to 100% by mass.

Results/Discussion:

Un-standardized factor analysis of XRD and FTIR data matrices were performed to determine the physical/chemical rank of the sets. Both XRD and FTIR data matrices from incubated samples have a rank of 4 suggesting that 4 terms are required to model the variance (Fig. 1). The time evolution of the first factor corresponds to spectral features characteristic of DCPD hydrolysis (Phase 1). Phase 1 time evolution correlates to the rapid loss of lattice water bands associated with the dihydrate (DCPD) in the high energy region (3200-3700 cm^{-1}) of the FTIR spectra, and the corresponding loss of DCPD planes in the diffraction pattern. The origin of the spectral features correlated to factors 2, 3, and 4 (Phase 2) are thought to represent the rapid initial hydrolysis of ACP and subsequent growth of the apatite phase (3,4).

Diffraction patterns of the pure DCPD (initial) and PCHA (final) phases were used to decompose the XRD data matrix into ***Si*** (phase response factor) and ***Ki*** *(*phase constant*)*. Growth of PCHA and concurrent hydrolysis of DCPD as a function of time were determined by Rietveld analysis. Standardized models of both XRD and FTIR data show that a phase lag exists between DCPD hydrolysis and PCHA formation. This indicates that the conversion reaction is related to the primary dissolution of amorphous calcium phosphate (ACP), hydrolysis of crystalline DCPD and subsequent rapid growth of the apatite phase.

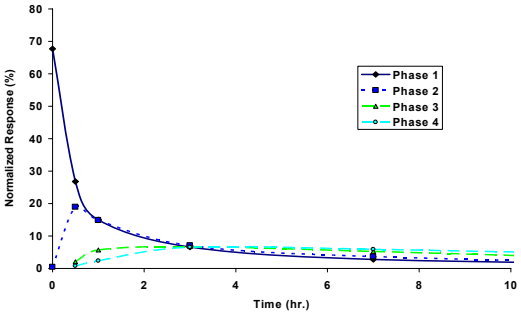

Fig. 1: Rank analysis of the nucleation and growth of poorly crystalline hydroxyapatite bone cement (37° C)

Conclusions:

Un-standardized rank analysis of both XRD and FTIR data indicate 4 terms (variables) are required to completely model the variance within the data sets. The coefficients for the first term correlate strongly to the to the spectral (& X-ray) features associated with the hydrolysis of DCPD. Any influence of ACP hydrolysis on XRD and FTIR spectra would be subtle if detectable. Therefore, the statistical weight of larger sample sets is required to resolve the physical origin of the other terms. Standardized models of both XRD and FTIR data show that a phase lag exists between DCPD hydrolysis and PCHA formation confirming that the conversion reaction is related to the primary dissolution of amorphous calcium phosphate (ACP), hydrolysis of crystalline DCPD and subsequent rapid growth of the apatite phase.

References:

[1] Wikesjo U.M. et al., Clin. Implant Dent. Rel. Res. 4(4) (2002) 174-82.