Proceedings of the 2022 Design of Medical Devices Conference
DMD2022
April 12-15, 2022, Minneapolis, MN, USA

DMD2022-1051

EVALUATION OF SUSTAINABLE P4MCL/PLLA BLOCK COPOLYMERS AS PVC REPLACEMENT IN MEDICAL PLASTICS

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ABSTRACT

Aliphatic polyesters are potential sustainable alternatives to PVC for use in medical devices, such as IV bags. Our candidate replacement of PVC-based IV bags use P4MCL, a sustainable polymer with demonstrated uses in mechanically robust materials. The goal of our project was to compare the mechanical and biocompatibility characteristics of P4MCL/PLLA star block copolymer TPEs with commercial PVC-based IV bags. P4MCL/PLLA TPEs were synthesized according to previously reported methods. Uniaxial tensile testing was conducted pre- and post-autoclave. Impact and tear resistance testing was performed on non-autoclaved specimens according to ASTM standards. Cytotoxicity was examined using NIH 3T3 Fibroblasts with an AlamarBlue assay. A student's t-test was used to compare results with statistical significance of $P < 0.05$. PVC tended to be stiffer but P4MCL/PLLA was more extensible. The tensile properties for the P4MCL-based material did not change after autoclaving. When compared to PVC-based IV bags, the P4MCL/PLLA TPE demonstrated a lower peak force and average force but a greater elongation at break and total absorbed energy ($P<0.05$). P4MCL/PLLA, unlike PVC-based materials with DEHP plasticizer, was non-cytotoxic. In summary, P4MCL/PLLA has desirable mechanical and biocompatibility advantages compared to PVC making the material a potential sustainable alternative for medical grade plastics.

Keywords: Sustainability, plastics, polymers, medical devices

NOMENCLATURE

PVC	Polyvinylchloride
IV	Intravenous
P4MCL	Poly(4-methyl-ε-caprolactone)
PLLA	Poly(L-lactide)
TPE	Thermoplastic Elastomer
ASTM	American Society for Testing and Measurement
MTCO2e	Metric Tons Carbon Dioxide Equivalent
NIH	National Institutes of Health
DEHP	Di(2- ethylhexyl) phthalate
T_g	Glass Transition Temperature
T_m	Melting Temperature

1. INTRODUCTION

Plastics are ubiquitous in healthcare comprising about 50% of medical waste, including IV bags, infusion tubing, dialysis bags, and flexible tubing [1]. One of the most highly used plastics in healthcare, PVC, has serious environmental and human health implications. PVC production, transportation, and incineration amounts to approximately 3.24 MTCO2e per ton and is often combined with the harmful plasticizer DEHP to achieve desired mechanical properties [2,3]. DEHP exposure has been associated with adverse reproductive tract changes while dioxin pollution during incineration has been linked to carcinogenic effects [3]. Although alternatives to PVC have been developed, including polypropylene, polyamide, and polyethylene, they continue to be manufactured from non-renewable resources, disposed of in landfills or via incineration, and ultimately exacerbate greenhouse gas production [2].

Sustainable polymers that are synthesized from renewable biomass are rapidly growing in popularity, especially in the food service industry [4]. Sustainable polymers have the potential to be compostable and biodegradable, enabling microorganisms to break down the material into simple organic molecules that are non-hazardous to the environment [4]. There are no biodegradable IV bags commercially available, likely due to the rigorous requirements for non-toxicity, sterile processing, and specialized production as well as higher material and operational costs.

Research involving the use of TPEs composed of ABA star block copolymers as a sustainable alternative to petroleum-based materials has become an area of interest. The use of the aliphatic polyesters P4MCL and PLLA as the soft (low T_g) B and hard (high T_m or T_g) A blocks, respectively, in (AB)n star block polymers been shown to yield materials that are tough, resilient, and elastomeric while also sustainable and degradable [5]. This combination of properties makes these P4MCL based materials potential candidates for novel degradable medical plastics. The goal of our project was to compare the mechanical and biocompatibility properties of P4MCL/PLLA star block copolymers to a commercially available PVC-based IV bag material.

2. MATERIALS AND METHODS

2.1 Material Acquisition

PMCL/PLLA block copolymers were synthesized according to previously reported methods [6]. Commercial IV bags made of PVC with DEHP as a plasticizer were supplied by M Health Fairview – University of Minnesota for comparison.

2.2 Mechanical Testing

Uniaxial tensile testing of both materials was conducted pre- and post- autoclaving for 45 minutes at 121 °C with 15 psi of saturated steam to simulate terminal sterilization procedures. Impact testing was completed according to ASTM F1306 which resulted in peak force, average force, elongation at break, and total absorbed energy being measured with samples having a similar thickness of 0.30 mm. Per ASTM D1922, tear testing was conducted also with sample thickness of 0.30 mm.

2.3 Biocompatibility Testing

Initial biocompatibility testing involved an AlamarBlue cytotoxicity assay with NIH 3T3 Fibroblasts cultured for up to 72 hours. Prior to the assay, specimens were sterilized via autoclaving with conditions identical to those used before tensile testing. Statistical analysis was conducted with a student's t-test at a significance level of $P < 0.05$.

3. RESULTS AND DISCUSSION

3.1 Mechanical Testing

Tensile testing demonstrated different stress-strain profiles for the PVC-based commercial IV bag material compared to the P4MCL/PLLA polymer. The PVC-based material was stiffer compared to P4MCL/PLLA (Figure 1). However, the P4MCL/PLLA displayed a significantly higher strain at break.

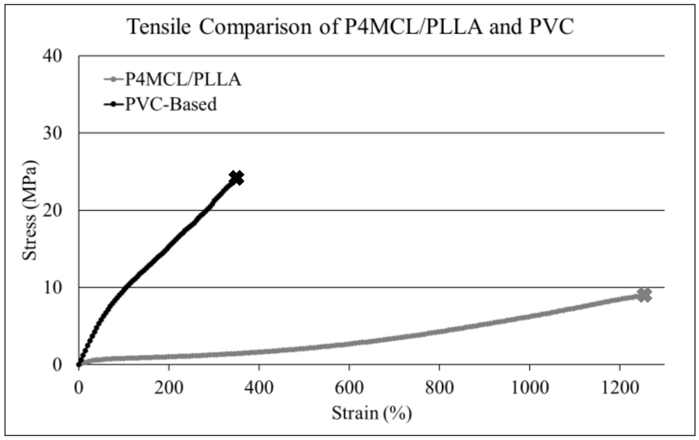

FIGURE 1: Tensile curve comparison of PVC-based commercial IV bag material and P4MCL/PLLA polymers. Material failure is indicated at points marked by 'X' symbol.

Plastics utilized in medical devices must be terminally sterilized prior to usage. A major method of sterilization, autoclaving, involves using temperature and pressure-controlled steam to eliminate microbes so that contamination or infection does not occur. Tensile testing of P4MCL/PLLA pre- and post-autoclaving showed minimal changes to the tensile properties after exposure to autoclaving conditions (Figure 2). This data suggests autoclaving is an acceptable sterilization technique for the polymer and does not result in diminished mechanical properties.

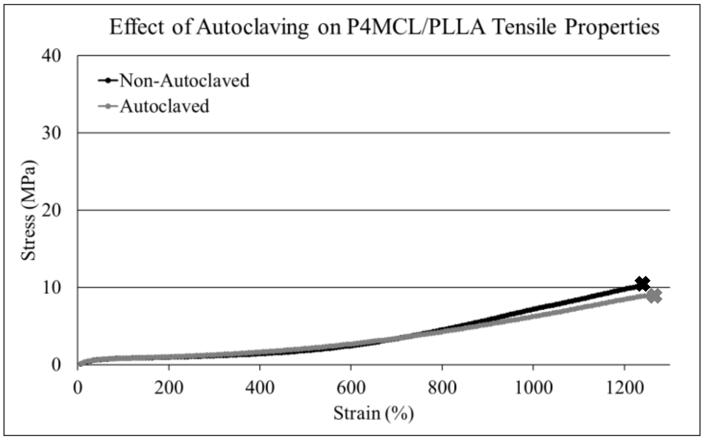

FIGURE 2: Tensile curve comparison of autoclaved and non-autoclaved samples of P4MCL/PLLA showed autoclave sterilization had minimal effects on mechanical properties. Material failure is indicated at points marked by 'X' symbol.

In the context of medical containers such as IV bags, the ability for the device to withstand mechanical rupture when dropped or impacted is an important feature. Impact testing according to ASTM F1306 was conducted for the PVC and P4MCL/PLLA materials. The PVC-based material withstood greater peak and average forces, whereas the P4MCL/PLLA polymer displayed significantly higher elongation at break and total absorbed energy (Table 1). These results suggest that the P4MCL/PLLA material may be even better equipped to resist rupture under impact than the commercial PVC IV bag as evidenced by the higher absorbed energy.

Characteristic	P4MCL/PLLA TPE, N = 4[1]	PVC, N = 5[1]	p-value[2]
Peak Force (N)	26 (3)	50 (4)	<0.001
Average Force (N)	12.8 (1.6)	20.8 (1.9)	<0.001
Elongation at Break (cm)	5.16 (0.70)	2.01 (0.14)	0.002
Total Absorbed Energy (N*cm/cm^3)	1,301 (271)	806 (105)	0.029
Thickness (mm)	0.29 (0.07)	0.32 (0.00)	0.4

[1] Mean (SD)
[2] Welch Two Sample t-test

TABLE 1: Impact testing parameters for P4MCL/PLLA and PVC-based materials collected according to ASTM F1306.

Tear resistance testing according to ASTM D1922 showed the PVC-based material was superior to withstanding a tearing force compared to P4MCL/PLLA (Table 2).

Characteristic	P4MCL/PLLA TPE, N = 4[1]	PVC, N = 3[1]	p-value[2]
Tear Test Resistance (g)	156 (15)	1,643 (98)	0.001

[1] Mean (SD)
[2] Welch Two Sample t-test

TABLE 2: Tear testing per ASTM D1922 of PVC-based material and P4MCL/PLLA.

3.2 Biocompatibility Testing

Biocompatibility with the underlying tissue that may be exposed directly or indirectly to a material is paramount. The AlamarBlue cytotoxicity assay showed that the P4MCL/PLLA material was non-cytotoxic as evidenced by the relative increase in NIH 3T3 fibroblast proliferation between 4 and 72 hours (Figure 3). These results indicate that the P4MCL/PLLA polymers could also be used as an implantable material for medical devices, however, in-vivo animal studies will be needed to confirm this. Conversely, the PVC-based material tended to inhibit fibroblast growth during the same time frame and demonstrated significantly higher cytotoxicity. The plasticizer DEHP used with the PVC-based materials has been shown to be harmful to an array of tissue types and was likely responsible for the cytotoxic effect [7].

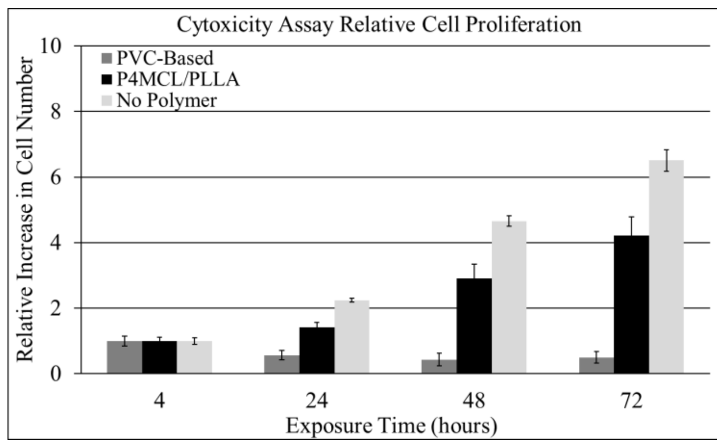

FIGURE 3: AlamarBlue cytotoxicity assay demonstrated increased NIH 3T3 fibroblast proliferation at 24, 48, and 72 hours for P4MCL/PLLA and the no polymer control while the PVC-based commercial IV bag material showed marked cytotoxicity. Increase in cell number is scaled relative to 4 hours.

4. CONCLUSION

P4MCL-based materials are viable candidates for use in medical plastics, especially IV bags that traditionally have been PVC-based. The novel P4MCL/PLLA polymers are softer and more extensible, have greater resistance to puncture, are non-cytotoxic, and have the potential to be bioderived and compostable [8]. Conversely, PVC-based materials with DEHP plasticizer were stronger but shown to be cytotoxic. Overall, the beneficial mechanical properties and biocompatibility of the

P4MCL/PLLA materials make these sustainable polymers possible candidates for a wide range of medical applications.

ACKNOWLEDGEMENTS
The project was funded by the Climate Change Innovation Grant sponsored by the University of Minnesota Medical School and College of Science and Engineering. Special thanks to Mark Hillmyer PhD and Rafael Andrade MD for their expertise and guidance.

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