LONG TERM POLYURETHANE CATHETER ALCOHOL COMPATIBILITY I, PHYSICAL AND RHEOLOGICAL STUDIES

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Abstract

Thermoplastic urethanes (TPU) offer broad property range, processing flexibility, and biocompatibility for medical applications. Alcohol based disinfectants have a long history of effective and safe use. Expanding on earlier rheology molecular weight data indicating minimal reduction, we conducted a long term compatibility study covering all known urethane types in a hemo-dialysis setting with a simulated clinical exposure protocol for 90 days. After 90 days exposure, minor changes in physical properties on the catheter body and components were detected, often similar to the saline control. Most importantly, resultant properties far exceeded ISO requirements for catheters.

Introduction

TPU catheters are prominent in device applications and increasingly, they are subjected to longer duration use, and exposed to a wide variety of chemically active agents. Alcohol based disinfectants are the most widely used for its long history of safety and effectiveness. To understand the compatibility of polyurethane devices and alcohol exposure, we conducted both fundamental material response and device performance studies. For example, it was pointed out in our earlier studies (1,2), that due to TPU's complex annealing behavior, vastly different properties can result from thermal history and could at least in part account for some of the reported variabilities on alcohol exposure.

The long term simulated clinical use study was aimed to demonstrate compatibility in actual devices while rheology indicated very limited molecular weight loss from hydrolytic degradation. The locking of the disinfectant between hemo-dialysis treatments, saline flush before three times weekly therapy sessions followed with disinfectant locking were all simulated in detail. In addition, to address limitations cited in literature reports where only the catheter body was evaluated (3), all components and connections exposed to the alcoholic disinfectant were studied.

Experimental

Continuing our previous studies where more detailed procedures are fully described, we evaluated hydrolytic molecular weight degradation upon exposure to alcoholic disinfectants with melt rheology with the well established relationship for linear polymers (4-5),

$$\eta = K\, Mw^{3.4} \qquad (1)$$

Where η is the steady shear limiting viscosity
Mw is the weight average molecular weight

Five TPU based hemo-dialysis long term indwelling catheters chosen to cover all known commercial polyurethane types were studied. They included (A) Tecoflex®, (B) Tecothane®, (C) Carbothane®, (D) Pellethane®, and (E) Chronoflex® (6-10). Sample A uses an aliphatic polyurethane with ether soft segments. Samples B and E are ether soft segment aromatic polyurethanes, Sample C contains a polycarbonate soft segment and Sample E's soft segment is also polycarbonate based but differs from C. These catheters range in size from 10 Fr to 14.5 Fr and from 24 to 55 cm in length. Figure 1 describes a typical catheter and all exposed area and testing locations indicated.

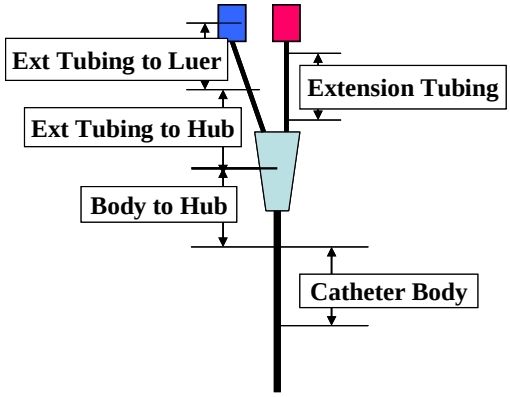

Fig. 1, Hemo-dialysis catheter testing locations

Physical testing was conducted on an Instron tester at 250mm min-1. The disinfectant solution studied contains ethyl alcohol at about 30 weight percent and an anticoagulant.
A long term simulated clinical use protocol was followed for 90 days. Briefly, the catheters were filled with the disinfectant and locked via the Roberts clamps on the extension tubing for 48 hours (72 hours on weekends) while immersed in a physiological saline bath at 37°C, flushed and filled with saline to simulate the dialysis treatment and refilled with the disinfectant and locked. In addition to t=0 sampling, catheter samples at exposure times of 7, 30 and 90 days were collected. For all time periods, a parallel set of saline locked catheters served as control. Sample size of 12 was chosen at all time periods except at 90 days where 10 additional samples for pressure testing per ISO 10555-1 (11) were provided.

To address the issue of environmental stress crack resistance (ESCR) where failure occurs under the simultaneous application of tensile stress and active chemical agents a screening study was first conducted where a catheter segment was crimped into a 180° sharp bend, immersed in the disinfectant for 72 hours and examined under a stereo microscope for evidence of cracks and surface damages. In addition, at each time point in the long term study, every mating surface (Luer to cap, Roberts clamp to extension tubing, etc.) were carefully examined for any ESCR damage and observations recorded.

Result and Discussions

Melt Rheology

As discussed in previous studies, the TPU hydrolytic degradation follows an exponential decay profile with a limiting plateau behavior, thus under a given testing condition, the plateau value viscosity, corresponds to weight average molecular weight, undergoes very little reduction with additional exposure. When this limiting viscosity was scaled against the time zero viscosity and compared with available manufacturers published melt flow specifications, Figure 2 resulted.

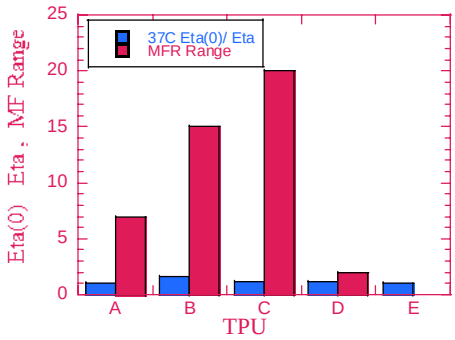

Fig 2, Viscosity ratios and specified MF range

Thus it can be seen that hydrolytic Mw reduction with disinfectant is minimal compared with raw material variability.

Environmental Stress Crack Resistance (ESCR) Testing

In both the 72 hr immersion screening study and during the 90 day long term exposure, no remarkable damage attributable to environmental stress cracking was observed on catheter body, extension tubing, and all connections.

Physical Testing

All data generated on each test locations at various time points were summarized in the graphical form. The left hand group is the saline control data, while the disinfectant group on the right (saline data at 7 days was not taken). The ISO 10555-1 requirement for vascular catheter for tensile strength is also indicated on the graph. Error bars covers the 95% confidence interval of the mean for the data set. Figure 3 below is for Sample A body.

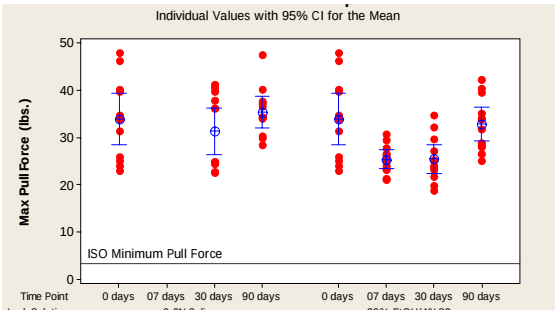

Fig 3, Sample A catheter body tensile strength

For Sample A, it is seen that there was a reduction in tensile strength upon disinfectant exposure up to about 30 days, then a pronounced up turn took place. A milder similar trend is also noted for the

saline control group. The initial softening is possibly due to hydration and plasticization from water and alcohol, and the later up-turn in strength is most likely caused by the annealing effect of 37°C long term conditioning. We also noted, the minimum data point is at least 400% higher than the ISO requirement for catheters.

Figure 4 is the corresponding catheter body elongation with time. Again, after an initial reduction possibly due to hydration and plasticization, a marked upward shift was seen for both saline and the disinfectant group. Long term annealing is the probable cause. It is noted that the 1500% minimum elongation to break is nearly impossible to achieve in a clinical setting (for example, for a 10 cm (4 in) catheter segment, 1500% elongation is 1.5 meter (5 ft).

For the Sample A extension tubing (Figure 5), near identical strength reduction was seen for both saline and the disinfectant exposure with no evidence of property improvement with time. Since the extension tubing was kept outside the 37°C bath to accurately simulate patient use, little annealing due to elevated temperature could be expected. Further, the extension tubing, for the majority of time in the 90 day period, are subjected to the severe deformation from the Roberts clamp. Thus the property reduction was likely from clamp induced softening. The near quantitative agreement between saline and the disinfectant is a strong indication that chemical and ESCR effects from the disinfectant are minimal. Again, the minimum data point far exceeded the ISO requirement by more than 400%. Likewise, a similar trend was noted for the extension tubing elongation in Figure 6.

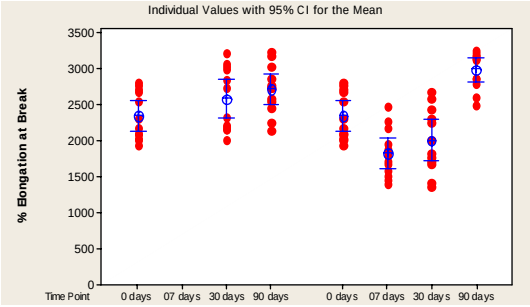

Fig. 4, Sample A catheter body elongation

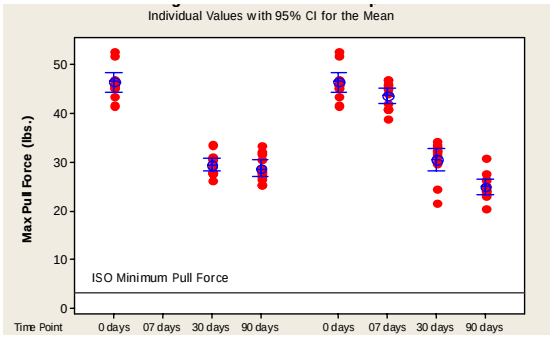

Fig. 5, Sample A extension tubing strength

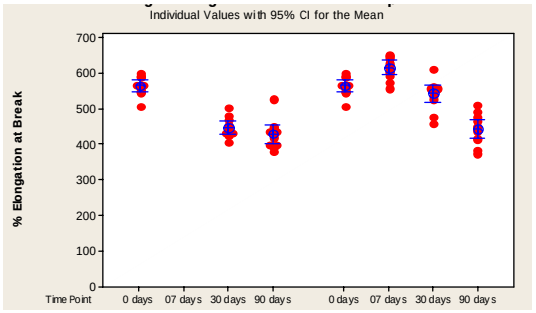

Fig. 6, Sample A extension tubing elongation

In Figure 7, the catheter tubing to hub bond strength exhibited a noticeable initial upward shift with disinfectant likely from polymer chain rearrangement from plasticization. And the subsequent reduction is also seen on the saline control.

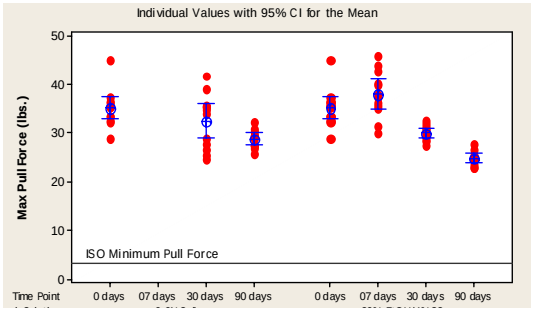

Fig. 7, Sample A catheter-hub bond strength

The extension tubing to Luer bond strength in Figure 8 was seen to undergo mild reduction and later increase with time possibly caused by polymer chain movements after plasticization.

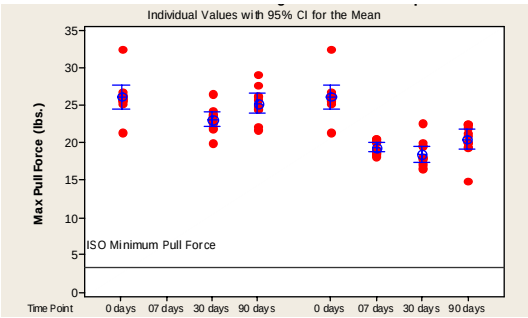

Fig. 8 Sample A extension tubing- Luer bond

Post 90 day exposure catheter leakage pressure data in Figure 9 conformed to normal distribution and tight variances. The ISO catheter requirement is seen as 17 standard deviations below the mean.

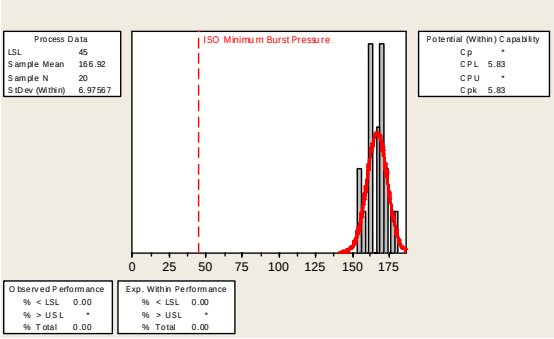

Fig 9, Sample A 90 days leakage pressure.

To accommodate the massive data set generated, for samples B-E only the catheter strength data are shown, and the 90 day disinfectant data tabulated in Table 1 as an appendix.

On the Sample B saline data at 90 days (Figure 10), there is an outlier data point possibly caused by Instron tester jaws. In addition, after the initial reduction in strength possibly attributed to hydration, there is a distinct strength upturn at 90 days, most plausible explanation is the annealing under prolonged conditioning at 37°C.

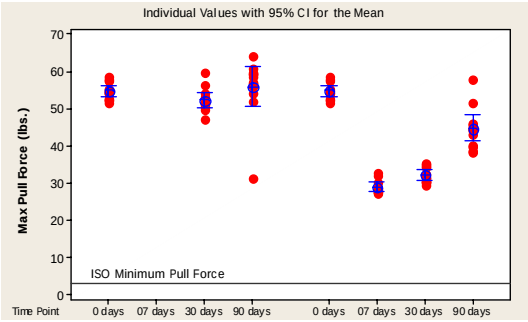

Fig. 10 Sample B catheter body strength

In Figure 11, Sample C, the Carbothane catheter strength exhibited rather high values with minimum variation with time, confirming literature reports on Carbothane®'s stability (11)

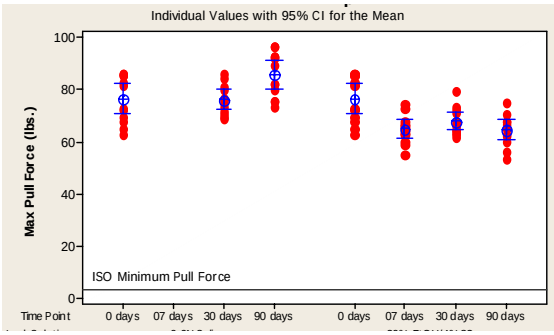

Fig.11, Sample C catheter body strength

Sample D and E's results (Figures 12-13) followed similar trends except the Chronoflex® based catheter body exhibited notable initial plasticization effects with the disinfectant and pronounced annealing at longer times.

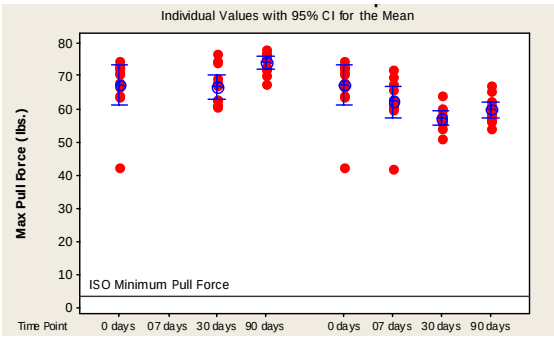

Fig. 12 , Sample D catheter body strength

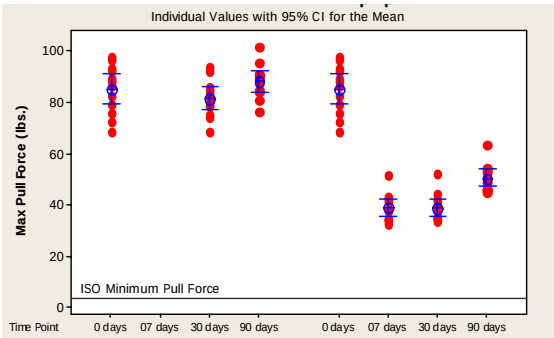

Fig.13, Sample E catheter body strength

Data summarized in Table 1 in the Appendix for other testing locations, followed the general trend described with a only observation that in comparison to others in the group, Sample A's catheter body and catheter to hub strength appeared lower. This was due to its smallest diameter (10 Fr) in the group. And the resulting strength after 90 days disinfectant exposure was still 400% above the ISO-10555 requirements.

Summary

In addition to the previously initiated rheological Mw study showing minimal hydrolytic degradation with an 30% alcohol based disinfectant, ESCR study detected no adverse observations, the comprehensive long term simulated clinical exposure covering all known TPU types for hemo-dialysis over 90 days.

Physical testing data detected subtle and minor changes at times mirroring the saline control. In nearly all cases, the catheter body, long term exposure led to improvements of physical properties most probably arising from annealing effects of the 37° body temperature bath.

The minimum values for all aspects of the catheter performance, exceeded the ISO requirement by a wide margin thus supporting the physical and mechanical compatibility of the disinfectant with hemo-dialysis catheters of diverse TPUs.

References

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2. L. Woo and W. Anderson, "Thermal Analysis and Rheological Studies on Thermoplastic Urethanes, SPE ANTEC (2009).
3. See for example and references in: M. Maiefski, Mark Rupp, E. Hermsen, "Ethanol Lock Technique: Review of the Literature", Infection Control and Hospital Epidemiology (2009), Vol 30, no 11, p. 1096.
3. G.C. Berry and t. G. Fox, adv. Polymer Sci. (1968) vol 5, p.261.
4. P. G. de Gennes, *Scaling concept in Polymer Physics*, (2003) Cornell University Press, Ithaca, NY.
5. Tecoflex ® is a trademark of Lubrizol Corp.
6. Tecothane® is a trademark of Lubrizol Corp.
7. Carbothane® is a trademark of Lubrizol Corp.
8. Pellethane® is a trademark of the Dow Chemical Company.
9. Chronoflex ® is a trademark of AdvanSource Biomaterial Corp.
10. ISO Standard 10555-1 Amendment 2, (2004) " Sterile Single Use Vascular Catheters"
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Key Words: TPU, Hemo-dialysis Catheters, Long Term Compatibility, ISO 10555-1, Physical Properties, Alcohol Disinfectant, Rheology

Appendix

Table 1, 90 day disinfectant exposure physical testing data.

Sample	ISO Req*	A	B	C	D	E
Catheter. Body (N)	15	146	199	288	262	224
Elongation (%)	NA	2993	1644	2165	1746	22184
Ext Tubing (N)	15	111	97	116	114	112
Elongation (%)	NA	444	770	699	655	6688
Catheter- Hub (N)	15	60	163	166	210	146
Ext Tubing to Hub (N)	15	91	95	123	147	152
Ext Tubing to Luer (N)	15	111	106	122	122	117
90 days Leakage P (KPa)	300	1152+-47	717+-34	1011+-34	1118+-300	900 +-99

*ISO 10555 requirements: 15 Newtons, and 300 KPa leakage pressure