In vitro and *In vivo* Evaluation of Absorbable, Self-setting Composite Adhesive Bone Cement

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Statement of Purpose: Growing interest in developing absorbable forms of bone cements and related compositions led to a number of early investigators to study (1) a self-setting bone cement which was described as a resorbable calcium phosphate; (2) PMMA/calcium phosphate composites; and (3) calcium silicate.[1,2] However, the success of these and similar compositions as absorbable orthopedic products was limited primarily because of the low fracture resistance of these systems. This prompted Poly-Med to explore the development of inorganic/organic hybrid absorbable self-setting composite adhesive bone cements/fillers.[3,4] Results of a preliminary study conducted at this laboratory demonstrated the feasibility of producing new self-setting adhesive bone cements based on inorganic phosphates and methoxypropyl cyanoacrylate.[5] The present communication deals with further studies on the system and its evaluation as a viable material for broad-based orthopedic applications.

Methods: Self-setting, absorbable bone cements were prepared from methoxypropyl cyanoacrylate and either (1) calcium phosphate with either potassium phosphate or polyglycolide (SCC-P) or (2) calcium phosphate in combination with calcium silicate (SCC-PS). Using molds constructed from stainless steel and Teflon, samples of 7.6 cm x 7.6 cm x 2 mm were prepared for multiple SCC-P type and SCC-PS type bone cements. Samples of approximately 1 cm x 5 cm x 2 mm were then cut from original molded samples and evaluated by mechanical three-point bending and *in vitro* mass loss. From each of the SCC-P and SCC-PS groups, a single composition was chosen for *in vivo* evaluation. The *in vivo* study was initiated using New Zealand white female rabbits as the animal model. Artificial defects were produced on the medial face of three tibias in a cross pattern using precise measurements that were repeated for each bone. Empty defects were filled with either SCC-P, SCC-PS or Simplex P (Stryker) bone cement as a PMMA control. One tibia was left intact as a control. After up to 3 days, the rabbit was euthanized and the tibias removed. Three-point bending was performed on each tibia, with the load applied at the site of the defect.

Results: Various compositions (Table I) of SCC-P and SCC-PS bone cements were analyzed using three-point bending. The initial three-point bending results indicated that the K_2HPO_4-containing SCC-P12 and the $CaSiO_3$-containing SCC-PS3 composites possessed the best mechanical profiles (Table II). They also had the greatest mass loss over 28 days for their respective composite types (Table III, comparison data not shown). Based on these results, they were evaluated by *in vivo* analysis (Table IV).

Table I. SCC-P and SCC-PS Compositions

Sample Type (SCC-)	Solid / MPC, g/mL	Composition of Solid Component; weight ratio
P7	50/50	95 / 5, $CaHPO_4$ / Polyglycolide
P10	60/40	95 / 5, $CaHPO_4$/ Polyglycolide
P12	60/40	95 / 5, $CaHPO_4$/ K_2HPO_4
PS1	50/50	90 / 10, $CaHPO_4$ / $CaSiO_3$
PS2	50/50	70 / 30, $CaHPO_4$ / $CaSiO_3$
PS3	50/50	50 / 50, $CaHPO_4$ / $CaSiO_3$

Table II. Three-point bending results

Sample Type (SCC-)	Peak Load (N)	Peak Stress (psi)	Modulus (N/mm^2)	Energy Under Curve (Nm/cm^3)
P7	18	131	20	139
P10	23	183	24	168
P12	29	217	32	131
PS1	41	296	70	28
PS2	49	353	74	42
PS3	51	356	76	39

Table III. *In vitro Mass Loss at Various Time Periods**

Sample Type (SCC-)	% Mass Loss at 7 Days	% Mass Loss at 14 Days	% Mass Loss at 21 Days	% Mass Loss at 28 Days
P12	2.4	4.2	6.2	8.8
PS3	34.8	38.2	41.0	43.1

*Incubated at 50 ºC in water

Table IV. Preliminary *In Vivo* Data**

Sample	Peak Load (N)	Peak Stress (psi)	Modulus (N/mm^2)	Energy Under Curve (Nm/cm^3)
Simplex P	408	888	215	353.8
SCC-PS3	361	995	268	495
SCC-P12	269	709	114	1051
Intact Tibia	414	1087	271	640

**Post-Implantation mechanical properties

Conclusions: Novel self-setting absorbable adhesive bone cements (SCC-P12 and SCC-PS3) show promising data that is comparable to non-absorbable bone cements currently on the market.

References:
1. Lin, J-H.C. et al., U.S. Patent 6,379,453 (2002).
2. Antonucci, J.M. et al, U.S. Patent 5,508,342 (1996).
3. Shalaby, S.W. et al., U.S. Patent app. 11/601,994 (2006).
4. Shalaby, S.W. et al., U.S. Patent app. 12/080,649 (2008).
5. Shalaby, S.W. et al., *Trans Soc Biomater*, 31, 519 (2009).

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