Development of a silica-free silicone system for medical applications

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Filler-free silicones are believed to be more blood-compatible than those containing fillers. An ultrapure silica-free room temperature vulcanizing silicone system was prepared and characterized using a swelling experiment, an infrared spectrometer, an x-ray spectrometer, a scanning electron microscope and neutron activation analysis. The polymer was found to be suitable for medical applications needing an extremely smooth surface.

INTRODUCTION

Silicones have found wide acceptance in the fabrication of medical devices where blood and tissue compatibility is of prime concern. For practical applications, mechanical properties of silicones are improved tenfold by incorporating filler materials into them. Most commercially available medical-grade silicones contain 20% to 40% by weight of silica filler.

Recently, some workers\(^1,2\) have conclusively demonstrated that incorporation of fillers, even of very fine particle size, adversely affects the blood compatibility of silicones. For many medical applications where mechanical strength is of secondary concern, or where silicone is used as a coating on a supporting substrate, an interest is being shown in the use of filler-free silicones.

Most filler-free silicones available to date for medical applications are of radiation-cure type.\(^2\) This is a major inconvenience to medical technicians who do not have in-house capability for radiation curing. An ideal blood-compatible material should also be easy to handle and easy to cure.

This paper discusses in detail an approach taken in the development of an RTV type filler-free silicone system for blood contacting surfaces.

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Chemical nature

A silicone polymeric system containing polydimethylsiloxane as the main backbone and terminated in acetoxy groups was chosen to be synthesized for various reasons. Low-energy "methyl clouds" on silicones have been known to be nonresponsible to blood components, whereas phenyl and other H-bonding groups are quite reactive to blood. Therefore, an essentially 100% dimethyl backbone was selected. Acetoxy termination needs moisture from the atmosphere for curing, and therefore, room temperature vulcanization is made possible. It also gives the added advantage of being a one-component system with a long shelf life; thus making the fabrication process still easier. Average functionality per chain was kept greater than or equal to three so that on curing, a crosslinked network having minimal tack is obtained.

Physicochemical nature

The system contains a catalyst, an organotin complex containing butyl and laurate groups, which accelerates the curing reaction. The amount of catalyst in the system would influence the degree of crosslinking in the final network. Molecular weight of the silicone fluid would also affect the degree of crosslinking, since at a given functionality per chain, the number of functional groups per unit weight increases with decreasing molecular weight.

![Figure 1. Effect of catalyst on crosslink density of cured silicone.](image-url)
An experiment was carried out where three silicone fluids of different molecular weights were each catalyzed at four different concentrations of the catalyst. Five slides were coated with each of these 12 formulations. They were allowed to cure for 24 h at room condition (20–25 °C and 30%–35% relative humidity), and 8 h at 80 °C to assure maximum curing. They were then dipped in a toluene bath for 15 h at 25 °C. Data obtained on the amount of swelling and the amount leached in toluene were used to calculate molecular weight between crosslinks and percent extractables in toluene using the following relationship:

$$\overline{M_x} = \frac{-V_1 p_2 (c^{1/3} - c/2)}{\ln(1 - c) + c + \chi c^2}$$

Figure 2. Effect of catalyst on percent extractables of cured silicone.

Figure 3. IR transmittance of Si-OAc at different time intervals.
Figure 4. Progress of Si-OAc hydrolysis.

where $\bar{M}_x$ = molecular weight between crosslinks, $V_1$ = molar volume of solvent, $\rho_2$ = density of polymer, $c$ = relative concentration = $W_o/\rho_2 V_e$. $W_o$ = initial weight of polymer, $V_x$ = swollen volume of polymer = $W_o/\rho_2 + (W_s - W_o)/\rho_1$. $W_s$ = swollen weight of polymer, $\rho_1$ = density of solvent, and $\chi$ = Flory–Huggins constant.

Keeping in mind that lower molecular weight between crosslinks means higher degree of curing, it can be seen from Figure 1 that at catalyst concentrations much below 0.01%, not enough curing is achieved. At approximately 0.01%, a sharp increase in the degree of curing is observed; however, beyond 0.01% no further increase is noticed. Figure 2 shows that the percent extractables of the system are at their minimum when the catalyst concentration is around 0.01%, and further increase in catalyst concentration does not reduce the percent extractables any further.

When the data were subjected to a statistical analysis (two-way analysis of variance), the results showed that it is 99.9% probable ($p < 0.001$) that the amount of catalyst present has an effect on the degree of curing, and it is 90.0% probable ($p < 0.1$) that molecular weight of silicone fluid also affects the extent of crosslinking.

It should be noted that toluene is a very good solvent for silicone, and therefore, much smaller percent extractables would occur during actual use than those found in toluene. Most of the well-established medical-grade silicones, when subjected to similar experiments in this laboratory, recorded approximately 10% by weight of extractables in toluene.
Addition of a metal-based catalyst also raises the question of the amount of metal coming up on the surface, and thus changing the surface characteristics. It is very difficult to define an absolute tolerance limit in this respect. Therefore, a comparison experiment was carried out on the new material under development and on some of the well-established medical grade silicones. A quantitative elemental analysis was done on these materials using the neutron...
activation analysis technique.* Approximately 5 \( \mu \)m thick films were cast from these materials, and were then irradiated (bombarded with neutrons) in a nuclear reactor. The induced radioactivities of the metal were identified and quantitatively measured using gamma ray spectrometry. The material under development showed 17.4 ppm of the metal, whereas the reference material recorded 56.2 ppm of the metal.

* This work was done at General Activation Analysis, Inc., 11575 Sorrento Valley Road, San Diego, CA 92121.
Figure 7. SEM of air-side cured Avcotane 51 surface (control for comparison of required degree of smoothness).

Curing period

Silicone coatings on microscope slides became tack-free within 30 min at 25 °C and 40% RH. However, to determine the time for completion of the curing reaction, time-driven infrared spectrum was run monitoring the Si-OAc peak at 1740 cm⁻¹ as a function of time. Figure 3 illustrates the depletion of IR transmittance of Si-OAc as time progresses, and Figure 4 translates this data quantitatively into the time dependency of the Si-OAc concentration. Change in concentration of Si-OAc is believed to be directly related to the progress of the curing reaction since, during the curing, Si-OAc is hydrolyzed to Si-OH which on further condensation gives Si-O-Si crosslinks.

Figure 8. SEM of mandrel-side cured Avcotane 51 surface cast on silica-free silicone (degree of smoothness suitable for exposure to flowing blood).
On the basis of these results, it was concluded that a 2-h curing period at 25 °C is sufficient (ca. 99% curing). This time can be further reduced by working at higher temperatures.

Surface smoothness

For many medical applications it is very important that, besides being ultrapure, the coatings be extremely smooth. The importance of microscopic imperfections, such as dust particles or other surface inclusions, in triggering thrombus formation has been demonstrated in previous studies.\(^5\) Figures 5(a) and 5(b) clearly show that the absence of fillers in silicone significantly improves the surface smoothness. The importance of purity is seen when Figures 6(a) and 6(b) are compared. The former represents the silicone system made under extremely pure conditions where, for example, spectrograde solvents were redistilled and filtered before use, silicone polymer was filtered through 0.2-\(\mu\)m size filters, etc. Figure 6(b) corresponds to the silicone polymer made under a typical commercial production environment where no particular care about purity was taken. The difference in surface smoothness could be quite significant at microscopic levels.

Rate of evaporation of solvents and viscosity of the system are also important in creating a smooth surface. Rate of drying is controlled for optimum results by using a mixture of tetrahydrofuran and \(p\)-dioxane as solvent. Depending on applications, viscosity of the system can be easily adjusted by varying the amount of solvents.

![SEM of mandrel side cured Aycote 51](image)

**Figure 9.** SEM of mandrel-side cured Aycote 51 surface cast on silica-filled silicone (degree of smoothness unsuitable for exposure to flowing blood).
Applications

The polymer which was derived as a result of this study has been used for varieties of medical applications where creation of a smooth surface is of prime importance. For example, it is used as an intermediate material during the fabrication of a left ventricular assist device. "Melt-out" mandrels of polyethylene glycol are cast in a female mold, deflashed and coated with the subject silicone polymer prior to dipping in a copolymer.* After vulcanizing to a rubbary film, the silicone coating provides a smooth substrate for deposition with the copolymer.* It also provides good release properties when stripping the completed bladder. Previously, when a commercially available silicone polymer containing silica filler was used, unsuccessful trials resulted due to the generation of rough surfaces. Figures 7, 8, and 9 illustrate these results.6

The material has also been used successfully in the development of seamless trileaflet valves.7 Here, smooth plastic epoxy replicas of sinus-contoured conduits, generated from stainless steel molds, are coated with the subject silicone to obtain medically acceptable smooth surfaces. Lederman et al.8 have described the use of this material in the development of discontinuity-free integrally valved left heart blood pumps.

The subject silicone polymer can also be used in implantable devices to flatten out sharp corners. This would help eliminate regions of low shear rates and separated flows which are known to lead to the formation of thrombi and clots.

For applications where mechanical strength is necessary, a stronger backing of silica-filled silicone overcoated with silica-free silicone has been successfully prepared and used.9

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* The copolymer used was Cardiothane 51 (formerly Aveothane 51) and is available from Kontron Cardiovascular Inc., Everett, MA.
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