PRODUCTION OF BIOMEDICAL POLYMERS, II,
PROCESSING TECHNOLOGY/PRODUCT PROPERTY CORRELATIONS
OF HEMOCOMPATIBLE AVECOITHANE® ELASTOMERS

Emery Nyilas
Avco Everett Research Laboratory, Inc., Everett, MA 02149

Robert S. Ward, Jr.
Avco Medical Products, Everett, MA 02149

Presented at International Conference on
Polymer Processing
8/77 @ M.I.T.
PRODUCTION OF BIOMEDICAL POLYMERS. II.
PROCESSING TECHNOLOGY/PRODUCT PROPERTY CORRELATIONS
OF HEMOCOMPATIBLE AVCOTHANE ELASTOMERS

Emery Nyilas
Avco Everett Research Laboratory, Inc., Everett, MA 02149
Robert S. Ward, Jr.
Avco Medical Products, Everett, MA 02149

ABSTRACT

A member of a series of proprietary hemocompatible materials introduced earlier, the Avcothane 51 elastomer has been used to provide both flexible and stationary blood-contact surfaces in various types of circulatory assist and other prosthetic devices. This elastomer has been the standard material of construction of intra-aortic balloon pumps made by Avco, of which about 25,000 were implanted to date in cardiac patients without inducing clinically intolerable hematologic effects. As an inherently nonthrombogenic material, the hemocompatibility of Avcothane 51 elastomer does not depend on added anticoagulants but on a specific type of surface molecular architecture that gives rise to a randomized dispersion force field designed to minimize interaction energies with native plasma proteins known to form a priming layer on surfaces exposed to blood.

For routine clinical applications in implantable or extracorporeal devices, an Avcothane 51 processing technology has been devised that simultaneously assures required bulk properties and the molecular architecture of blood-contact surfaces yielding optimum hemocompatibility, by employing nonconventional methods. In this paper, a description is presented of the application of molecular engineering principles, applied in the development of Avcothane 51 elastomer, to a production-scale processing of this material into implantable devices under controlled conditions.

Production of prosthetic devices made of, or coated with, Avcothane 51 elastomer is most feasibly accomplished using prepolymer solutions under clean-room conditions, which allows for the formation of immediately hemocompatible surfaces. In a 2:1 mixture of absolute tetrahydrofuran and dioxane, standardized prepolymer solutions contain 11-15% solids composed of relatively high molecular weight poly(ether urethane) (PEU, 90%) and a poly(dimethylsiloxane) (PDMS, 10%) having initially a relatively medium molecular weight and, at least, three acetoxy end-groups per chain. Both solvents are dehydrated and purified until nonvolatile contaminants are about 1-2 ppm. Monitored by GPC, the polymeric components are purified to remove low molecular weight substances potentially leachable under physiologic
conditions and interfering with desired bulk and surface properties. During prepolymer synthesis performed under anhydrous conditions, a partial coupling of PDMS to the PEU yields a block-copolymer stabilizing the mixture of otherwise immiscible polymers. The extent of this reaction, also monitored by GPC, is maintained at levels optimized to prevent phase separation since excessive copolymerization leads to formation of an insoluble gel adversely affecting the surface micromorphology of cured elastomers.

In the conversion of prepolymer solution films to solid Avcothane 51 elastomer, the kinetics of solvent removal by evaporation and/or diffusion into an underlaying substrate fundamentally affects the molecular structure of resulting surface layers. Depending upon conditions, at variable rates a gel-like "skin" is formed, from which other still soluble polymeric components are gradually excluded resulting in an anisotropic distribution of PDMS verified by IR attenuated total reflectance spectra, electron-microprobe analysis and ESCA. Since optimum hemocompatibility is associated with a specific range of PEU/PDMS ratios in Avcothane 51 surface layers, and the PDMS distribution is a function of solvent removal rates, a first-order approximation is presented to correlate the rates of "skin" formation determining surface molecular composition with relevant processing parameters.
INTRODUCTION: INHERENTLY NONTHROMBOGENIC POLYMERIC MATERIALS

Extracorporeal and implantable prosthetic devices can provide therapeutic benefits unattainable by other conventional modes of drug therapy. In the course of the past decade, the development of several types of cardiac assist devices has been initiated for the treatment of various forms of reversible cardiac conditions. However, as compared to the conditions involved in the use of other types of prostheses, these new methods of providing cardiac assistance are significantly more invasive inasmuch as they routinely employ implantable blood pumps constructed, by necessity, from man-made materials.

Of the variety of circulatory assist devices proposed and/or carried to the stage of testing in experimental animals, there are so far only a very few that have reached the level of routine clinical application in humans. This limitation is attributable to essentially two causative factors. First, when removed from its natural environment constituted by the intact endothelium, native blood immediately recognizes foreign surfaces resulting in thromboembolic phenomena which can easily reach clinically intolerable levels and defeat the purpose of the implanted device. Secondly, there are several current polymeric materials available whose bulk properties would qualify them for use in circulatory assist devices but, as a rule rather than the exception, their compatibility with blood is poor, at best. This condition is not improved by the conventional processing techniques generally requiring the incorporation of considerable amounts of additives which are usually leachable under physiologic conditions. These additives have been designed to protect the material processed but not to improve hemocompatibility.

A substantial number of approaches have been suggested to improve the hemocompatibility of polymeric materials having the desired physical properties but insufficiently compatible with blood. For a variety of reasons, most of these methods which are based on the deposition or coupling of various types of coatings, such as ionically or covalently bonded heparin (a known anticoagulant), grafted hydrogel layers, etc., have not as yet proceeded beyond the developmental stage.

In contrast to the use of hemocompatibility-improving additives and coatings, another entirely different approach is the development of inherently nonthrombogenic materials whose hemocompatibility is attained by means of their specific surface molecular structure alone. To function as flexible blood contact surfaces in cardiac assist devices, inherently nonthrombogenic elastomers are subject to a spectrum of different requirements. In combination with each other, they represent a most stringent set of complex specifications. First, the macromolecules employed in these elastomers should be capable of imparting the desired bulk physical properties such as tensile strength and elasticity. The second condition of equal importance involves
that, while meeting the prerequisites of bulk properties, the same macromolecules should also give rise to specific surface molecular structures which render the elastomer hemocompatible enough such that, in actual short- or long-term implantsations, it does not induce any intolerable hematologic or toxic effects under clinical conditions. Thirdly, the elastomer has to be fatigue-resistant not only in terms of its bulk structure, but also in terms of its effective surface molecular architecture which is defined by the surface number density and spatial arrangement of various moieties constituting the top layer of the material. This architecture must be dynamically resistant to possible enzymatic attacks in the physiologic environment, as well as to stress-induced rearrangements of polymeric chains to maintain hemocompatibility at constant levels.

A series of proprietary materials, (1) introduced earlier under the name of Avcothane R, were found to display significant degrees of inherent non-thrombogenicity both in vitro and in vivo. (2) By the combination of appropriate polyurethanes with poly(dimethylsiloxane) in variable ratios, Avcothane elastomers have been obtained whose properties surpass those of their components as a result of synergistic effects. (3) Both polyether and polyester urethanes can be used in these elastomers. However, for circulatory assist devices requiring blood pumps with flexing membranes and designed for long-term implantsations, the former type is preferred because polyester urethanes display inadequate hydrolytic stability in the physiologic environment. (4)

The working hypothesis defining the specifics of the surface molecular structure of Avcothane elastomers has been based on the physicochemical aspects of the interaction arising between native blood and a foreign surface. Using diffusion kinetics, it has been shown (2) that the arrival of plasma proteins, at any freshly exposed contact surface, precedes that of the cellular blood components such as platelets. This theoretical result is consistent with experimental evidence. (5-8) Depending both upon their own nature and the molecular structure of the surface they encounter, native plasma proteins undergo adsorption with or without ensuing adsorption-induced conformational changes. The "intensity" of native protein/surface interaction or the binding energy of proteins released upon their adsorption, which can be determined using direct microcalorimetric measurements, (9-11) are a function of the effective molecular architecture of the contact surface, (12) and influence the degree of conformational changes induced as well as the mean residence time of sorbed proteins. Thus, in a sense, the sorbed protein layer acts as a proportional transformer mitigating the effects of the original surface on the rest of the blood. A contact surface can be inherently non-thrombogenic if it minimizes its interaction energy with native plasma proteins. This avoids the causes of platelet adhesion resulting in the release of platelet factors which activate the cellular pathway of the intrinsic coagulation mechanism, as well as the activation of the enzymatic pathway of the same mechanism. The way this principle is embodied in Avcothane surfaces is the construction of a surface molecular architecture composed of a variety of groups which establish a force field mainly of the dispersion type with field intensities fluctuating as a function of locus, and interact with plasma proteins via van der Waals-London forces only. Placed into such a force field, plasma proteins can be expected to be in an energetically unstable state that would hinder their irreversible attachment.
In the development of inherently nonthrombogenic Avcothane elastomers, the combination of poly(ether urethane) with organosiloxanes has been assumed to simultaneously meet the requirements specified earlier for bulk physical properties as well as of a surface structure having a randomized dispersion force field. A member of this series is the Avcothane 51 elastomer. Following establishment of its in vivo performance in a number of different prosthetic devices chronically implanted in experimental animals, (13) this elastomer has been the standard material of construction of all intra-aortic balloon pumps (IABP) made by Avco. The in vivo hematologic effects of Avcothane 51 IABP's in humans have been assessed in two series of statistical analyses. (14, 15) To date, a total of approximately 25,000 of these temporary circulatory assist devices were used in cardiac patients in more than 500 hospitals located in this country and numerous others. Despite the fact that a large number of human implantations were performed under a variety of clinical conditions, no case has been reported so far in which either a fatigue failure occurred or, the effects of Avcothane 51 blood contact surfaces combined with those of pumping induced clinically intolerable thromboembolic phenomena. In other experimental applications, total artificial hearts made essentially from this elastomer sustained calves for 75 (16, 17) and 122 (18) days. Another type of blood pump made of Avcothane 51 elastomer, the Elliptical Left Ventricular Assist Device which is under development at the 2nd Surgical Clinic of the University of Vienna, Austria, (19) sustained a calf for 87 days without any appreciable hematologic trauma, and was recovered with its blood contact surfaces virtually free of any adherent thrombi or fibrinaceous deposits.

The routine clinical application in implantable circulatory assist devices, with a reproducibly high degree of safety, requires an Avcothane 51 elastomer processing technology that assures not only the bulk physical properties of each of the products, but also the molecular architecture of their blood contact surfaces optimized to yield maximum hemocompatibility. The achievement of this two-fold objective is accomplished by the application of nonconventional methods. This paper presents a description of the transfer of molecular engineering principles and techniques which have been applied in the attainment of inherently hemocompatible surface structures, to a production-scale processing of Avcothane 51 elastomer into implantable prosthetic devices under controlled conditions.

**FUNDAMENTAL PROPERTIES OF AVCO THEANE 51 ELASTOMER DETERMINED BY PROCESSING TECHNOLOGY**

The completely cured Avcothane 51 elastomer is composed of a poly(propylene glycol)-based urethane (90%) essentially void of urea groups, and a poly(dimethylsiloxane) (10%). Although the elastomer displays some properties typical of thermoplastic materials, such as heat or ultrasonic sealability, it does contain a substantial gel-phase when fully cured. Since the inherent nonthrombogenic properties of the elastomer depend on the particulars of its surface composition, processing of the material into implantable devices by conventional thermoplastic technology that requires the use of additives generally detrimental to hemocompatibility, is conceivable
under certain conditions, but not feasible at all. Among others, the application of conventional methods is negated by the uncertainties that would be involved in the quantitative removal of such additives prior to implantation. As a result of these factors, one of the most feasible methods for the preparation of Avcothane 51 films, sheets or other items involves the use of a prepolymer solution in which all components had been purified as determined by the requirements of implantability as well as the chemical nature of the material. By means of dip-molding or solvent-casting under clean-room conditions followed by curing at ambient temperatures, the prepolymer solution yields finished products that are immediately implantable.

In a 2:1 mixture of absolute tetrahydrofuran (THF) and dioxane (DXE), the standardized Avcothane 51 prepolymer solution contains typically 11-15% (by wt) solids, depending upon the intended applications. In addition to the poly(ether urethane) of relatively high molecular weight, the solids include the poly(dimethylsiloxane) in an initial state characterized by a relatively medium molecular weight and the presence of a minimum of three reactive acetoxy terminal groups per chain. The solids also include a certain amount of urethane/siloxane block copolymer which, as discussed later, is formed in the course of prepolymer solution synthesis under anhydrous conditions, and stabilizes the homogeneous mixture of two otherwise incompatible polymers for long periods of time (viz., 6 months minimum).

The bulk structure of solid Avcothane 51 elastomers obtained from the standardized prepolymer solution can be best described as a lightly cross-linked matrix, with small nodular domains of poly(dimethylsiloxane) homopolymer dispersed in, and bound by chain entanglement as well as the polyurethane/silicone block-copolymer to, the urethane continuous phase. In addition to high magnification transmission electron micrographs published elsewhere, (20) this structure is supported, as shown in Fig. 1, by Rheovibron viscoelastic measurement data recorded at 110 Hz. The variation of the complex modulus, \( E'' \), with temperature displays a relatively broad transition peaking at \( T_g = -50^\circ + 2^\circ C \), considered to be the glass transition of the dominant component. Since this transition is quite broad, the peak of tan \( \delta \) occurs, at a higher temperature, viz., at approx. -25°C. The Young's modulus, \( E' \), continues to change with temperature on both sides of the transition, but the absence of separate plateaus in its curve indicate a significant degree of phase interpenetration. In contrast to the known behavior of homogeneous polymers under identical conditions of testing, the trends in \( E' \), \( E'' \) and tan \( \delta \) noted above are characteristic of polyblends as well as block copolymers. Other bulk properties of Avcothane 51 elastomer are in Table I.

As indicated by their IR attenuated total reflectance (IRATR) spectra, the effective surface molecular structure of Avcothane 51 elastomers is generally a function of parameters employed in processing technology. Depending upon the conditions of curing the standardized prepolymer solution, elastomer surfaces can give rise to two entirely different types of spectral characteristics in the 11.0 - 13.5 \( \mu m \) range of their IRATR spectra, illustrated as extremes in Figs. 2a and 2b. Depending upon the conditions involved in particular applications, the IRATR spectral characteristics of resulting Avcothane 51 surfaces can vary between those shown in these diagrams.
The spectrum displayed in Fig. 2a is characteristic of the surface molecular structure usually obtained on the air-facing (AF) side of an Avcothane 51 elastomer when the prepolymer solution is cured, under ambient conditions, on a material impenetrable to the standardized THF/DXE solvent mixture. Although the prepolymer solution was homogeneous at the time of its deposition, the substrate-facing (SF) side of the same film obtained under identical conditions gives the spectrum shown in Fig. 2b. The doublet at 12.26 and 13.00 μm, seen in Fig. 2a, corresponds to the "breathing motion" of multisubstituted aromatic rings present in the urethane component of the material. If the reactive poly(dimethylsiloxane) component used in the prepolymer is separately converted into a homopolymer, the 11-13.5 μm range of the IRATR spectrum of this material displays, as shown in Fig. 2c, a single strong absorption band that is peaking at 12.82 μm and is attributable to the silicon/methyl "wagging motion." Thus, the spectrum in Fig. 2b is a complex envelope obtained by the superposition of this silicone peak over the doublet due to the polyurethane, causing the latter to appear as only shoulders on the single peak displayed by the SF-side. These spectral variations indicate that, within the surface layer penetrated by the evanescent IR beam whose depth is on the order of a few μm, the concentration of the silicone component in the elastomer sample specified is greater on the SF-side than that of the AF-side. Comparison of the two spectra also implies that the distribution of silicone is anisotropic throughout the cross-section of the elastomer, and the degree of anisotropy is determined by factors of processing technology.

The molecular structural characteristics of any Avcothane 51 surface can be quantitatively described using a parameter defined as the IRATR index. For any given surface yielding an IRATR spectrum under standardized conditions, the value of this parameter can be computed by dividing the optical absorptivity at 13.00 μm by that obtained at 12.62 μm. A typical AF-side spectrum has an IRATR index ≥ 1 since its %T (13.00 μm) < %T (12.62 μm) while, for typical SF-sides obtained on solvent-impenetrable substrates, this index ≤ 1.

The anisotropic distribution of silicone in cured Avcothane 51 elastomers has been also verified by evidence obtained with other instrumental methods of surface analysis. By its definition given above, the IRATR index is inversely proportional to the concentration of siloxane chains. Electron microprobe analysis was employed to determine to the silicon atom concentration, proportional to that of polysiloxane chains, in the top layers of elastomers which were prepared from the standardized prepolymer solution using different processing techniques to attain different IRATR indices. As illustrated in Fig. 3, the silicon atom counts which were measured with the electronprobe having a penetration depth on the order of 2.5 μm, give a satisfactory direct linear relationship with the inverse of the IRATR indices. These data independently confirm the difference between surface layer molecular structures resulting from the anisotropic distribution of components. In addition, the surface characteristics of Avcothane 51 films have been assessed by ESCA (electron spectroscopy for chemical analysis) providing information on the structure of surface layers whose depth is only 40-60Å. Figure 4a shows the carbon 1s electron spectrum obtained for a typical AF-side, after the
instrumental output was resolved by envelope analysis using a computerized curve deconvolutes. In Fig. 4b, the SF-side carbon 1s electron spectrum of the same elastomer sample is displayed. In both spectra, the 286.8 eV peak corresponds to etheric C-O bonds which, in the cured elastomer, can be present only in macroglycol segments of the polyurethane component. The areas under the C-O peaks represent 12% and 4% of the total integrated carbon 1s peak areas obtained for each of the AF- and SF-sides, respectively, indicating that the SF-side has a relatively smaller urethane component concentration due to the relatively greater concentration of polysiloxane chains.

The significance of the different effective molecular structures of Avcothane 51 surfaces is that their degree of hemocompatibility appears to be different, at least under in vitro or ex vivo conditions. For example, in terms of modified Lee-White clotting times of fresh human venous blood, which were obtained using systematically alternated normal donors and statistical evaluation methods, these data correlate with the IRATR index showing maxima in the range of 1.3 - 1.6 considered to be optimal. Other correlations between this index and measures of hemocompatibility have been given elsewhere by this Laboratory (20) as well as others. (21) Using the standardized Avcothane 51 prepolymer solution, the anisotropic polysiloxane distribution with the corresponding IRATR index, as well as the degree of hemocompatibility associated with that index become a direct function of processing techniques applied to the prepolymer.

PREPOLYMER SOLUTION PREPARATION

With respect to the requirement that prosthetic devices made of the Avcothane 51 elastomer under clean-room conditions should be implantable without any further materials processing operations, the preparation of prepolymer solutions commences with extensive purification and characterization of each starting material as well as solvent. All process equipment employed in these operations is made of materials of construction which have been selected not only to eliminate contamination of processed substances with wear particles or corrosion products, but also to withstand the release of any leachables.

The polymeric components required for Avcothane 51 prepolymer solution synthesis are purified and vacuum dried to remove any low molecular weight impurities and additives. These may not only be leachable under in vivo conditions, but can also affect bulk properties as well as alter the desired surface composition of cured elastomers by increasing the surface number density of polar terminal groups. For example, Fig. 5 illustrates the stainless steel reprecipitation kettle and tumbling vacuum dryer used in polyurethane purification. Gel permeation chromatography (GPC) is utilized to monitor both raw and purified polymeric materials. In addition to the detection of low molecular weight impurities, with the appropriate column set, polymer molecular weight distributions can be obtained from the same chromatogram. This data is useful in predicting solution viscosities and polymer functionalities.
With respect to the implantability requirements as well as the use of acetoxyl-terminated poly(dimethylsiloxane), both THF and DME utilized in the prepolymer solution must be free of nonvolatile contaminants and water. After fractional distillation and drying over molecular sieves, which are performed in an all-glass apparatus shown in Fig. 6, nonvolatile contaminants are typically in the range of 1-2 ppm of anhydrous solvent.

The synthesis of prepolymer solutions is conducted under anhydrous conditions in glass reaction vessels, as illustrated in Fig. 7. Under a dry nitrogen blanket, the viscous product is subsequently subjected to high pressure filtration using stainless steel filters with a nominal pore size of 2.0 μm. In the course of prepolymer solution synthesis under the specified conditions, varying amounts of a block copolymer can be formed by coupling of the polyfunctional poly(dimethylsiloxane) and the essentially difunctional, hydroxy-terminated urethane. GPC is also used to monitor the extent of the copolymerization reactions. As shown in Fig. 8, a strongly UV-absorbing, high molecular weight shoulder appears on the molecular weight distribution curve of the original polyurethane. This is taken as evidence of copolymerization since the poly(dimethylsiloxane) is nearly transparent to UV light at the detector sensitivities employed.

Under anhydrous conditions, the block-copolymer formed stabilizes the prepolymer solution that consists of an emulsion of the remaining unreacted silicone in the urethane, by acting as a "surfactant." On the other hand, if the copolymerization is allowed to proceed to high extents of reaction, this will result in the formation of a gel phase. In turn, insoluble gel present in the prepolymer solution will adversely effect the surface morphology of cured Avcothane 51 elastomer films, as illustrated in Fig. 9. Thus, based on GPC data, processing parameters are adjusted to assure the formation of a copolymer quantity optimized to prevent phase separation in the prepolymer solution.

PREPOLYMER SOLUTION CONVERSION: THE KINETICS AND MECHANISMS AFFECTING AVCOTHANE 51 SURFACE STRUCTURE FORMATION IN PROCESSING

Avcothane 51 prepolymer solution films having the standardized composition specified earlier are usually converted to the solid elastomer under ambient conditions. After evaporation of most of the solvents, penetration of atmospheric moisture into the prepolymer gel film initiates an autocatalytic curing reaction similar to that in a one-component silicone RTV system. However, the rate at which a prepolymer solution film undergoes decreases in its solvent content in the process of solidification, can fundamentally affect the effective surface molecular architecture of resulting elastomers, as previously demonstrated by IRATR spectroscopy, electron-probe analysis and ESCA. As a result of this, the conversion of prepolymer solution films into solid elastomers or, coatings applied to other materials represents an integral part of the processing technology applied in the preparation of hemocompatible Avcothane prosthetic devices.
The rate of removal of solvents from a liquid Avcothane 51 prepolymer solution film is a complex function of a large number of variables, some of which are interrelated. For the purposes of the treatment that follows, it is convenient to classify these variables into essentially two main categories: (1) factors affecting the rate of transport of solvent components to, and their rate appearance at, the bounding surfaces of the prepolymer solution film; and (2) factors influencing the irreversible removal of solvent components from the immediate vicinity of the bounding surfaces of prepolymer films. By the foregoing definitions, factors classified into the second category represent the controllable process variables affecting those grouped into the first category.

Described in qualitative terms, the first category of factors influencing the rate of solvent removal includes, among others, the effective temperature, the heat capacity and conductivity, and the composition of the prepolymer solution film. All of these are interrelated and time-dependent variables determining the effective vapor pressure of solvents at the immediate bounding surface of the prepolymer film; and the effective vapor pressure influences, to a great extent, the rate at which these solvents can be removed from the vicinity of bounding surfaces. In a closed system not subject to overall temperature fluctuations, the heat capacity and conductivity of the prepolymer solution film affects the extent to which the effective film temperature undergoes changes if, for example, the solvents are allowed to evaporate and their heat of vaporization is supplied by the heat capacity of that film. The time-dependent composition of the prepolymer solution film also affects the rate of appearance of solvents at the bounding surfaces since the solute content of the film acts as to reduce the vapor pressure of solvents. The relationship between the factors influencing the rate of appearance of solvents at the film bounding surfaces becomes a more complex function if the liquid prepolymer solution film does not remain homogeneous and solvent molecules experience hindrance by a barrier in their migration to the bounding surfaces.

The second category of factors includes the controllable process variables determining the rate at which these solvents are transported away from the prepolymer solution film bounding surfaces. In general, two different cases can be distinguished. At a prepolymer film/gas phase interface or at the AF-side of films, these factors entail the composition, pressure, and temperature of the gas phase, as well as the conditions of flow in that phase, if any, which can also involve the existence of a boundary layer. At a prepolymer film/solid phase interface, factors affecting the rate of solvent removal from prepolymer solution films are inconsequential if the solid is not penetrable to the solvents, i.e., the substrate is of the "nonsink" type. This is the case, for example, at the SF-side of single prepolymer solution films directly deposited on metal mandrels or glass casting trays. However, removal rate factors come to the fore when prepolymer solution films are deposited on solids penetrable to the solvents. On these "sink" type substrates, solvent depletion also occurs on the SF-side via diffusion into the underlaying solid phase. This is the case, for example, when the prepolymer solution is coated onto certain other polymeric materials or, onto a semi-cured Avcothane 51 layer, as is done in multiple dip-coatings to attain specified wall thicknesses.

For the purposes of establishing correlations between processing technology parameters and product surface properties, a quantitative relationship
between factors affecting the rate of solvent removal from liquid Avcothane 51 prepolymer solution films is developed in the Appendix. The treatment presented there is a simplified one because it is based on the assumption that the prepolymer solution film temperature, \( T \), which affects the effective vapor pressure of that film, remains constant throughout the entire period of solvent removal. This obviously represents only a first-order approximation. If only a part of the solvent removal proceeds via evaporation, the heat of vaporization is extracted from the heat capacity of the prepolymer film rendering \( T \) a time-dependent variable. On the other hand, if adjustments are made in the derivations to define \( T \) as a time-dependent function of all major factors affecting it, the resulting complex functions are tractable only by computer and exceed the scope of this paper.

Thus, according to the first-order approximation described in the Appendix, the time-dependent change due to vaporization alone, in the solvent content of a liquid Avcothane prepolymer solution film deposited on a solvent-impenetrable, "nonsink" type substrate, is given by

\[
\eta_S \ln \left( \frac{W_{L0}}{W_L} \right) + \frac{W_{L0} - W_L}{M_L} = \frac{\eta (P_{TD})_T}{M_L} t \tag{24}\]

where \( \eta_S \) is the mole number of polymeric solids (as defined in the Appendix); \( W_{L0} \) is the weight of removable solvents in the prepolymer film at the time of its deposition; and \( W_L \) represents the weight of solvents in the film after a \( t \) period of elapsed solvent removal time. In the form as is written, Eq. (24) is valid for Avcothane 51 prepolymer solutions having the standardized 2:1 THF/DXE solvent mixture and hence, \( M_L \) represents the mean nominal molecular weight of that mixture equal to \( 3 M_T M_D/(2 M_D + M_T) \) where \( M_T \) and \( M_D \) are, respectively, the molecular weights of THF and DXE. The term \( (P_{TD})_T \) signifies the vapor pressure, at a temperature, \( T \), of the THF/DXE mixture specified above. In Eq. (24), \( \eta \) is a proportionality factor that is a function of, among others, the flow characteristics of gas over the prepolymer solution film, and is determined experimentally as given below.

With respect to its terms, Eq. (24) implies that the prepolymer solution film remains homogeneous throughout the entire duration of the solvent removal process. Provided this requirement is met, the data which is obtained by the substitution of values of \( W_L \) into the left-hand side of Eq. (24), should give a straight line as a function of \( t \), with a slope equal to \( \eta (P_{TD})_T/M_L \). At a given \( T \) temperature (assumed to remain constant in this approximation), \( (P_{TD})_T \) is a known constant computable from Eq. (3) given in the Appendix, and \( M_L \) is also a known constant. From the slope specified above, the numerical value of the proportionality constant, \( \eta \), can be determined for the particular gas flow conditions employed over the prepolymer film to remove the vapors.

In contrast to the behavior predicted by this approximation, the actual experimental values of removable solvent content, \( W_L \), plotted vs \( t \) according

\*The number of this equation is (24) to be consistent with the numbering of equations given in the Appendix.
to Eq. (24), give curves which are generally straight only for relatively short, initial periods of elapsed solvent removal time. Nonetheless, the slopes of the initial straight portion of these curves allow for the determination of corresponding \( \eta \) values characteristic of the vapor removal conditions applied in the particular experiments.

**Surface Formation Kinetics on Solvent-Impenetrable Substrates**

For the case of solvent removal, by vaporization alone, from a prepolymer solution film deposited on a "nonsink" substrate, Fig. 10 illustrates the change in solvent content as a function of elapsed removal time. To render these data comparable to those obtained from prepolymer solution films on "sink" type substrates, the normalized solvent content of these films, \( \frac{W_L}{W_L^0} \), has been plotted. As indicated in Fig. 10, in a laminar flow of air at \( \sim 200 \) cm/min which has been established to give rise to AF-side surfaces having IRATR indices in the optimum range, the normalized solvent content of a prepolymer solution film on a "nonsink" substrate decreases, as predicted by Eq. (24), during the first 2 min of evaporation time. After this, the experimental data deviate from the theoretical curve indicating continuously decreasing rates of solvent removal. While, as noted earlier, the theoretical curve is based on the assumption that the film temperature, \( T \), remains constant, it can be shown that decreases on the order of 10 - 15°C in \( T \) do not account for continuing decelerations in solvent removal rates as large as those indicated by the experimental data.

The reduction of solvent removal rate by evaporation becomes explicable if, as opposed to that implied in Eq. (24), the prepolymer solution film does not remain homogeneous. Inhomogeneities arise if, at the gas phase interface, rapid gelation takes place due to removal of solvents from the immediate top layer of the film at rates which are greater than the flux of solvent from the bulk of the film that is generated by the solvent concentration gradient across the film. Thus, the "unbalanced" removal of solvent from layers in the near vicinity of the film bounding surface results in the formation of a "skin" rendering the film inhomogeneous. As indicated by the experimental data given in Fig. 10, under the conditions specified, "skin" formation on the AF-side of a prepolymer solution deposited on a "nonsink" substrate can be taken to require about 2 min, i.e., the period after which the experimental curve begins to deviate from the theoretical. Following this, the arrival of solvent molecules at the film bounding surfaces becomes a diffusion-controlled process that is a function of the properties of the "skin" layer.

While "skin" formation on the AF-side of Avcothane 51 prepolymer solution films can be easily demonstrated experimentally, the incidence of this event and its controlling effect on the rate of further solvent removal can be verified by the following simplified method. Since the initial solids, \( W_S \), and solvent, \( W_L^0 \), contents of the prepolymer film are known quantities,
the amount of solvent evaporated, \((W_L, 0 - W_L)\) during any \(t\) elapsed removal time can be converted into a proportionate nominal quantity of solid film formed at the AF-side. In this model, the approximation is made that solvent evaporation occurs always from the immediate top layer of the film and, in the domains under that layer, the total solvent content remains quasi unaffected. Using the area of the prepolymer solution film and the density of the solid film forming the top layer, which are known quantities, the thickness of the "skin" can be computed as a function of \(t\). For the prepolymer solution film on a "nonsink" substrate, whose change in its normalized solvent content has been given in Fig. 10, the computed growth of its "skin" thickness is given as a function of \(t\) in Fig. 11. Since deceleration in the rate of solvent vaporization occurred after about 2 min of elapsed removal time, it can be estimated from Fig. 11 that the "skin" thickness was on the order of 15 \(\mu\) at the time when it began to retard the evaporation rate.

If experimental conditions as well as the state of the "skin" remain unaltered, the rate of solvent removal by vaporization should linearly decrease with increasing "skin" thicknesses because of the increasing length of the diffusion path. In Fig. 12, the computed rates of evaporation for the same prepolymer solution film are shown as a function of its "skin" thickness which has been calculated as described above. Within the error involved in the determination of evaporation rates, the data given in Fig. 12 indicate this linear relationship. The line displayed in that diagram is the best fit obtained by the least-squares method.

The correlation between surface formation kinetics and the processing technology of implantable hemocompatible devices can be easily assessed from the physical significance of "skin" formation. In the case of Avcothane 51 prepolymer solution films, the "skin" formation induces concentration gradients not only for the solvents, but also for each of the polymeric solutes. These gradients, in turn, result in a gradual exclusion and migration of polymeric components which are still in solution, in the order of their solubility and size, from the semi-solid "skin" phase whose thickness is increasing with elapsed solvent removal time. Following "skin" formation at the gas phase interface and the gradual exclusion of polymeric solutes from that layer, the domain of prepolymer solution film that is adjacent to the "nonsink" substrate becomes depleted of its solvent content last. This effect coupled with the exclusion phenomena account for the anisotropic distribution of the silicone component within cured Avcothane 51 films demonstrated earlier.

The overall result of these concurrent phenomena is that the rate of solvent removal from the near vicinity of Avcothane 51 prepolymer solution film bounding surfaces, as well as the rate of "skin" formation, determine what type of polymeric species become fixed in the "skin" layer. The composition of that layer determines the effective surface molecular architecture of resulting solid elastomers, which affects, in turn, the apparent hemocompatibility of those surfaces.

In view of its impact on processing technology, the kinetics of "skin" formation on any side of a prepolymer solution film, which becomes a blood-contact surface, obviously requires accurate description so that process
parameters can be appropriately adjusted. The accurate description of surface kinetics is also necessary if the mechanisms controlling the formation of surfaces on prepolymer solution films deposited on solvent-penetrable, "sink" type substrates are to be approached, and relevant process parameters for those conditions are to be defined.

With the approximation $\tau$ remains constant, the correlation expressed in Eq. (24) has been derived essentially from first principles, as described in the Appendix. Also using first principles, it is possible to correct that equation to account for the changes in film homogeneity as well as the retarding effect of "skin" formation on solvent removal rates. One possible method is to amend Eq. (24) with terms describing the loss in solvent removal rates as a function of the kinetics of "skin" formation, which can be based on the relationship shown in Fig. 12. However, this approach introduces a number of interrelated variables resulting in a complex set of equations solvable only by computer. On the other hand, for the purposes of this treatment, it has been possible to determine an empirical equation that satisfactorily describes the variation of the solvent content as function of elapsed removal time for prepolymer solution films on impenetrable "nonsink" substrates. This equation which implicitly accounts for the retarding effects of "skin" formation on solvent removal is

$$W_L = W_{L_0} \exp (t \log k)$$  \hspace{1cm} (25)

where $k$ is a constant $< 1$, which can be experimentally determined for each set of particular conditions used.

Using Eq. (25) with $k = 0.971$, the variation of the solvent content of the same prepolymer solution film deposited on a "nonsink" substrate has been recomputed as a function of elapsed removal time. In Fig. 13, this is shown by the filled circles of the lower curve. The open circles in the same curve indicate the experimental data from which the value of the constant, $k$, has been determined for the experimental conditions specified. As seen from this diagram, the correlation between the two sets of data is satisfactory indicating that Eq. (25) reasonably accounts for the deceleration of solvent removal rates caused by the "skin effect" on the AF-side of Avcothane 51 prepolymer solution films.

Surface Formation Kinetics on Solvent-Penetrable Substrates

In certain applications, prosthetic devices are required having parts made of machined or molded plastic materials with hemocompatible surfaces. These requirements can be met if standard engineering plastics, whose physical properties are acceptable but whose hemocompatibility is usually poor, are overcoated with the Avcothane 51 elastomer. In these cases, however, prepolymer solution films are deposited on substrates which are penetrable by
the THF/DXE solvent mixture and act as "sinks" for those liquids. Thus, on the AF-side of "sink" type substrates, the attainment of Avcothane 51 blood contact surfaces having IRATR indices in the range considered to be optimal, is influenced by the rate of solvent removal by diffusion into the underlaying material.

Another relevant case of the effect of "sink" type substrates is represented when specified layer thicknesses of cured Avcothane 51 elastomer are to be attained by deposition of multiple coatings with the prepolymer solution. Although the initial substrate, in these cases, may be of the "nonsink" type, in the second and any subsequent coatings, the prepolymer film is deposited on the first layer which converts the substrate to the "sink" type.

In Fig. 10 presented earlier, the upper solid line shows the decrease of normalized solvent content, effected by vaporization alone, from a prepolymer solution film deposited on a "sink" type substrate. This curve has been computed using Eq. (24) with the appropriate proportionality constant, \( \eta \). The experimental conditions applied are identical to those used for the prepolymer solution film deposited on a "nonsink" substrate, yielding the lower solid curve in the same diagram. As seen from Fig. 10, the experimental rate of solvent removal by vaporization from the "sink" type substrate also begins to deviate from the theoretical values roughly after the same period of elapsed removal time, \( t \), as this deviation occurred for the film on the "nonsink" substrate. After this, however, the deceleration of solvent removal by vaporization from the "sink" type substrate becomes increasingly greater with increasing values of \( t \), indicating the combined retarding effects of "skin" formation as well as the diffusion of solvent into the "sink".

Using Eq. (25) as described earlier, which takes into account the "skin effect" on solvent removal rates by vaporization on the AF-side, the curve indicated by filled diamonds in Fig. 13 is generated. The difference between the curve of actual experimental data, shown by open diamonds in this diagram, and the curve determined by Eq. (25) represents the net vaporization rate retarding effect arising from solvent diffusion into the "sink" type substrate. While this difference is variable according to the nature of the particular "sink" and has to be evaluated experimentally, it can be utilized to determine process parameters to insure appropriate rates of "skin" formation on the AF-side.

The diffusion of solvent into an underlaying "sink", particularly if the diffusion rates can be accelerated, results in a rapid "skin" formation on the SF-side of prepolymer films. This phenomenon is deliberately exploited in the technology of dip-molding or casting of items which are formed easier on positive mandrels but whose blood-contact surface is to be their SF-side. As noted earlier, for maximum hemocompatibility, IRATR indices within the range considered to be optimal are preferred. These indices, however, are displayed by Avcothane 51 surfaces with molecular architecture characteristics corresponding to that of the AF-side formed on "nonsink" type substrates. To promote the formation of surfaces with AF-side characteristics on the SF-side of prepolymer films, solvent-impenetrable substrates can be converted into "sink" type substrates. This is performed by deposition of a priming layer that is insoluble in, but is capable of absorbing substantial amounts of, the THF/DXE solvent used in the prepolymer solution.
The development of AF-side surface characteristics on the SF-side can be demonstrated by the following example. In the preparation of seamless, spherical or ellipsoidal blood pump chambers having one or two ports for connections, disposable, hollow polyethylene (Epolene) mandrels are primed with a polynvinylalcohol (PVA) layer of predetermined thickness. Upon deposition of prepolymer solution coatings over the dried PVA layer, this acts as a solvent "sink," and gives rise to the formation of elastomers having SF-sides with IRATR characteristics comparable to those of the AF-side shown earlier in Fig. 4a. Figure 14 shows an Ellipsoidal Left Ventricular Assist Device (ELVAD) developed by F. Unger, et al., at the 2nd Surgical Clinic of the University of Vienna, Austria, (19) using the Avcothane 51 elastomer. The entire pumping chamber of this device is prepared, by the PVA technology described above, in the course of a single procedure including the deposition of a varying number of prepolymer solution films as required by the designed variations in wall thickness. After an adequate period of curing, the chamber made according to the principles of monolithic construction, is obtained by simply cracking the Epolene mandrel and peeling off the PVA priming film. The SF-sides of these pump chambers have demonstrably AF-side characteristics with IRATR indices in the range of 1.0-1.4. These optimized surface characteristics have led to significant degrees of in vivo hemocompatibility, as demonstrated in Fig. 15, by the absence of any fibrinaceous or thrombotic deposit on the inner blood-contact surfaces of an ELVAD recovered from a calf after 87 days of functioning implantation.

The production of implantable-quality Avcothane 51 intra-aortic balloons requires a multiple-dip technology. Although their blood-contact surface is their AF-side, except the first layer of prepolymer solution film, all subsequent coats are deposited on a "sink" type substrate constituted by the same but partially cured material. To perform the deposition of prepolymer films on stainless steel mandrels under controlled conditions, and to assure the rate of "skin" formation required for optimized IRATR indices on the AF-side, the apparatus shown in Figs. 16 and 17 has been designed and used at Avco Medical Products for the automated mass production of intra-aortic balloon casings. The operational chamber of this apparatus, constructed entirely of stainless steel, represents a better than Class A clean-room environment (count of airborne particles $< 10^3/m^3$), and allows for solvent removal rates by vaporization as to optimize the rate of "skin" formation.

SUMMARY

A series of proprietary elastomers, known as Avcothanes, has been developed earlier to provide both flexible and stationary blood-contact surfaces in various types of circulatory assist and other prosthetic devices. A member of this series, the Avcothane 51 elastomer has displayed a considerable degree of in vivo hemocompatibility in terms of the ultimate test for any implantable prosthetic material: about 25,000 intra-aortic balloon pumps made of it were implanted to date in cardiac patients, without causing clinically intolerable hematologic trauma or other toxic effects. The elastomer is inherently non-thrombogenic inasmuch as its hemocompatibility does not depend on added
anticoagulants but on a specific surface molecular architecture which gives rise to a randomized dispersion force field designed to minimize interactions with native plasma proteins.

To be useful for routine clinical applications with a reproducibly high degree of safety, as inherently hemocompatible materials, the Avcothane 51 elastomer has to comply simultaneously with two basic requirements. It has to exhibit a combination of desired bulk physical properties with surface characteristics yielding the demonstrated degree of blood compatibility. This two-fold requirement is, in part, met by the composition of the elastomer which is derived from a combination of a poly(ether urethane) with poly(dimethylsiloxane). However, since the apparent hemocompatibility of Avcothane 51 surfaces is a function of their molecular structure which is affected by the process parameters employed in the synthesis of prepolymer solutions as well as their conversion into the cured material, processing technology is an equally significant factor because of its direct bearing on the in vivo performance of the elastomer. Thus, for prosthetic devices made of, or coated with, the Avcothane 51 elastomer, a technology has been established that is capable of simultaneously assuring not only the desired bulk properties of each of the products, but also the molecular architecture of their blood-contact surfaces optimized to yield maximum hemocompatibility. As a result of the nature of objectives to be accomplished, the Avcothane 51 technology devised is an integrated assembly of methods not conventionally applied in current polymer processing.

APPENDIX

For the purposes of describing correlations between parameters of processing technology and the surface properties of finished Avcothane 51 products, the prepolymer solution can be defined as a three-component system, with respect to its composition given earlier. By this definition, the solvent THF is the "solvent" for the system in which the solutes are: (a) DXE (despite the fact that it functions as a solvent), and (b) the polymeric nonvolatile components including both the poly(ether urethane), the poly(dimethylsiloxane) and their block copolymer. Regardless of their actual relative proportions, the cumulative weight fraction of these polymeric materials is defined as the total solids content. The definition of DXE as a so-called "volatile solute" is based on its physical effect inasmuch as its presence decreases the vapor pressure of the prepolymer solution from that which would be exerted, at the same temperature, if the solution would contain only THF as the solvent. As shown later, the rate of solvent removal by vaporization is a function of the effective vapor pressure over the prepolymer solution. As a result of reducing this pressure, as solutes do in general, DXE decreases that rate.

Thus, for a "solution" which is composed of a $W_D$ quantity or $W_D/M_D = n_D$ moles of DXE, in a $W_T$ quantity or $W_T/M_T = n_T$ moles of THF, the corresponding mole fractions are:

-15-
\[ X_D = n_D \left( n_D + n_T \right) \] \hspace{1cm} (1)

and

\[ X_T = n_T \left( n_D + n_T \right) \] \hspace{1cm} (2)

where \( M_D \) and \( M_T \) represent, respectively, the molecular weights of DXE and THF. At a given temperature, \( \tau \), both pure DXE and THF exert finite vapor pressures equal to \( (P_D)_\tau \) and \( (P_T)_\tau \), respectively. The equilibrium vapor pressure of the "solution" will be given by Raoult's Law,

\[ (P_{TD})_\tau = (P_D)_\tau X_D + (P_T)_\tau X_T \] \hspace{1cm} (3)

if the "solution" is ideal.

In Fig. 18, the measured equilibrium vapor pressures of 4 different "solutions" of known amounts of absolute DXE in absolute THF are given at ambient temperature. This condition has been selected to be relevant to that usually prevailing when the removal of solvents commences from Avcothane 51 prepolymer solutions in various types of operations. As shown, within experimental error, these pressures fall with good agreement on the straight lines predicted by Eq. (3), indicating ideal behavior. Under these conditions, this is as can be more or less expected since neither DXE nor THF has any functional groups. The energy of their intermolecular interaction can arise only from relatively weak dispersion forces also controlling the capability of any of these molecules to escape into the vapor phase.

During solvent evaporation, the mean surface temperature of a prepolymer solution film decreases because, at least, a part of the heat of vaporization is extracted from the film's heat content. Thus, for the purposes of surface formation kinetics, vapor pressures are to be expressed as some function of temperature. This can be performed using the well-known correlation,

\[ P = \exp(\alpha \tau + C) \] \hspace{1cm} (4)

where \( P \) is the equilibrium vapor pressure of any particular pure substance; \( \alpha \) and \( C \) are its characteristic constants; and \( \tau \) now denotes the Kelvin temperature. Substituting either \( P_D \) or \( P_T \) for \( P \) in Eq. (4), each of the values of \( \alpha \) and \( C \) for DXE and THF can be found, respectively, by standard methods. With these values, the temperature-dependent equilibrium vapor pressure of DXE solutions in THF can be expressed as

\[ P_{TD} = X_D \exp(\alpha_D \tau + C_D) + X_T \exp(\alpha_T \tau + C_T) \] \hspace{1cm} (5)

For a prepolymer solution containing \( W_D \) and \( W_T \) quantities of DXE and THF, respectively, and a total solids content, \( W_S \) of polymers, the corresponding mole fractions are:
number of moles of polymeric substances present not be defined by any of their 3 possible molecular weights. Instead, as a first-order assumption, \( M_g \) can be taken equal to 27.1, the group weight of urethane moieties which effectively interact with both DXE and THF, and hence, \( n_S = W_S/27.1 \).

In the establishment of correlations with experimental data, it is convenient to introduce a number of simplified notations. This involves that the separate DXE and THF contents, \( W_D \) and \( W_T \), respectively, of a prepolymer film are not distinguished from each other but taken as the total removable liquid content, \( W_L = W_D + W_T \). On this basis, the weight fraction of removable liquids which is usually determined in experiments, can be expressed as

\[
c_L = \frac{(W_D + W_T)}{(W_D + W_T + W_S)} = \frac{W_L}{W_L + W_S} \quad (11)
\]

Since the standard composition of Avcothane 51 prepolymer solutions involves a 2:1 by weight THF/DXE mixture,

\[
W_L = W_D + W_T = 3W_D \quad (12)
\]

and hence, the number of moles of removable solvents can be expressed as

\[
n_L = 2 \frac{W_D}{M_T} + \frac{W_D}{M_D} = W_D \left(2 \frac{M_D}{M_D + M_T}\right) \quad (13)
\]

Using the foregoing expressions, the mole fraction of removable solvents becomes

\[
x_L = \frac{n_L}{(n_L + n_S)} \quad (14)
\]

and that of the solids content is

\[
x_S = \frac{n_S}{(n_L + n_S)} \quad (15)
\]

To correlate the vapor pressure of a prepolymer solution, which has been measured at a fixed \( \tau \) temperature, with the experimentally determined weight fraction of its removable solvent contents, Eq. (9) can be written using the expressions given in Eqs. (14) and (15),

\[
\left(\frac{P_{TD}}{P_{TD}}\right)_\tau x_L = \left(\frac{P_{TD}}{P_{TD}}\right)_\tau \frac{n_L}{(n_L + n_S)} \quad (16)
\]

Figure 19 shows the equilibrium vapor pressures, determined at \( \tau = 25.5^\circ C \), of an Avcothane 51 prepolymer solution in the standard 2:1 by weight THF/DXE mixture, as a function of the weight fraction of removable solvent contents, \( c_L \). If, as postulated above, \( n_S = W_S/27.1 \) is substituted into Eq. (16), the upper solid line in Fig. 19 results. If curve fitting
is applied to the measured vapor pressure data, the lower solid curve is obtained. Using the fitted curve, regressive analysis gives $n_5 = W_5/32.4$, which appears to be within reasonable agreement with the value estimated for $M_5$ according to the first-order assumptions described earlier. This agreement implies that $(P TD)_T$, as expressed in Eq. (16), can be applied with reasonable confidence toward the derivation of a treatment for the kinetics of solvent removal from, and solid surface formation of, liquid Avcothane 51 prepolymer solutions.

The simplified treatment presented below for solvent removal kinetics is based on the assumption that the prepolymer solution film temperature, $T$, remains constant throughout the entire period of solvent removal. Obviously, this represents only a first order approximation because, if part of the solvent removal proceeds via evaporation, the heat of vaporization of solvents is supplied by the heat capacity of the prepolymer film, which renders $T$ a time-dependent variable. It can be shown that, in Eq. (10) having the proper form, adjustments can be made to define $T$ as a time-dependent function of all major variables affecting it. The resulting expressions are tractable only by computer.

Thus, according to this simplified approach, let $W_F$ be the weight of a prepolymer solution film deposited over a known area, at a $T$ temperature taken to remain constant. According to definitions introduced earlier,

$$ W_F = W_D + W_T + W_S = W_L + W_S \quad (17) $$

As a result of solvent removal, $W_L \to 0$ and $W_F \to W_S$. The quantity of solvent removed in $dt$ time is

$$ -dW_L = W_L, 0 - W_L, t \quad (18) $$

where $W_L, 0$ denotes the solvent content at $t = 0$.

For the case of a prepolymer solution film deposited on an impenetrable or "nonsink" type substrate, solvent removal occurs only via evaporation. Under the conditions that the vapors released by the film are removed from the immediate vicinity of the film bounding surfaces at a constant rate, the rate of solvent removal by evaporation becomes a function of the vapor pressure, $P TD$ defined in Eq. (16). The quantity of evaporated solvent can be expressed as

$$ - (dW_L)_T = \eta (P TD)_T \left[ n_L/(n_L + n_S) \right] dt \quad (19) $$

where $\eta$ is a proportionality factor which, among others, is a function of the flow characteristics of gas over the prepolymer solution film, and can be experimentally determined for a particular set of conditions. The substitution of previously derived expressions into Eq. (19) gives
\[- (dW_L)_T = \eta (P_{TD})_T \frac{W_L}{M_L} \frac{1}{(W_L/M_L)} + n_S \text{ } \frac{dt}{dt} \tag{20}\]

where \(M_L\), the mean nominal molecular weight of the standardized 2:1 THF/DXE mixture is defined as

\[M_L = \frac{W_L}{n_L} = \frac{3}{M_T} \frac{M_D}{(2 M_D + M_T)} \tag{21}\]

As a result of the fact that the total weight of solids in the film, \(W_S\) remains constant throughout the removal of solvents, \(n_S\) is also a constant. Upon rearrangement, Eq. (20) can be written as

\[- \left(\frac{dW_L}{W_L}\right)_T = \eta (P_{TD})_T \frac{1}{M_L} \frac{1}{(W_L/M_L)} + n_S \text{ } \frac{dt}{dt} \tag{22}\]

which can be integrated for a \(t\) period of elapsed solvent removal time to give

\[- \frac{W_L}{M_L} - n_S \ln W_L = \left[\eta (P_{TD})_T t/M_L\right] + Q \tag{23}\]

where \(Q\) is the integration constant. After substitution of \(n_L\) for \(\frac{W_L}{M_L}\) into Eq. (23), and determination of \(Q\) on the basis that when \(t = 0\), \(W_L = W_L, 0\), the solvent content of a prepolymer solution film is given as a function of \(t\), the elapsed solvent removal time as

\[n_S \ln (W_L, 0/W_L) + \frac{W_L, 0 - W_L}{M_L} = \frac{\eta (P_{TD})_T}{M_L} t \tag{24}\]
REFERENCES


<table>
<thead>
<tr>
<th>Property</th>
<th>ASTM No.</th>
<th>Avcothane 51</th>
<th>PEU*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (g/cm³)</td>
<td>D-1505</td>
<td>1.09</td>
<td>1.18</td>
</tr>
<tr>
<td>Tensile Strength (psi)</td>
<td>D-882</td>
<td>6200</td>
<td>6500</td>
</tr>
<tr>
<td>Ultimate Elongation (%)</td>
<td>D-882</td>
<td>980</td>
<td>600</td>
</tr>
<tr>
<td>Indentation Hardness (Shore &quot;A&quot;)</td>
<td>D-2240</td>
<td>72</td>
<td>80</td>
</tr>
<tr>
<td>Graves Tear Resistance (lb/in.)</td>
<td>D-1004</td>
<td>490</td>
<td>400</td>
</tr>
<tr>
<td>Dielectric Strength (volts/mil)</td>
<td>D-149</td>
<td>1500</td>
<td>800</td>
</tr>
<tr>
<td>Lee-White Clotting Time (min)</td>
<td>N.A.</td>
<td>45-65</td>
<td>24-28**</td>
</tr>
</tbody>
</table>

* Represents a typical poly(ether urethane), presented only for comparison.

**Solvent-cast film of polymer purified by reprecipitation.

N.A. = Not applicable.
FIGURE CAPTIONS

Fig. 1  Loss ($E'$) and Storage ($E''$) Moduli of Avcothane 51 Elastomer Determined with a Rheovibron Viscoelastometer at 110 Hz.

Fig. 2a-c  The 11 - 13.5 µm Ranges of IR Attenuated Total Reflectance (IRATR) Spectra Obtained from (a) Air-Facing Side and (b) Substrate-Facing Side of an Avcothane 51 Elastomer; (c) Same Spectral Range of Homopolymer Derived from Polyfunctional Poly(dimethylsiloxane) Used in Avcothane 51 Prepolymer Solutions.

Fig. 3  Correlation between the Inverse IRATR Index and Electron-Microprobe Silicon Atom Count Proportional to Polysiloxane Content.

Fig. 4a,b  Computer-Deconvoluted Carbon 1s Electron Spectra Obtained by ESCA from (a) Air-Facing Side, and (b) Substrate-Facing Side of an Avcothane 51 Elastomer Prepared from Standardized Prepolymer Solution.

Fig. 5  "Reprecipitation Kettle and Tumbling Vacuum Drier Used in Purification of the Poly(ether urethane) Component of Avcothane 51 Elastomer.

Fig. 6  "Fish-Eye" View of Purification Plant for Solvents Used in Avcothane Prepolymer Solutions. A combination of fractionation (distilling columns on the right) with molecular sieves (packed columns in center) is employed.

Fig. 7  Custom-Equipped Glass Reactor for Avcothane Prepolymer Solution Synthesis.

Fig. 8  Gel Permeation Chromatograms of Poly(ether urethane) Used in Avcothane 51 Prepolymer Synthesis and Avcothane 51 Prepolymer Showing High Molecular Weight Shoulder.

Fig. 9  Correlation Between Extent of Copolymerization Reaction Monitored by Gel Permeation Chromatography and Micromorphology seen in the Scanning Electron Microscope on Avcothane 51 Elastomer Surfaces Cured under Identical Conditions.

Fig. 10  Decreases of Removable Solvent Content by Vaporization, Determined Experimentally or Predicted by Eq. (24), for Avcothane 51 Prepolymer Solution Films as a Function of Elapsed Removal Time. Lower pair of curves indicate the change in solvent content for a prepolymer solution film.
Fig. 10  placed on a solvent-impenetrable, "nonsink" type substrate leading only to the "skin effect." Upper pair of curves show the same change but for a prepolymer solution film deposited on a solvent-penetrable, "sink" type substrate leading to a combination of "skin" and "sink" effects.

Fig. 11  Growth of "Skin" on the Air-Facing Side of an Avcothane 51 Prepolymer Solution Film Deposited on a "Nonsink" Type Substrate. (Air flow ~ 210 cm/min, air temperature ~ 25.5°C).

Fig. 12  Decrease of Experimentally Determined Rate of Vaporization as a Function of "Skin" Layer Thickness Computed for an Avcothane 51 Prepolymer Solution Film Deposited on a "Nonsink" Type Substrate.

Fig. 13  Comparison Between Experimentally Determined Changes in Removable Solvent Content due to Vaporization, and Changes in Same but Computed Using Eq. (25). Lower pair of curves (circles) indicate the change in solvent content for an Avcothane 51 prepolymer solution film placed on a "nonsink" substrate leading only to the "skin effect." Upper pair of curves (diamonds) indicate the same change but for a prepolymer solution film deposited on a "sink" type substrate leading to both "skin" and "sink effects."

Fig. 14  The Ellipsoidal Left Ventricular Assist Device (ELVAD) as Developed at the 2nd Surgical Clinic of the University of Vienna, Austria. Except for the connecting Dacron outflow graft, all other blood-contact surfaces are made of Avcothane 51 elastomer. Pumping chamber is made according to monolithic construction utilizing the "sink effect" of poly(vinyl alcohol) priming layers for the attainment of optimized blood-contact surfaces.

Fig. 15  Pumping Chamber Blood-Contact Surface of an Ellipsoid Left Ventricular Assist Device Recovered from a Calf after 87 Days of Functioning Implantation.

Fig. 16  Automated Apparatus Designed and Built by Avco Medical Products for Dip-Molding Intra-Aortic Balloons with Standardized Avcothane 51 Prepolymer Solution.

Fig. 17  Closeup of Station No. 3 in Automated Balloon-Dipping Apparatus. On clean stainless steel mandrils, having a mirror-finished surface, a coat of the Avcothane 51 prepolymer solution has been deposited at each of Station Nos. 1 and 2. At Station No. 3, the "fingers" of pneumatically operated arms remove the mandril having 2 coats from the turntable, and rotate the mandril by 180° for dipping in the reverse direction.
Fig. 18  Equilibrium Vapor Pressure Diagram of Tetrahydrofuran/Dioxane Mixtures at Ambient Temperatures

Fig. 19  Equilibrium Vapor Pressure of Avcothane 51 Prepolymer Solution as a Function of its Solvent Content at 25.5°C.
DECONVOLUTED CARBON 1s ELECTRON PEAKS OF AVCOTHANE 51 ELASTOMER

a) AIR-FACING (AF) SIDE

b) SUBSTRATE-FACING (SF) SIDE

COUNTS PER SECOND

ENERGY (eV)

C-C
C-N

C-O BOND
PRESENT ONLY IN POLYETHER URETHANE COMPONENT

~12% OF TOTAL INTEGRATED PEAK AREA

~4% OF TOTAL INTEGRATED PEAK AREA

Fig. 4
AIRFLOW ~ 210 cm/min
AIR TEMP ~ 25.5°C

"SINK" TYPE SUBSTRATE
"SKIN+SINK" EFFECTS

NORMALIZED SOLVENT CONTENT OF FILM, \( W_L/W_L,0 \)

"NONSINK" TYPE SUBSTRATE
"SKIN" EFFECT ONLY

ELAPSED REMOVAL TIME (MIN)
FINAL THICKNESS OF RESULTING DRY SOLID FILM

"SKIN" THICKNESS [\(\mu\)]

ELAPSED REMOVAL TIME (MIN)

D3332
AIRFLOW $\sim 210$ cm/min
AIR TEMP $\sim 25.5^\circ$C

EVAPORATION RATE OF SOLVENT CONTENT, $\Delta W^L / \Delta t$ (gm/30 secs)

"SKIN" THICKNESS [$\mu$]
"SINK" TYPE SUBSTRATE
"SKIN + SINK" EFFECTS

EXPERIMENTAL
PREDICTED WITH "SKIN" EFFECT
BUT NOT WITH "SINK" EFFECT

"NONSINK" TYPE SUBSTRATE
"SKIN" EFFECT ONLY

EXPERIMENTAL
PREDICTED WITH "SKIN" EFFECT

AIR FLOW ~ 210 CM/MIN
AIR TEMP. ~ 25.5°C

WEIGHT FRACTION OF SOLVENT CONTENT OF FILM, W_L/(W_L+W_S)

ELAPSED REMOVAL TIME (MIN)
EQUILIBRIUM VAPOR PRESSURE, $P_{Td}$ (mm Hg)

- @ 25°C
- @ 24°C

$X_T$ and $X_D$ with THF/DXE WT. RATIO (3/1, 2/1, 1/2, 1/3)
Robert S. Ward, Jr.

Mr. Ward is Biomaterials Production Manager for Avco Medical Products. He received his B.S. Ch.E. from the Lowell Technological Institute in 1971, and is currently enrolled in the Masters Program in Engineering Management at Northeastern University.

Since 1971, he has been responsible for the production of Avcothane 51 elastomer, including scale up as well as plant design and construction. Recently he has developed new characterization methods for biomedical polymers employing exclusion chromatography as well as several correlations between polymer bulk properties and surface blood compatibility. As a member of the Senior Staff of the Medical Products Division his duties include all phases of materials development, production and specification in the manufacture of cardiovascular devices.

He is a member of the American Chemical Society.
EMERY NYILAS

Dr. Nyilas joined the Avco Everett Research Laboratory, Inc. in 1966, and has been Chairman of the Medical Research Committee since 1973. His activities included the invention and development of proprietary Avcothane elástomers as well as participation in the development of various types of implantable prosthetic devices of which the Avco Intra-Aortic Balloon Pump has reached the level of routine clinical application in cardiac patients. In addition, he has been directing basic research programs concerning the physico-chemistry of blood/foreign surface interfacial phenomena.

After he obtained his degree at the Technical University of Budapest, Hungary, he served as an Assistant Professor at that institute. At the Massachusetts General Hospital/Harvard Medical School, he was a Research Fellow engaged in the synthesis of new organo-boron compounds for neutron-capture therapy of brain tumors and some nitrogen-mustards for cancer chemotherapy. At American Plastic and Chemical Corp., where he was a partner, his work entailed high-temperature polymers, nonconventional plastics and plastic additives.

He is a member of the American Chemical Society, American Society for Artificial Internal Organs, the New York Academy of Sciences, and the Society for Biomaterials.