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Evaluation of Ethyl Salicylate as a Plasticizer for Vascular Bioresorbable Stent Application

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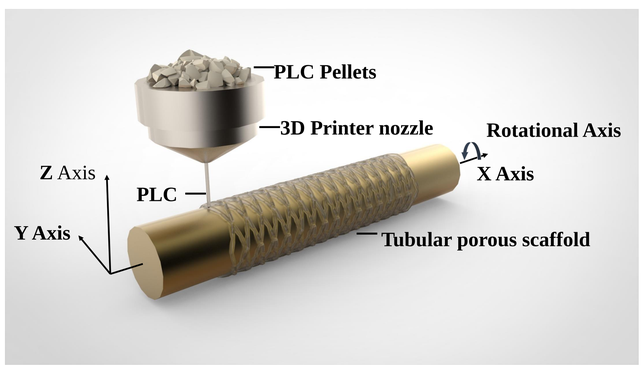
Statement of Purpose

Interventional vascular stenting is one of the most widely used therapy for arterial atherosclerosis treatment. The development of bioresorbable stents (BRS) has drawn much attention in the past decades with the hope that BRS could overcome the limitations of traditional permanent stents, such as chronic inflammation. Biodegradable polymers, including poly-l-lactic acid (PLLA) and poly(lactic-co-glycolic) acid (PLGA), are among the most widely studied materials for BRS application because of their good biocompatibility. However, these materials have poor fatigue resistance, therefore, they are vulnerable to fracture, which limits their applications in peripheral vascular disease treatment. Using plasticizers is an effective way to improve the mechanical properties of a biomaterial. The goal of this study is to evaluate the effectiveness and biocompatibility of ethyl salicylate (ES) as a plasticizer for BRS application.

Methods

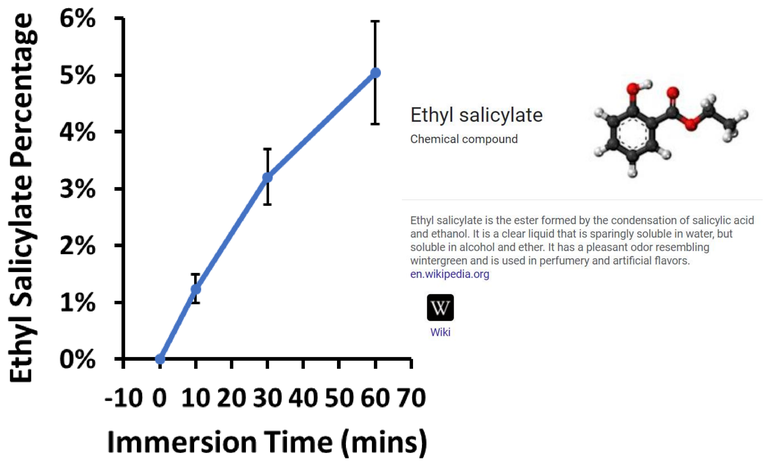
Both fibers and stents made from copolymer poly(lactide-co-caprolactone, 95:5) (PLC) (Corbion, Amsterdam, NL) were used in this study. PLC fibers were melt extruded from an extruder (Ø0.23mm) and collected at room temperature. PLC fibers were annealed at 150 °C for 1h followed by immersing in ES (TCI, Tokyo, Japan) for 0, 10, 30 or 60 mins at 50°C. Excess ES on the surface of the fibers was blotted with tissue paper. The amount of ES in each group were determined by a HPLC method. Tensile tests were performed for each group at a strain rate of 10% by length per minute. A custom-made multi-axial 3D printer was used to fabricate closed-cell structured stents from PLC raw material as reported previously. The PLC stent or BRS was annealed and incorporated with ES (2-3% by weight) by a method similar to the one described above. The BRS samples with or without ES treatment (sized 6mm x 76mm, n=5 each) were subjected to a flexural fatigue test with bending angles ranging from 0 to 60 degrees at 1 Hz for up to 3.5 million cycles in PBS at 37 °C. To evaluate stent performance *in vivo*, the ES treated BRS samples (5.5mm x 36mm, n=8) were mounted on balloon catheters and implanted in the iliofemoral arteries of pigs for up to 3 months.

Fabrication of Closed-Cell Structured Stent from PLC Raw Material

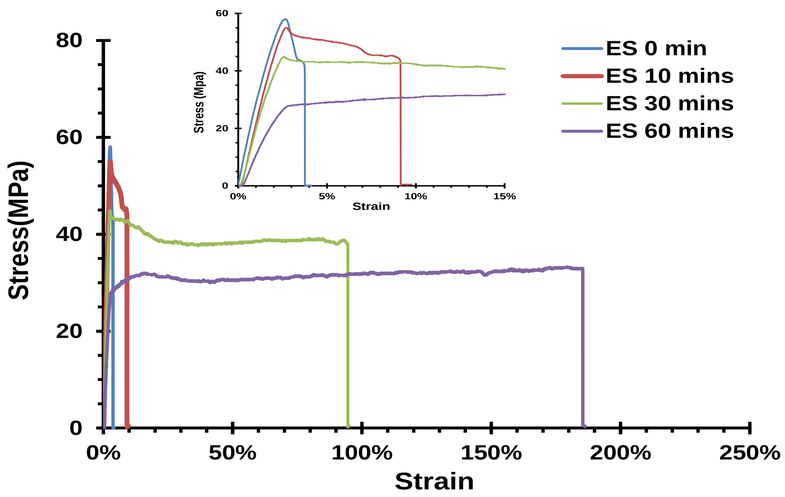


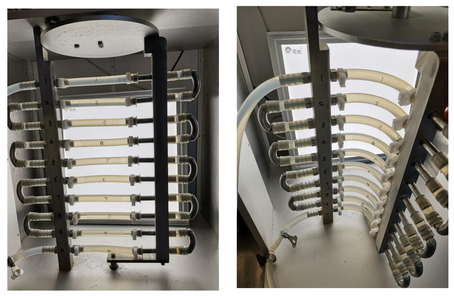
Results

Diffusion Curve of Ethyl Salicylate Into PLC Fibers at 50 °C

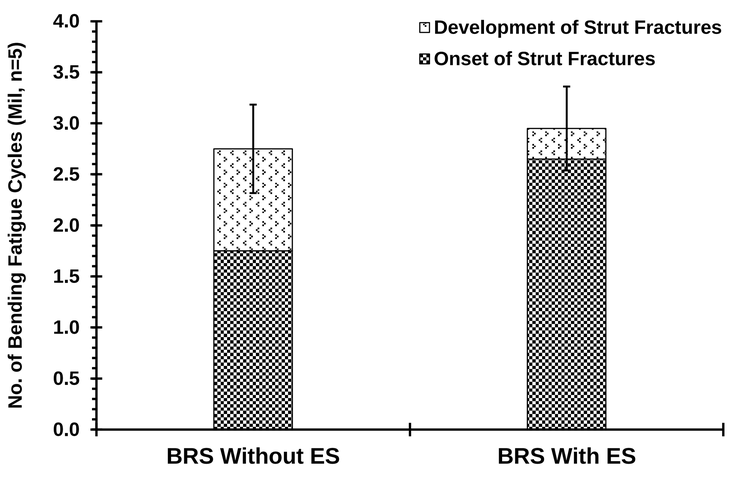


Stress-Strain Curves of ES Treated PLC Fibers

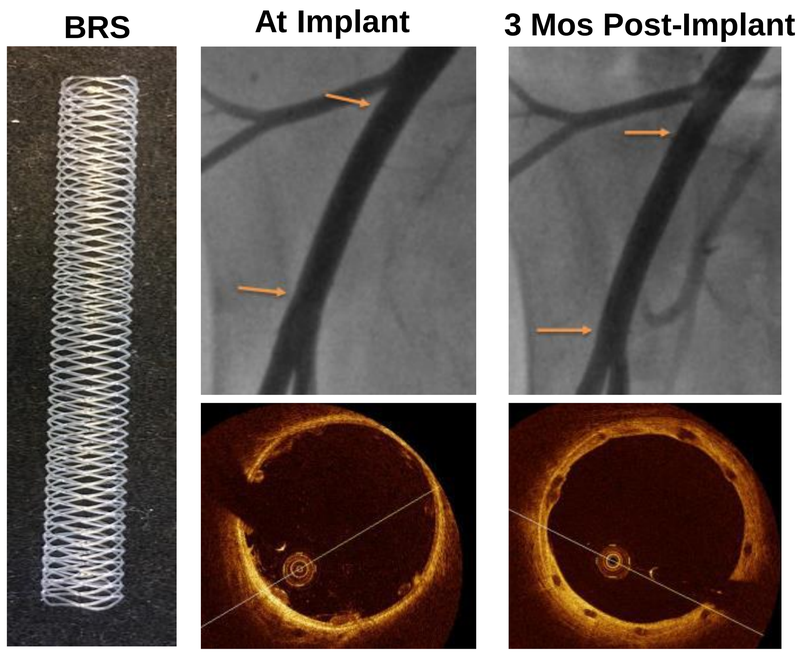




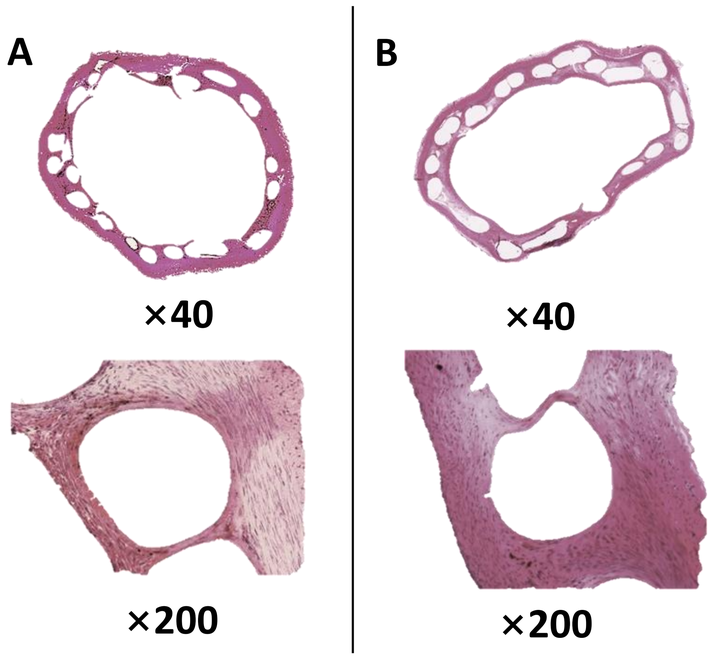
Bending Fatigue Lives of PLC Stents or BRS



Angiographic and OCT Images of PLC BRS Implants



Histopathological H&E Staining. A) 1 Month; B) 3 Months post-implantations



Conclusions

Results of this study demonstrated that ethyl salicylate was an effective yet biocompatible plasticizer for enhancing ductility of PLC devices. ES incorporated PLC BRS retained sufficient mechanical strength to keep iliofemoral artery patent and supported arterial remodeling and endothelialization.

References

H. Zhao, J. Zhang, X. Weng, N. Yu, Q. Liu, B. Liu, Z. Chen. *Evaluation of Multi-Axial 3D Printed Bioresorbable Vascular Scaffolds for Peripheral Vascular Interventional Application.* Society for Biomaterials Annual Meeting, Atlanta GA, 2018.