PERMEABILITY OF DECAMETHYLTETRASILOXANE THROUGH A SEGMENTED POLYETHER POLYURETHANE INTO BLOOD

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INTRODUCTION

In many Ventricular Assist Devices a flexible membrane (for example, Biospan, which is a segmented polyether polyurethane) separates the blood from the hydraulic fluid (in this instance a silicone oil, decamethyltetrasiloxane) that drives the pump. The use of hydraulic fluids (silicone oil) in VADs presents the possibility for diffusion of the hydraulic fluid out of the device into the blood [1]. The loss of silicone oil from the device may result in health problems, reduced pumping performance and the need to refill the device after a given duration of operation.

The experiments presented in this paper were designed to measure the volume of decamethyltetrasiloxane (silicone oil) that would permeate through a segmented polyether polyurethane membrane into blood. The experimental parameters were chosen to model the environmental and physical characteristics found in a typical Ventricular Assist Device. The characteristics affecting permeability that were considered in this study were temperature, diaphragm thickness, donor fluid, receiving fluid and boundary conditions on both sides of the diaphragm. Effects resulting from motion of the membrane, such as, fluctuating pressure, fluctuating stress and flexing of the diaphragm were not taken into consideration.

The results from the experiments presented in this paper show that the silicone oil/polyurethane/whole blood system has a permeability coefficient of $4.1x10^{-11}\frac{cm^2}{s}$, a diffusion coefficient of $3.1x10^{-8}\frac{cm^2}{s}$ and a solubility coefficient of 0.0013. Using these values the loss of silicone oil through a $50cm^2$ diaphragm with a thickness of $0.056cm$ over two years would be $2.15ml$. This is approximately 1% of the total volume of hydraulic fluid in a typical device and is not expected to have any effect on pumping performance.

BACKGROUND

Ficks law (e.g. [2]) is often used to model permeability problems. Ficks first law is applicable to diffusion in the VAD since the concentration of silicone oil (donor fluid) in the device will remain constant (100%) and the continuous flow of blood (receiving medium) is expected to maintain an negligible concentration of silicone oil (0%). The following equation was found for a permeating volume using Ficks law and assuming one dimensional diffusion.

$$Q = \frac{PAt(C_r - C_d}{l} \quad (1)$$

where:

Q	permeant volume passing through the polymer
P	permeability coefficient of the system
A	area available for permeation
t	time
C_r	permeant concentration in the receiving chamber
C_d	permeant concentration in the donor chamber
l	is the thickness of the polymer

From equation 1 we can see that P, the permeability coefficient is required to predict the volume of silicone oil permeating through the polymer. This value further depends on the diffusion (D) and solubility (S) coefficients that can be calculated using the time lag method as outlined by Comyn [2]. The experiment performed to determine the permeability of silicone oil through the flexible diaphragms was designed to provide information that could be used to calculate the permeability, diffusion and solubility coefficients of the system.

EXPERIMENTS

The flexible polymer membrane used was a segmented polyether polyurethane, Biospan, supplied by The Polymer Technology Group, Incorporated, Emeryville, CA, USA. The diaphragms were cast following the techniques used for the diaphragms in the VAD. Only diaphragms with a thickness in the range of 0.480 to 0.660 mm were accepted for testing. The hydraulic fluid used in the VAD was a silicone oil, decamethyltetrasiloxane. The receiving fluid used to model human blood was CPDA (Citrate Phosphate Dextrose Adenine) treated bovine blood. The volume of bovine blood used in each test was $7.5ml$ and the area of the model diaphragms was $3.14cm^2$.

In the test setup (see Figure 1) the model diaphragms are located on the bottom of the test tubes. The blood samples were contained inside of the glass test tubes and the silicone oil was located in the large acrylic reservoir. The diaphragms were bonded onto the glass using Biospan. The tops of the test tubes were sealed with Teflon caps to control the evaporation of blood out of the tubes and to prevent the contamination of the samples with silicone oil. All tests were performed at body temperature, $37°C$. In order to assure that the boundary conditions induced on both sides of the diaphragm had flow rates similar to those expected in a typical VAD, magnetic stirring bars were used. A large magnetic stirring bar was located in the silicone oil reservoir and one small magnetic stirring bar was located in each test tube. During testing, the apparatus was placed on a magnetic stir tray where the magnetic stir bars continuously mixed the fluids. In addition to providing constant flow over the diaphragms the blood was sufficiently mixed to avoid precipitation of the red and white blood cells out of the plasma.

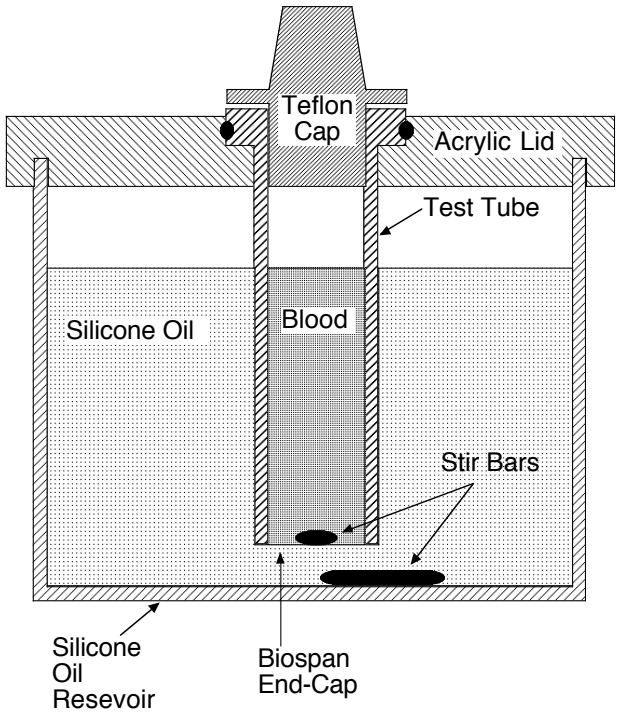

Figure 1: Schematic of Permeability Test Apparatus. Note that, for clarity, only one test tube is shown. In the actual device seven tubes were incorporated into the same reservoir.

Twenty two independent samples were tested using the same procedure. The reservoir containing the silicone oil was preheated to $37°C$ and model diaphragms were bonded onto the ends of the test tubes. $7.5ml$ of bovine blood was added to each test tube and the tubes were suspended in the test apparatus reservoir. The silicone oil level in the reservoir was adjusted so that the level of oil was even with the level of blood in the test tubes. The process of permeation of silicone oil was from the silicone oil in the reservoir into the model diaphragms then into the blood contained in the tubes. This process was allowed to take place for twenty two samples with varying times from 8 hrs up to 18 days.

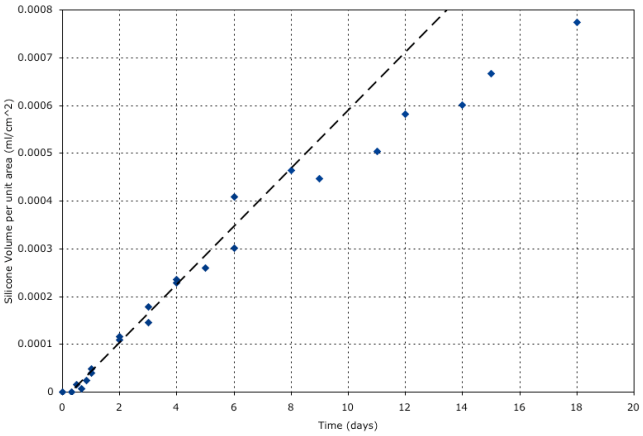

Figure 2: Permeability Test Data up to Day 18

To test the receiving fluid (blood) for permeant (silicone oil) with a concentration expected in the parts per million range Gas Chromatography with a Mass Spectrometric detector (GC/MS) was chosen. GC/MS provides results which specifically identify the silicone oil, decamethyltetrasiloxane [4] without contamination from other sources of silicone (such as the glass tubes or the silicone that is naturally found in the blood [7]).

To prepare the blood samples for GC/MS testing the blood was transfered from the test tubes to a glass bottle. A volume of extraction solvent (hexane) ranging from 5 to $10ml$ was added to the blood and agitated. The mixture was then centrifuged at approximately $825g$ and the extraction solvent was pipetted off and put in a glass bottle. The blood was then extracted and centrifuged 2 more times with the solvent. The total volume of extraction solvent ranged from 15 to $30ml$.

The extraction solvent was then tested for silicone oil using gas chromatography. The results from the GC tests permitted calculations of the volume of silicone oil that had permeated through the model diaphragms into the blood volume (see Figure 2).

RESULTS AND DISCUSSION

To determine the permeability and diffusion coefficients, a graph was prepared of all of the permeability test samples (see Figure 2) that shows the volume of silicone oil passing through the diaphragm per unit area ($\frac{ml}{cm^2}$) as a function of time (s). The results generally followed the expected results dictated by theory. The linear portion of the curve, from day 1 to day 6 (see Figure 2), is used to determine the permeability and diffusion coefficients. The method of least squares ([6]) was used to find the most accurate linear approximation to the permeability test data. Eleven data points from day 1 to day 6 were used in the linear approximation. The data after day 6 indicated a decreasing permeation rate which may have been due to an increasing concentration of silicone oil on the receiving side of the end-caps which would resist permeation.

Using the Time Lag Method, ([2]) the permeability coefficient (P) was determined to be $4.1x10^{-11}\frac{cm^2}{s}$. The solubility coefficient (S) of the permeability test system was $.0013g/g$. The diffusion coefficient (D) of the system was found to be $3.1x10^{-8}\frac{cm^2}{s}$.

The diffusion and solubility coefficients were determined from experiments. If the area (A) of the blood chamber diaphragm is assumed to be $100cm^2$ and the thickness (l) is $0.056cm$. The concentration of silicone oil in the device (Cd) is 100% or $1.0ml/ml$. The volume of silicone oil permeating through the diaphragm was calculated at different times (t) using Equation 1. Using the coefficients found with the permeability test model the volume of silicone oil that may be lost through a diaphragm with an area of $50cm^2$ over one year is $1.08ml$ and over two years the volume lost would be $2.15ml$. The volume of silicone oil in a typical VAD is several hundred ml. The loss of $2.15ml$ over two years a small percentage of the volume of fluid in the device and is not expected to have any effect on pumping performance.

Random sampling of the thickness of the end-caps before and after the permeability tests showed that no significant change in end-cap thickness due to swelling could be observed. The consistently linear portion of the curve indicates that there is not sufficient swelling of the polymer to introduce channels which permit increased diffusion of silicone oil through the end-cap. Silicone oil completely saturates a Biospan sample in under 24 *hours* and a steady state permeation rate commences at approximately 24 *hours*. No problems were encountered with respect to clotting of the CPDA treated bovine blood in the test apparatus even after 18 *days*. Bonding of the Biospan end-caps to the glass surface was effective. This was determined through random pressure testing of the tubes.

CONCLUSIONS

The purpose of the permeability test was to determine the permeability, solubility and diffusion coefficients of the system and to predict the volume of silicone oil that would be lost through the blood chamber diaphragm of the VAD over two years. The solubility, diffusion and permeability coefficients of silicone oil in a blood/Biospan/silicone oil model of the VAD are $0.0013g/g$, $3.1x10^{-8}\frac{cm^2}{s}$ and $4.1x10^{-11}\frac{cm^2}{s}$ respectively. The permeability test apparatus demonstrated a permeation rate of $1.08\frac{ml}{year}$ for a diaphragm of equal area to a typical VAD blood chamber diaphragm.

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