Development of an Absorbable Synthetic Bone Wax

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Statement of Purpose: Surgical bone wax is a relatively safe and inert hemostatic agent that is commonly used in a variety of surgical procedures to mechanically plug bleeding bony structures and elicit immediate hemostasis. Since commercial bone wax typically consists of beeswax, isopropyl palmitate and softening agents such as paraffin, the material is minimally resorbable and remains in the body for the lifetime of the patient following surgery. In recent years there have been case reports of bone wax-related complications that include the development of post-thoractomy paraplegia[1,2], a foreign body granuloma[3], and a retroperitoneal tumor[4]. The continued post-operative persistence of bone wax is the most critical issue regarding the potential for future complications. The persistent foreign bone wax can elicit foreign body reactions in rare cases. Furthermore, the residual bone wax can migrate out of the original site of application following surgery. Migrated bone wax can exert compressive forces on the spinal cord, leading to debilitating paraplegia that requires a second operative procedure to remove the displaced bone wax. Complications resulting from bone wax persistence can be eliminated by engineering novel bioabsorbable polymeric materials with similar physical properties to conventional bone wax. Poly-Med has developed such a material from a polyaxial copolymer of poly[(*p*-dioxanone-co-trimethylene carbonate) to serve as a substitute to conventional bone wax.

Methods: Polymer synthesis was performed in a two-neck flame-dried 250 mL glass reaction flask, fitted with a stainless steel stir rod and a nitrogen gas connector. *Para*-dioxanone was melted at 50°C overnight; then, the trimethylolpropane initiator, molten *p*-dioxanone and crystalline trimethylene carbonate were added to the reaction flask at room temperature. Monomer and initiator were dried under vacuum, and then the system was purged with nitrogen gas. Upon mixing, stannous octoate catalyst was added to the reaction, followed by increasing the temperature to 130°C to commence polymerization. After five hours, the reaction was stopped and polymer was removed from hot reaction flask with a spatula. Collected polymer was dried in a room temperature vacuum oven. Purified polymers were prepared by dissolution of polymerized material in dichloromethane (0.25 grams polymer per 1 mL solvent) followed by precipitation in -70°C isopropyl alcohol while blending. Precipitated polymer was filtered and dried under in a vacuum oven (>28 in. Hg) at 40°C. Novel compositions were analyzed by DSC and GPC. Functional streak tests were performed on all polymers in order to qualitatively compare novel compositions to commercial Ethicon® bone wax. Streak tests were performed by kneading polymer by hand for 5 minutes to increase temperature, then spreading a streak of polymer across a clean glass surface. The spreadability of each polymer was assessed visually.

Results: Two prototype polymers were developed as bioresorbable bone wax substitutes: TPDX1 and TPDX2. Thermal data analysis is shown in Table I. GPC analysis indicates that of the two polymers, TPDX2 had a better polydispersity (see Table II). Streak tests that were performed with both polymer prototypes demonstrate that TPDX1 performs more comparably to commercial bone wax. TPDX1 made a relatively clean, smooth streak across the glass plate, whereas TPDX2 produced uneven streak marks (see Figure 1).

Table I. Thermal data analysis of bone wax formulations.

Bone Wax Formulation	T_m (°C)	ΔH (J/g)
Ethicon® Bone Wax	54, 60	142
TPDX1	70	53
TPDX2	60	44

Table II. GPC results for bone wax formulations.

Composition	Mn	Mw	PDI
TPDX1	4,900	9,000	1.8
TPDX2	5,500	7,100	1.3

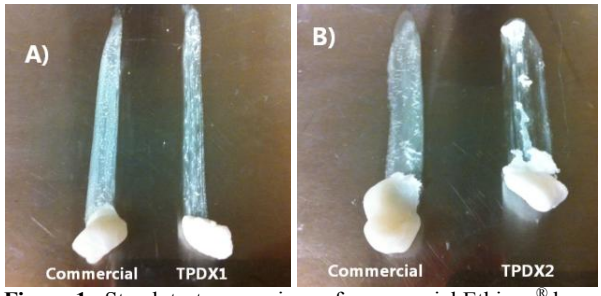

Figure 1. Streak test comparison of commercial Ethicon® bone wax vs. (A) TPDX1 and (B) TPDX2.

Conclusions: Our investigation into a bioabsorbable bone wax has led to the development of polyaxial copolymers of poly[(*p*-dioxanone-co-trimethylene carbone)]. Two polymer candidates were developed during our research: TPDX1 and TPDX2, both of which demonstrated similar analytical results according to DSC and GPC; however, only TPDX1 performed comparably to commercial bone wax in our streak test. Therefore, we present TPDX1 as a novel bioresorbable bone wax that demonstrates similar performance to commercially available non-absorbable bone wax.

References:

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