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Silicone elastomers: study of their mesh size by thermal analysis

J. C. MOREAU, G. MADELMONT, B. LECLERC, J. MAZAN, G. COUARRAZE
Laboratoire de Physique pharmaceutique, U.R.A. C.N.R.S. 1218 Université Paris-Sud, 92296 Châtenay-Malabry Cedex, France

Silicone elastomers are often used as a base for controlled-release systems material for drugs. The modulation of drug diffusion by varying the mesh size of a silicone elastomer network has already been studied. In this work we have investigated the influence of vulcanization conditions and chemical modifications on the network mesh size by thermal analysis and measurement of the swelling ratio. In parallel, the influence of these same parameters on the diffusion of model drugs has been studied.

1. Introduction

Silicones now occupy an important place among biomaterials, especially for the formulation of therapeutic systems [1, 2]. Vulcanized silicone elastomers are particularly suitable for the manufacture of controlled drug release matrices.

However, the chemical compatibility of silicones is limited to a few lipophilic drugs. In order to improve this compatibility and to extend it to more hydrophilic drugs, modifications of their chemical structure has been investigated by grafting organic side-chains along the PDMS backbone.

The formulation of the matrices can influence the release of the included drugs [3]; Ayeni [4] and Bogner [5] showed that the degree of vulcanization can greatly influence the bioavailability of progesterone from elastomers. Lee [6, 7] studied the influence of the elastomer network structure on steroid permeation and, especially, the grafting of alkyl chains on to the polymer backbone.

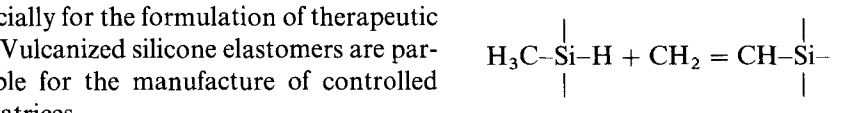
All these parameters lead to important modifications of the network conformation, especially their tridimensional structure which is determined by the crosslink points. Nevertheless, few studies have been carried out to determine the real evolution of the mesh size and its influence on drug mobility [8].

In this work, we have used thermal analysis to study the influence of the vulcanization conditions and the influence of grafting of organic side-chains along PDMS chains on the mean mesh size and its distribution in silicone elastomers. A correlation between this size distribution and the intrinsic diffusivity of a model drug was investigated.

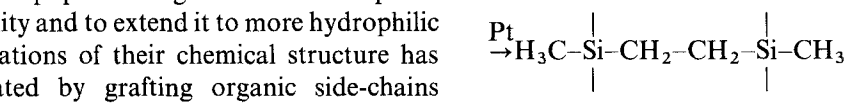
2. Materials and methods

2.1. Elastomers studied

Elastomers are systems which can be vulcanized at room temperature by Pt room temperature volcanizing systems (RTV). They are obtained by hydrosilylation between two polydimethylsiloxane oils (PDMS): a silane oil and a vinyl oil.



Silane oil Vinyl oil



A reference elastomer was prepared with the following PDMS oils:

SiH oil: $Me_3SiO(MeHSiO)_{10}(Me_2SiO)_{140}SiMe_3$

SiVi oil:
$Me_3SiO(MeCH_2CHSiO)_8(Me_2SiO)_{292}SiMe_3$
with $Me = CH_3$.

This reference network was vulcanized by three different processes: in each case, the SiH/SiVi ratio was 0.5; this condition leads to an elastomer with good mechanical properties.

Reference 1: catalyst ratio 5×10^{-4} mol Pt/mol PDMS and vulcanization for 2 h at 100 °C.

The faster the vulcanization, the faster the increase of medium viscosity, and the faster the decrease in chain mobility. So, this phenomenon leads to a lower degree of vulcanization. In order to avoid this, a second reticulation process was used.

Reference 2: catalyst ratio 10^{-3} mol Pt/mol PDMS and time–temperature gradient. 2 h at 20 °C, 2 h at 40 °C, 4 h at 70 °C and 10 h at 100 °C.

Reference 3: same conditions as reference 2 with the addition of a short SiH oil: $Me_2HSiO(Me_2SiO)_{20}SiHMe_2$ in order to adjust the SiH/SiVi ratio to near one. Under these conditions, a better vulcanization degree is expected.

In order to develop improved elastomers for hydrophilic drugs, modified compounds were prepared

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by grafting ether organic groups on to the reference composition:

SiH oil:

$Me_3SiO(MeHSiO)_{10}(MeRSiO)_{10}(Me_2SiO)_{130}SiMe_3$

SiVi oil:

$Me_3SiO(MeCH_2CHSiO)_8(MeRSiO)_9(Me_2SiO)_{292}SiMe_3$

where $R = -(CH_2)_3-(O-CH_2-CH_2)_2-O-C_2H_5$

Elastomers "Ether 1", "Ether 2" and "Ether 3" were obtained, respectively, with the same vulcanization processes as described for the three reference systems.

Since all the studied systems have the same number of SiH and SiVi groups on their constitutives oils (respectively, 10 and 8), theoretically they should yield a similar mesh and any differences observed would be the result of the vulcanization conditions or of the grafting of side-chains.

2.2. Evaluation of elastomer mesh size

2.2.1. Thermal analysis

The network was first swollen in an appropriate organic solvent (benzene). The measure (DSC Dupont de Nemours 990) consists of the determination by differential enthalpic analysis of the decrease in the crystallization temperature ΔT between free benzene and solvent trapped in the matrix. This temperature decrease can be related to the size of the crystals formed; the size of crystals is itself limited by the size R of the network meshes [9]. Therefore

$$R = \frac{A}{\Delta T}$$

where A is a characteristic factor of the solvent.

For each elastomer, five experiments were carried out under the following conditions: cooling at $-30\,^{\circ}C$, heating speed $0.5\,^{\circ}C$/min

2.2.2. The degree of swelling

The elastomer degree of swelling (G) was measured as the ratio between the solvent volume (benzene, 48 h at $20\,^{\circ}C$) and the dry volume of the elastomer. An average value was determined for three samples.

Knowing G, it is then possible to obtain an average value of vulcanization density by reference to Flory's theory [10] and, assuming a regular geometry of the mesh, we can determine the mean mesh size R_m of the elastomer from the density of reticulation ν:

$$\nu = \frac{-[\ln(1-V_2)+V_2+\chi_{12}V_2^2]}{V_1(V_2^{1/3}-V_2/2)} \quad (1)$$

$$R_m = (\nu N_A)^{-1/3} \quad (2)$$

where V_1 is the molar volume of benzene, $V_2 = 1/(G+1)$, the partial volume of silicone, χ_{12} the interaction coefficient silicone–benzene and N_A is Avogadro's number.

2.3. Evaluation of diffusional properties of elastomers

2.3.1. Diffusing molecules

Two model ^{14}C-labelled drugs were used:

Progesterone $M_W = 314.5$

Metronidazole $M_W = 171.2$

These molecules were chosen for two reasons: their different hydrophobic and physico-chemical characteristics.

2.3.2. Determination of the diffusion coefficient

The concentration profile of the diffusing molecule was determined in the presence of a concentration gradient [11, 12]. The evolution with time of these concentration profiles was followed with a multichannel linear radioactivity counter providing good spatial resolution. Two methods of interpretation of this evolution allow us to calculate the intrinsic diffusion coefficient of the molecule in the elastomer. Each experiment was carried out in triplicate at $37\,^{\circ}C$.

3. Results and discussion

3.1. Determination of the elastomer mesh size by differential enthalpic analysis

Fig. 1 shows a fusion thermogram of benzene in an elastomer of type 2. The width of the fusion peak depends on the crystal size distribution and therefore on the mesh size of the network. Like the reference elastomer number 2, all systems tested demonstrated considerable heterogeneity of their mesh size.

In order to quantify the mesh size, several interpretations are possible: (1) it is likely that the top of the fusion peak corresponds to the most frequent mesh size; (2) as the smallest mesh size is the limiting factor for drug diffusion in the elastomer, it is essential to take this into account [13, 14]. We considered the onset melting point of benzene contained in the elastomer. This temperature was determined by the junction point of the baseline with the thermogram. The measured ΔT will then correspond to the highest temperature decrease observed, i.e. to the smallest crystals formed, or to the smallest mesh size of the elastomer.

Table I shows the smallest mesh size of the elastomers studied. Because of the error inherent in the ΔT determination, the smallest mesh size value is given as an interval.

It seems that neither the modification of the cross-linking conditions, nor the grafting of an organic group can modify the smallest mesh size of the elastomers.

3.2. Determination of the mean mesh size of the elastomers from their degree of swelling

The degree of swelling in benzene (G), vulcanization density ν and mean mesh size (R_m) deduced from Equations 1 and 2 for the different networks are given in Table II.

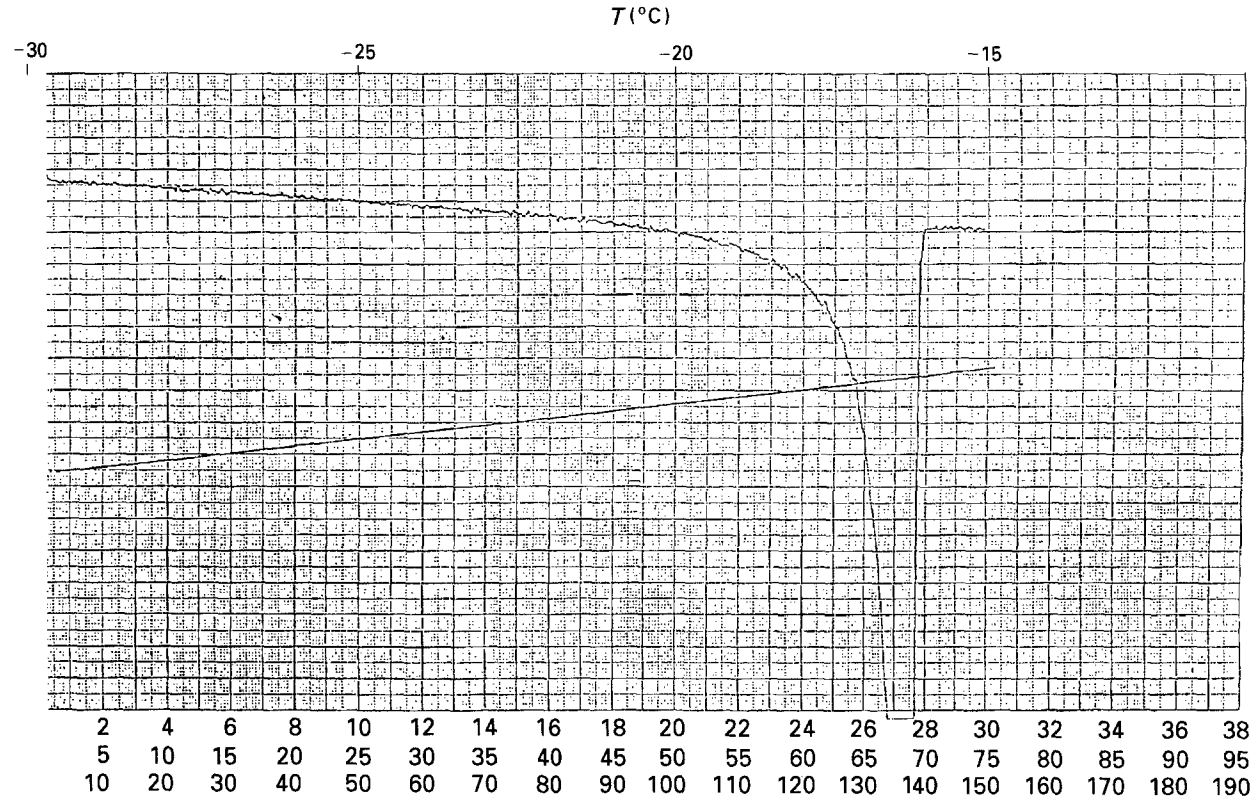

Figure 1 Fusion thermogramme of benzene contained in the swollen reference 2 elastomer.

TABLE I Mesh sizes of silicone networks determined by DSC

Elastomer	Ref. 1	Ref. 2	Ref. 3	Ether 1	Ether 2	Ether 3
Smallest mesh size (nm)	2.3 to 3.5	2.6 to 3.3	2.9 to 3.4	2.5 to 3.6	2.6 to 3.5	2.6 to 3.1

TABLE II Mesh sizes determined from swelling rates

Elastomer	Ref. 1	Ref. 2	Ref. 3	Ether 1	Ether 2	Ether 3
G (benzene)	4.2	4.2	1.7	5.5	3.3	2.6
$v \times 10^6$ (mol cm^{-3})	7.1	6.9	130	2.5	16.3	37
R_m (nm)	6.2	6.2	2.35	8.7	4.7	3.6

3.2.1. Influence of vulcanization conditions

In order to improve the crosslinking yield, vulcanization conditions were modified in the case of reference 3 and ether 3 elastomers, such that the stoichiometry of the reaction was restored.

It seemed that when changing from the first reticulation process (reference 1 and ether 1) to the second or third process, a decrease in degree of swelling was observed, as well as an increase in vulcanization densities, and a decrease in mean mesh sizes. These modifications resulted from a higher frequency of crosslinks.

3.2.2. Influence of organic group grafting

The mesh size seemed to be slightly affected by the grafting of organic groups. With the same vulcanization conditions, the grafting of ether groups led to an increase in G and therefore to an increase in the mean mesh size. This was probably due to steric hindrance which prevents SiH and SiVi units from reacting. This phenomenon was not observed with reference 2 and ether 2. We noticed that the vulcanization process number 2 was not perfect since the reticulation characteristics of the reference network were not improved compared to those obtained with the first vulcanization process.

These two studies showed that the smallest mesh size remained the same under different vulcanization conditions or with side-chain grafting. However, it is likely that the characteristics of the size distribution were modified, since the mean mesh size is not the same for all systems. Thus larger meshes would be obtained with the first reticulation process or in the presence of side-chains.

3.3. Diffusional study of the elastomers

The diffusion coefficients (D) of progesterone and metronidazole obtained with reference 1, ether 1, reference 3 and ether 3 elastomers are displayed in Table III.

In spite of a more important hydrodynamic volume, the diffusivity of progesterone in the reference elastomers was higher than that of metronidazole. Consequently, the meshes of this elastomer are not restrictive for the diffusion of these molecules. For metronidazole, it seems that other factors must be considered, such as chemical interactions between polymer and drug (while the lipophilic characteristics of progesterone lead to a good compatibility of this drug with silicone networks) [15].

TABLE III Diffusion coefficients of studied molecules

Elastomer	Reference 1	Ether 1	Reference 3	Ether 3
$D_{progesterone} \times 10^8$ ($cm^2 s^{-1}$)	66 ± 2	66 ± 2	1.8 ± 0.3	1.4 ± 0.2
$D_{metronidazole} \times 10^8$ ($cm^2 s^{-1}$)	48 ± 3	1.7 ± 0.2	0.48 ± 0.02	0.15 ± 0.04

Modification of the vulcanization conditions (ether 1 and ether 3) led to a drastic decrease in the diffusion coefficient for both molecules. This phenomenon can be related to the mesh size; in fact, the mean mesh size decreased considerably from ether 1 to ether 3 (from 8.7 nm to 3.6 nm. Furthermore, the increase in cross-linking density has a direct influence on the mobility of the solutes within the networks.

4. Conclusions

Thermal analysis of silicone polymer networks after swelling with an organic solvent has been carried out in order to evaluate the influence of vulcanization conditions and organic group grafting on the mesh size of the networks. It seems that these parameters can affect the mean mesh size, but not the lower size limit of the mesh. This later parameter depends on the chemical structure of the two polydimethylsiloxane oils of the silicone networks. On the other hand, the grafting of side-chains on the backbone of the polymer or the use of imperfect vulcanization conditions can lead to the presence of larger meshes in the elastomer. In this case, a clear mesh effect, resulting from the modification of vulcanization conditions, was observed with respect to the diffusivity of model drugs in these elastomers.

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