Absorbable Self-setting Composite Adhesive Bone Cement/Filler

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Statement of Purpose: Since the development of the non-absorbable polymethyl methacrylate (PMMA) bone cement, there has been consistent efforts to develop absorbable forms of bone cement and related compositions for use as bone fillers or in bone repair.[1] These included (a) self-setting, inorganic bone cement described as a resorbable calcium phosphate,[2] which suffers from being fragile and susceptible to fracture; (b) PMMA/ calcium phosphate composites[3] for use in dentistry to protect against demineralization; and (c) calcium sulfate, which has a low fracture resistance. However, the success of these and similar compositions as orthopedic products was limited. This evoked the need for a novel composition of bone cement/filler which is preferably absorbable. Such need and Poly-Med's successful development of absorbable cyanoacrylate tissue adhesives[4] and our consistent interest in absorbable phosphate glasses and related compositions,[5] prompted the pursuit of the present study. The study integrates the absorbable tissue adhesive attributes with the osteoconductivity of absorbable, inorganic phosphate materials to produce self-setting, bioactive cyanoacrylate phosphate-based composites as preferred substitutes to the non-absorbable PMMA bone cement.

Methods: The composites were constructed in a 3 in. x 3 in. Teflon compression mold to produce 2 mm or 3 mm thick sheets. A typical absorbable bone cement (ABC) was prepared by mixing an aliquot of dibasic calcium phosphate (DBCP) with a second aliquot of methoxypropyl cyanoacrylate (MPC) in a polypropylene container. The DBCP was used in three different amounts to prepare three different cements. The concentrations used of the DBCP were 50, 40, and 35 wt percent of the total mixture with MPC. The cement components were mixed for one minute or until homogenous and transferred to the mold. The mold was placed in a 37°C incubator to cure. The sheet from each mold was cut into 1 cm x 5 cm test specimens, which were tested to failure by three-point bend on an MTS Synergie 200. A total of four samples were tested in each set. To evaluate the degradation profile, specimens of the ABC-1 were incubated in deionized water at 37°C for predetermined periods of time. The mass loss and mechanical properties were measured on the solid samples at different periods. The liquid phase including any degradation products was tested for pH and cytotoxicity. The liquid media were changed weekly and the pH was measured. The cytotoxicity testing was conducted according to ISO standards in terms of the effect on cell viability using a fibroblast cell culture.

Results: The mechanical results of testing of three different cements, ABC-1 to ABC-3, are summarized in Table I. Incremental increase in the amount of the DBCP was associated with significant effects on the mechanical properties over the concentrations tested. The properties of a typical ABC change significantly with small changes in DBCP content. More specifically, as the amount of DBCP decreases from 50% to 35%, increases of about 200% and 300% in modulus, and about 100% to 200% in strength, respectively, were observed. Compared with the 50% DBCP system, the 35 and 40 wt. % DBCP counterparts revealed significantly faster cure time, and were somewhat difficult to work with or manipulate. The ABC-1 was therefore chosen for the *in vitro* study for its ease of manipulation and high strength. The results for the ABC-1 *in vitro* study are summarized in Table II. By 4 weeks at 37°C, the samples have lost about half of their strength while only losing 0.8% of their initial mass. The effect of the liquid phase on cell viability at different periods indicated no significant difference from their media controls.

Table I. Initial Results of Calcium Silicate Samples

ABC	DBCP Amount (wt. %)	Peak Stress (psi)	Modulus (N/mm^2)	Strain at Break (%)	Thickness (mm)
-1	50	260.6 ± 6.4	37.7 ± 4.5	8.4 ± 2.0	2
-2	40	304.6 ± 3.6	55.4 ± 1.5	5.1 ± 0.3	2
-3	35*	461.7 ± 36.9	132.2 ± 12.1	3.8 ± 0.2	3

*Thickness was 3 mm

Table II. Results for ABC-1 *In Vitro* Samples at 37°C

Sample Name	*In vitro* Temperature	*In vitro* Time Period	Percent Weight Loss (%)	BSR (%)	Cell Viability* (%)
ABC-1	37°C	1 wk.	0.45	60.7	116
		4 wk.	0.80	47.9	99
		8 wk.	1.26	35.6	94
		17 wk.	3.82	28.9	120

*Normalized to media controls

Conclusions: Available results demonstrate the feasibility of producing new, self-setting, potentially cytocompatible, absorbable adhesive/phosphate composites with promising properties for use as a bone cement/filler.

References:

[1]Kuhn, K-D, *Bone Cement*, Springer, NY, 2000.
[2]Lin, J-H, C. et al, U.S. Patent No. 6,379,453 (2002).
[3]Antonucci, J.M. et al, U.S. Patent No. 5,508,342 (1996).
[4]Shalaby, S.W. & Vaughn, M.A., U.S. Pat. Appl. 11/601,994 (2006).
[5]Shalaby, S.W. et al., U.S. Patent No. 5,874,509 (1999).