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BIORESORBABLE AND BIOMIMETIC BONE ADHESIVE FOR DEFECT REPAIR AND REGENERATION OF BONE

Tzagiollari, A.[1,2,3], Levingstone, T.J.[1,2], Insley, G.[3], Dunne, N.[1,2]

[1] School of Mechanical and Manufacturing Engineering, Dublin City University, Dublin 9, Ireland, [2]Centre for Medical Engineering Research, Dublin City University, Dublin 9, Ireland, [3]PBC Biomed, Accelerating Medical Innovation, Limerick, Clare, Ireland

INTRODUCTION

Bone defects and complex fractures present significant challenges for orthopaedic surgeons [1]. Current surgical procedures involve the reconstruction and mechanical stabilisation of complex fractures using metal hardware (i.e. wires, plates) resulting in poor healing, such as mal-unions. An injectable, biocompatible, biodegradable bone adhesive that could glue bone fragments back together would present a highly attractive solution [2]. A bone adhesive that meets many clinical requirements for such an application has yet to be developed. This study aims to develop a new bioresorbable and biomimetic bone adhesive, comprised of alpha-tricalcium phosphate (alpha-TCP), phosphoserine and deionised water, with bone regenerative properties. Specifically, a bone bioadhesive based on a phosphoserine-modified calcium phosphate cement (PM-CPC) will be developed and through chemical and biomechanical characterisation, the formulations that provide suitable injectability and adhesive properties for use in the repair of challenging bone voids and fractures will be identified.

MATERIALS AND METHODS

The alpha-TCP powder was prepared by mixing calcium phosphate ($CaHPO_4$) and calcium carbonate ($CaCO_3$) at a 2:1 molar ratio (both from Sigma Aldrich) [3]. The mixture was turbo-blended, and heat treated in a furnace (Elite BRF1600º, Elite Thermal Systems Ltd., UK) for 6h at 1400ºC. Following rapid quenching using compressed air, the powder was subjected to particle attrition using a planetary mill (Pulverisette 6, Frisch, Germany) at a rotating speed of 600 ± 5 RPM for 5 min periods over 6, 11, 13, 15, 17 cycles. Initially, the physicochemical properties of the alpha-TCP powder were characterised in terms of particle size, zeta potential (laser diffraction particle analysis), morphology (SEM), phase purity (XRD) and chemical composition (FTIR spectroscopy) Alpha-TCP and phosphoserine (Flamma, S.p.A. Italy) at different molar percentage (20, 27.5, 32.5, 45 mol%) were combined with deionised water at liquid:powder ratio (LPR) ranging from 0.2, 0.35, 0.5 mL/g. The resultant various compositions of PM-CPC based bone adhesive will be characterised in terms of physical (SEM), chemical (XRD and FTIR spectroscopy), rheological (parallel plate rheology), setting (Gilmore needle), static mechanical (compressive, shear and bond strength) and biodegradation properties.

RESULTS AND DISCUSSION

The XRD refinement technique (i.e. Rietveld analysis) confirmed the alpha-TCP demonstrated a phase purity of 99.9%. The particle size of the alpha-TCP powder reduced as a function of number of attrition cycles (Fig.1a). A D_{50} particle size of 4.0 ± 0.5 µm resulted following 17 cycles of particle attrition. SEM analysis (Fig. 1b) demonstrated the TCP-powder was spherical in morphology and further confirmed the correlation between the particle size and the attrition time. The zeta potential of the alpha-TCP ranged from -21 to -37 mV, and this difference was a function of the D_{50} value for the powder. Valentim *et al.* reported similar findings [4]. The initial (t_i) and final (t_f) setting time of the PM-CPC also increased as a function particle size (Fig. 1d). This observation agrees with previous studies investigating the influence of powder particle size and the setting properties of calcium phosphate cement [5].

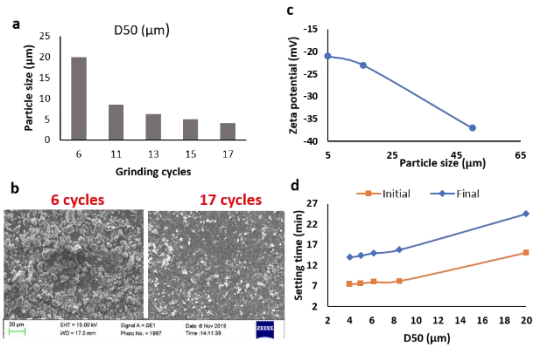

Figure 1: Particle size (a), SEM analysis (b), zeta potential (c) and setting properties (d) as function of particle attrition cycles.

CONCLUSION AND FUTURE PROSPECTIVES

Various compositions of PM-CMC have been successfully prepared. Initial results indicate the important role that the particle size of the alpha-TCP powder plays in influencing the setting properties of the resultant PM-CMC. This finding offers the potential to tailor the rheological and setting properties of the proposed bone adhesive for the treatment of bone fractures. Future work will focus on optimising the rheological, setting, mechanical and biodegradation properties and also the *in vitro* and *in vivo* biocompatibility of the PM-CPC based bone adhesive.

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