Reduction of Absorption Time for a Polydioxanone Homopolymer Using Polyethylene glycol

D.R. Ingram, J.T. Corbett, D.E. Linden, M.S. Taylor
Poly-Med, Inc. Anderson, SC 29625

Introduction: PDSII is a monofilament suture indicated for general soft tissue approximation, ophthalmic use, and pediatric cardiovascular surgery. It is used for closure to provide extended strength retention compared topolyglycolide based sutures. According to Ethicon package literature, 70% of the initial strength is retained at 2 weeks and 25% at 6 weeks (Break Strength Retention, BSR). Absorption is "essentially complete" within 6 months[1]

The focus of this communication is to demonstrate the successful integration of polyethylene glycol and p-Dioxanon (PDO) to improve upon the utility of PDSII by shortening the absorption time.

Methods: *Polymer Synthesis, Removal, and Purification* – Syntheses were performed in a 1L stainless steel kettle/stirrer enclosed by a 3-neck glass lid/ground glass fittings with a PTFE bearing, and sealed at the kettle interface with a PTFE gasket.

The polymer reagents (charge) comprised vacuum dried polyethylene glycol, PDO and glycolide, used without modification. Tin(II) 2-Ethylhexanoate was used to catalyze the reaction. This charge was heated under positive nitrogen pressure in an oil bath to perform the synthesis.

The reacted polymer was cooled with liquid nitrogen, ground, and purified using vacuum distillation.

Fiber Formation – Monofilament fibers were prepared using a melt extrusion process using a custom ¾" single screw extruder (Alex James and Associates). Extrudates were heated and drawn to reduce diameter and increase tensile strength by orientation of the polymer chains. Dimensional stability was achieved through a series of annealing and relaxation schemes.

Fiber Tensile Testing Method – A Universal Tester (MTS Minibonix) was used for all fiber testing, with an initial grip separation of 70 mm and a strain rate of 2.33 mm/s (As defined by the methods set forth in the United States Pharmacopeia).[2]

In vitro/in vivo BSR Testing – *In vitro* BSR test samples were aged by incubating fiber samples in 7.2 pH 100mM phosphate buffered solution at 37°C.[3] *In vivo* test sutures were implanted subcutaneously in Spraque Dawley rats.

The ultimate tensile strength (UTS) for *in vitro* and *in vivo* BSR samples was then measured before and after aging.

In vivo Absorption Testing - *In vivo* absorption suture samples were implanted in the gluteal muscle of Sprague Dawley rats. At varied timepoints, these rats were euthanized and samples were explanted, trimmed, and preserved in 10% neutral-buffered formalin. Subsequently, these specimens were stained using massons trichrome and imaged using an optical microscope.

Results: The developmental polymer compositions are as follows (glycolide comprises up to 10% of the graft):

PDO2 – 6 wt. % PEG 20,000, Approximately 94% PDO
PDO4 – 6 wt. % PEG 14,000, Approximately 94% PDO

Percent BSR profiles (Table 1) for all tested USP size 2-0 fibers were comparable out to six weeks. The strengths of PDO4 and PDSII™ are nearly equivalent for all timepoints while that of PDO2 is lower.

Images of gluteal explants are shown in Figure 1. Size O PDO2 absorbed substantially by 3 months, demonstrated by the active phagocytosis present around the suture periphery. The 4 month aged PDO2 samples indicates no presence of a foreign body. PDSII™, on the other hand, is still very present after 4 months, in accordance with package literature expectations. Because of the similarity of their compositions, the absorption of PDO4 is expected to be like that of PDO2.

Table 1. *In vitro/**in vivo*** BSR results (**Bold** indicated ***in vivo***)

Name	Diam., mm	Initial UTS, Mpa	% BSR / (UTS, MPa)		
			2 Wk.	4 Wk.	6 Wk.
PDO2	0.32	448	89 (490)	62 (345)	28 (152)
		374	**70 (414)**	**51 (303)**	**27 (159)**
PDO4	0.34	552	55 (138)	42 (103)	30 (76)
		592	**68 (200)**	**53 (159)**	**44 (131)**
PDSII ™	0.33	555	71 (228)	53 (172)	39 (124)

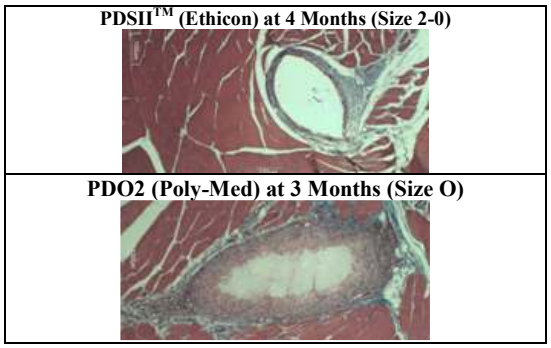

Figure 1. Microscopic Images (100X)

Conclusions: The claims made in Ethicon package literature are in accordance with the experimental results obtained by Poly-Med (*in vivo*). PDO4 is equivalent in strength and strength retention, compared to PDSII™. Although sutures exhibited similar strength retention to the PDSII control, mass loss is significantly faster in the PDO sutures.

Based on available data, an optimized version of the PDO suture line has great potential as an implantable device.

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References:

[1] PDS II (Polydioxanone) Suture Dyed and Clear Monofilament Instructions for Use (2012). Somerset, NJ: Ethicon, Inc.
[2] United States Pharmacopeia and National Formulary (USP 31-NF 28). Rockville, MD: United States Pharmacopeia Convention; 2009.
[3] ASTM F1635 - 11 Standard Test Method for *in vitro* Degradation Testing of Hydrolytically Degradable Polymer Resins and Fabricated Forms for Surgical Implants.