# Polyurethanes in Biomedical Engineering II

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PREFACE

Polyurethanes developed for industrial purposes, when exposed to static or dynamic load, show excellent long-term mechanical properties. Accordingly, they seem predestined for application in the area of medical technology.

It is for this reason that many research groups are using polyurethanes for medical applications. At first, polyurethanes used in other areas for technical products were used for medical applications also. In comparison with other biomaterials, they showed good blood compatibility, particularly with regard to long-term stability. On the other hand, degradation appeared and calcification limited the use of these polyurethanes. Consequently, a number of teams at universities and in industry began to develop new polyurethanes or to modify available polyurethanes in order to overcome these problems. Furthermore, processing of polyurethanes was optimized. To demonstrate the world-wide research activities on polyurethanes, the Institute of Textile Technology and Chemical Engineering in Denkendorf, Germany organized the 1st International Conference on "Polyurethanes in Biomedical Engineering" in 1983.

The presentations and discussions at that Conference made it clear that further research was needed in areas such as

- prediction of in-vivo performance by in-vitro and accelerated in-vivo tests;
- modification of existing polyurethanes or development of tailor-made polyurethanes for biomedical purposes;
- improvement of polyurethane processing to avoid degradation and surface alterations.

A real need for better cooperation and exchange of information was expressed. The Division of Biomedical Engineering of the Institute of Textile Technology and Chemical Engineering therefore arranged a second conference on polyurethanes at Fellbach/Stuttgart on 18-19

June, 1986. The main aim of this second conference was to answer questions brought up during the first conference. Papers were presented by scientists from Europe, USA, Australia and Japan.

The papers and the discussions following each presentation, as well as the round-table discussion, showed that many improvements were achieved but that a lot of problems still remain to be solved.

We would like to thank the participants for the good discussion and the speakers for the excellent papers.

To make this information more widely available, the papers and discussions are published in this Proceedings volume.

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C O N T E N T S

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# THERMOPLASTIC POLYURETHANES. MATERIALS FOR VASCULAR CATHETERS.

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## ABSTRACT

A series of segmented polyether polyurethanes in four nominal Shore D hardnesses was developed and evaluated in vascular catheters. These materials, coded VIALON® 510X-45, 55, 65, and 75, were produced with no catalysts or additives to ensure highest purity and blood compatibility.

The VIALON® 510X polymers compare very favorably with TEFLON® FEP and poly(vinyl chloride), currently the principal materials in peripheral and central venous catheters, respectively. The primary advantages of polyurethane catheters are (1) superior blood compatibility, (2) improved stiffness for insertion and softness after insertion for reduction of vascular wall irritation and mechanically induced phlebitis, (3) better combination of fluid flow rates, stiffness and kink resistance, (4) increased radiopacity, (5) wider applicability to a variety of catheters, and (6) reduced catheter assembly costs.

## INTRODUCTION

Vascular catheterization is a significant and critical part of worldwide health care. In the United States alone, more than 100 million peripheral fluorocarbon catheters annually are used routinely in hospital care. Longer central venous catheters also are utilized and are produced from softer materials such as highly plasticized poly(vinyl chloride). Many sophisticated devices, for applications such as cardiac output, angioplasty and biosensors, have been and are being developed to expand further the need for improved materials.

Polyethylene, polypropylene, poly(vinyl chloride) and nylon were early materials which have proved to be either thrombogenic or rather stiff. Fluorocarbons subsequently were introduced as more hemocompatible polymers. TEFLON® FEP now is used widely for peripheral catheters but it is relatively inelastic and kinks easily (ref. 1). Poly(vinyl chloride) can be formulated as a soft

material but it requires the addition of as much as 50 percent leachable plasticizers and additives. At the other extreme, silicone rubber is too soft, weak mechanically, and is currently restricted to heavy-walled, long-term central venous catheter lines.

An ideal catheter material would have the following characteristics, most of which can be ideally fulfilled by polyurethanes.

- superior hemocompatibility
- controlled softening in the body
- low extractables
- good kink resistance
- broad range of physical-mechanical properties
- good processibility
- smooth surfaces
- high acceptance of radiopaque filler
- long shelf life
- stability to long term degradation in the service environment

VIALON® MATERIALS

A number of polyurethane materials such as BIOMER®, PELLETHANE®, TECOFLEX®, and AVCOTHANE® are or have been available to the biomedical engineer. Most of these contain catalysts, stabilizers, processing aids or other additives. Some are available only in solution for casting applications. It is desirable to use minimal amounts of additives to obtain the maximum purity, low extractables, and highest achievable hemocompatibility for vascular catheters. In addition, the polymers must be extrudable and moldable to smooth tubings and components.

A new family of polyurethanes, consequently, was developed using polymerization, compounding, and fabrication processes which do not require added catalysts or additives. Materials made from this process have been trademarked VIALON®, the first series of which is based on conventional materials; namely, polytetramethylene ether glycol (PTMEG), 4,4'-diphenylmethane diisocyanate (MDI) and 1,4-butanediol (BDO). In order to provide the broad range of physical mechanical properties required for catheter applications, nominal hardnesses of 45, 55, 65, and 75 Shore D were formulated by variation of the hard segment content. Evaluation of these polymers as catheter materials is presented in the following sections.

The VIALON® 510X polymers were selected to demonstrate performance of thermoplastic polyurethanes as catheter materials. Physical-mechanical

properties, response to model physiological conditions, biocompatibility, blood compatibility and clinical performance were evaluated.

Tensile Properties

One of the outstanding properties of segmented polyurethanes is their high strength over a wide range of stiffness. This feature allows more freedom in optimizing catheter tubing dimensions such as wall thickness and inside diameter to obtain the best combination of fluid flow rates and strength.

Specimens were prepared from extruded ribbons to ensure high quality and freedom from defects. They were conditioned in the laboratory at 23°C and 50% relative humidity for seven days. An Instron Universal Testing Machine, Model 1122, with a 50 lb. load cell was utilized at a strain rate of 300 mm/min. Elongation was measured manually.

Table 1 summarizes tensile and tear properties and demonstrates excellent mechanical strength of VIALON® materials. Comparison with TEFLON® FEP and poly(vinyl chloride) in Table 2 shows the superiority of polyurethanes.

TABLE 1

Tensile Properties of VIALON® TPU

| Property | | 510X-45 | 510X-55 | 510X-65 | 510X-75 |
|---|---|---|---|---|---|
| Shore D Hardness | | 46 | 56 | 66 | 74 |
| Tensile Moduli (psi): | 5% | 150 | 210 | 650 | 2700 |
| | 25% | 570 | 810 | 1500 | 3100 |
| | 100% | 900 | 1300 | 2400 | 4000 |
| | 200% | 1200 | 2200 | 4300 | 6600 |
| Tensile Strength (psi) | | 7600 | 9600 | 10700 | 10100 |
| Ultimate Elongation (%) | | 640 | 470 | 400 | 330 |
| % Set (0/1 Minute) | | 46/41 | 16/16 | 36/32 | 170/150 |
| Die "C" Tear (pli) | | 490 | 500 | 680 | 880 |
| Slit Tear (pli) | | 270 | 310 | 420 | 270 |

TABLE 2

Comparison of Tensile Properties of common catheter materials

| | 100% Tensile Modulus (psi) | Tensile Strength (psi) | Ultimate Elongation (%) |
|---|---|---|---|
| VIALON® 510X-45 | 900 | 7500 | 640 |
| -55 | 1300 | 9600 | 470 |
| -65 | 2400 | 10700 | 400 |
| -75 | 4000 | 10100 | 330 |
| PVC | 3400 | 4800 | 200 |
| FEP | 2500 | 4000 | 250 |

Thermal Transitions

Segmented polyurethanes typically are phase separated, multiphase polymers having distinct, measurable thermal transitions for each phase. These $(AB)_n$ block copolymers normally separate into hard (A) and soft (B) microdomains with dimensions in the 100-250 angstrom range (ref. 2). The chemical composition and extent of microphase separation significantly affects the thermal properties (refs. 3, 4). These properties in turn have a marked effect on the performance of the material in catheters. This is especially true when transitions are in the room temperature to body temperature range.

The phase separated morphology in the VIALON® series was characterized by Differential Scanning Calorimetry (DSC) and dynamic-mechanical testing. A DuPont Thermal Analyzer, Model 990, operated at 20°C/min. and Rheometrics, RDS-7700, operated at a shear mode of 6.28 rad/sec., respectively, were utilized with extruded ribbon and injection molded specimens.

Table 3 summarizes the thermal transitions ascribed to the soft segment and hard segment domains and verifies the phase separated morphology. The dynamic-mechanical analysis results also are illustrated in Figure 1 and most likely would correlate better than DSC with observed softening of polyurethane tubings in the body temperature range. The Tan Delta $T_g$ given in Table 3 may more realistically reflect the combination of the DSC soft segment $T_g$ and hard segment $T_i$ or mixed phases at the domain's interface. These parameters affect the tubing stiffness at room temperature and in the body, a subject discussed in a later section.

TABLE 3

Thermal Transitions by DSC and Dynamic-Mechanical Analysis

| | VIALON® 510X, °C | | | |
|---|---|---|---|---|
| Transition | 45 | 55 | 65 | 75 |
| Soft Segment | | | | |
| DSC $T_g$ | -68 | -58 | -27 | 2 |
| Tan Delta $T_g$ | -45 | -22 | -12 | 40 |
| Hard Segment | | | | |
| DSC $T_i$ * | 76 | 73 | 67 | 52 |
| $T_g$ | 103 | 113 | 131 | 137 |
| $T_{II}$ ** | 164 | 177 | 90 | 192 |

* $T_i$ Dissociation of short range order.
** $T_{II}$ Dissociation of long range order.

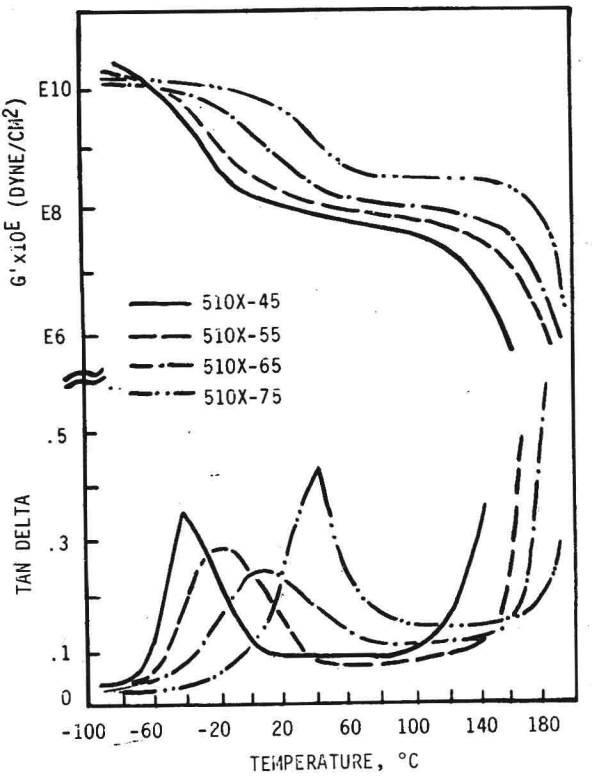


Fig. 1. Dynamic-Mechanical Curves for VIALON® Materials.

Long-Term Stability

The stability of polyurethanes is a critical parameter in long-term surgical implants such as pacemaker insulators (ref. 5), heart valves, and vascular grafts, and has been the subject of considerable study in the past few years (ref. 6). Polyether based polyurethanes are reasonably stable toward hydrolysis but are susceptible to autoxidation under certain circumstances (ref. 7). Polyurethanes also may be degraded in the body by enzymes, phagocytes and substances such as lipids (ref. 8). This sensitivity of polyurethanes to long-term degradation, unfortunately, has delayed their acceptance in implants requiring a minimum performance life of 10-15 years.

In vascular catheter applications, however, the indwelling times are much shorter and range from a few days to a few weeks or months for peripheral and central lines, respectively. Hickman and Broviac catheters are implanted in the central venous system for periods of 6-18 months.

VIALON® 510X-65 and 75 tensile specimens were immersed in a closed system of normal saline at 70° and 90°C. Samples were removed periodically and conditioned for 48 hours at 23°C and 50% R.H. before testing. The time required to reduce the tensile strength to one-half its original value was defined as the half life ($t_{½}$ in months). The data were fitted to the following Clausius-Clapeyron-type equation:

$$\log t_{½} = (3000/T) - 6.9$$

At 37°C, the calculated half life is about ten years. This value is consistent with the literature (ref. 9) and more than meets the performance requirements for catheters.

Softening Characteristics

The importance of using a flexible catheter to avoid damage to the blood vessel walls is well documented. Stiff catheters can cause thrombus generation and mechanically induced phlebitis (refs. 1, 10). Catheters which are placed over-the-needle, nevertheless, must have some stiffness for easy insertion. Long-line catheters also must have an optimum degree of flexibility for insertion and placement in tortuous vessels and yet have an appropriate degree of stiffness for kink resistance. Material design and selection, therefore, is a question of optimization for each application. Polyurethanes are ideally suited for this purpose.

In the 23-37°C temperature range, the VIALON® materials are already being softened by temperature as indicated by the declining slope of the rubbery plateau as may be seen from the storage modulus G'/temperature plot (Fig. 1). It is also well known that polyether polyurethanes absorb water and become reversibly plasticized. These effects have been described in an earlier paper (ref. 11).

To simulate the effect of temperature and water absorption on catheter performance, the softening of extruded ribbons (0.010 inch thickness) and rods (0.051 inch diameter) was determined in 37°C normal saline. Percentage decreases in tensile modulus and in the force required to bend the rods were calculated relative to 23°C and 50% R.H. Two hours immersion time achieved equilibrium. Table 4 shows the dramatic effect of softening produced by exposure to elevated temperature and water. The harder materials soften to a greater extent because the soft segment $T_g$ is in the body temperature region (see Table 3 and Fig. 1). It is apparent that structure and morphology have a significant effect on this plasticizing effect.

TABLE 4

Softening of VIALON® TPU after exposure to 37°C normal saline

| Property | Percent Softening | | | |
|---|---|---|---|---|
| | 510X-45 | 510X-55 | 510X-65 | 510X-75 |
| 5% Tensile Modulus | 44 | 38 | 68 | 77 |
| Bending Force | 30 | 45 | 71 | 88 |

Tubing Properties

Extrusion conditions were defined using a Brabender Plasti-Corder® extruder having a 3/4 inch screw (24/1 L/D ratio) and standard tubing die. Table 5 summarizes typical conditions for extrusion of 16 gauge tubing. The temperature profiles, however, are representative of those for general extrusion.

TABLE 5

Typical extrusion profiles of VIALON® TPU

| Extrusion Parameter | 510X-45 | 510X-55 | 510X-65 | 510X-75 |
|---|---|---|---|---|
| Solid Transport Zone Temp. (°C) | 140 | 140 | 140 | 140 |
| Melting Zone Temp. (°C) | 195 | 215 | 215 | 217 |
| Metering Zone Temp. (°C) | 200 | 210 | 215 | 221 |
| Die Temp. (°C) | 195 | 210 | 210 | 218 |
| Barrel Pressure (psi) | 3800 | 3800 | 3800 | 3300 |
| Torque (meter-gram, $10^{-2}$) | 35 | 38 | 37 | 35 |
| Screw RPM | 25 | 25 | 25 | 25 |

Tubing properties are illustrated in Table 6. The bending force and distance to kink were measured on the Instron, in a compression mode, using 2.0 inch long pieces of 16 gauge tubings. The bend force was recorded as the force required to initiate a bend in the tubing and is a measure of stiffness. The distance to kink is the length of travel required to collapse the tubing; consequently larger values indicate more kink resistance. Polyurethane tubings, in comparison with TEFLON® FEP, have excellent tensile strength and kink resistance.

TABLE 6

Properties of 16 gauge tubings

| Property | VIALON® | | | | TEFLON® |
|---|---|---|---|---|---|
| | 510X-45 | 510X-55 | 510X-65 | 510X-75 | FEP |
| Tensile Moduli (psi): 5% | 160 | 250 | 610 | 2300 | 1800 |
| 100% | 850 | 1300 | 2000 | 3300 | 2600 |
| Tensile Strength (psi) | 8400 | 10400 | 10500 | 11200 | 3700 |
| Ultimate Elongation (%) | 600 | 500 | 430 | 360 | 200 |
| Bend Force (g) | 13 | 25 | 45 | 256 | 310 |
| Distance-to-Kink (in) | 0.86 | 0.81 | 0.86 | 0.44 | 0.45 |
| Wall Thickness (mil) | 10.7 | 10.5 | 9.8 | 8.6 | 10.9 |

Radiopacity

Most catheters incorporate radiopaque fillers such as barium sulfate, bismuth trioxide, and bismuth subcarbonate in order to be detected by X-rays and fluoroscopy. In order to achieve smooth surfaces and high radiopacity for demanding applications, it is important to obtain a fine, uniform dispersion of the radiopaque agent. The low melt viscosity and good wetting characteristics of polyurethanes make them ideal materials for achieving these properties. Table 7 shows excellent retention of physical properties at levels up to 60 percent $BaSO_4$. At this filler level, materials such as PVC and TEFLON® FEP would have very little strength.

TABLE 7

Influence of $BaSO_4$ loading on VIALON® 510X-55 properties

| $BaSO_4$ Content % | 0 | 22 | 35 | 60 |
|---|---|---|---|---|
| Tensile Moduli (psi): 5% | 560 | 610 | 610 | 980 |
| 100% | 2200 | 2100 | 1800 | 1500 |
| Tensile Strength (psi) | 8800 | 7800 | 6000 | 2700 |
| Elongation (%) | 390 | 400 | 430 | 360 |

Surface Characteristics

The block copolymer nature of segmented polyurethanes allows microphase separation of hard and soft segments. This characteristic raises the issue of how the bulk and surface morphology compare with each other. This is especially important since blood/material interactions are highly dependent upon surface character. These effects have been studied and reviewed extensively (refs. 12, 13).

In order to study the bulk/surface composition of VIALON® materials we have determined the contact angles and critical surface tension on extruded

ribbons at ambient temperature and 50% R.H. A sessile drop technique, utilizing a Rame-Hart NRL Goniometer, Model 100, was used to obtain the contact angles at the solid-liquid-air interface. Zisman plots were used to obtain critical surface tension. Results are given in Table 8.

TABLE 8

Contact angles and critical surface tension of VIALON® 510X materials

| | Surface Tension (dyne/cm) | Contact Angles (°) | | | |
|---|---|---|---|---|---|
| | | 510X-45 | 510X-55 | 510X-65 | 510X-75 |
| Water | 72.8 | 80.8 | 76.3 | 80.0 | 80.2 |
| Formamide | 58.2 | 67.3 | 65.0 | 63.4 | 71.5 |
| 2,2'-Thiodiethanol | 54.0 | 58.2 | 57.8 | 56.3 | 54.5 |
| 1-Bromonaphthalene | 44.6 | 28.7 | 24.6 | 16.7 | 18.9 |
| 1-Methylnaphthalene | 38.7 | 18.4 | 16.8 | 11.5 | 13.7 |
| Critical Surface Tension (dyne/cm) | | 36.7 | 36.7 | 38.4 | 38.3 |

The critical surface tension for the bulk polymer was estimated in the following manner for comparison with the experimental values (see Table 8). Pure hard segment based on MDI and BDO was polymerized in bulk and extruded into ribbon. The critical surface tension using the outlined procedure was 41.8 dyne/cm. The critical surface tension for pure PTMEG is given by Van Krevelen (ref. 14) as 31.9 dynes/cm. Utilizing these values the critical surface tension was calculated based on the relative proportions of hard and soft segment. Table 9 shows that calculated bulk values are very close to those experimentally determined.

TABLE 9

Comparison of measured and calculated critical surface tension

| | Critical Surface Tension (dyne/cm) | |
|---|---|---|
| VIALON® | Measured | Calculated |
| 510X-45 | 36.7 | 36.4 |
| 510X-55 | 36.7 | 37.0 |
| 510X-65 | 38.4 | 37.8 |
| 510X-75 | 38.3 | 38.7 |

Biocompatibility Screening

The VIALON® materials met all the required standard tests, such as USP Class VI, USP Physicochemical, tissue culture, and hemolysis, to establish the baseline biocompatibility. In addition, the polymers were evaluated in final tubing form for hemocompatibility according to the following test procedures.