A New Catalytic Method for Crosslinking of Silicone Polymers

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ABSTRACT: The aim of our work was to develop a gelation process for polymerizing polydimethylsiloxane-α,ω-diols for pharmaceutical purposes. Three different gelling agents has been tried; among them, the prehydrolyzed tetraethoxysilane (TES 40) had the best performance. As initiators, several amines were investigated. The gelling time has been found to be correlated with the basicity, solubility, and diffusibility of the amines. The correlation between the thickness of the oligomer layer and the gelling time has also been investigated. The amount of the remaining initiator after the completion of the network formation has been determined, together with the time needed for its complete removal from the matrix. By using thermogravimetric methods it has been shown that no initiator is left in the matrix. The elastomers obtained by the present method were compared to those obtained by the usual catalysts, resulting in identical properties. The procedure developed is able to produce silicone oligomers for pharmaceutical purposes either in a continous or in a discontinous way. The procedure has several advantages in comparison with the conventional methods. © 1998 John Wiley & Sons, Inc. J Appl Polym Sci 69: 1705–1709, 1998

Key words: polydimethylsiloxane-α,ω-diol; network formation; crosslinking agents; initializing effect of amines; gas-phase reaction

INTRODUCTION

The transdermal therapeutic system, TTS, appeared in the middle of the 1970s. In the case of transdermal drug delivery, the drug penetrates across the skin, resulting in a constant drug level in the blood. In addition, the effective dose is lower than those of the traditional forms because the drug penetrates directly into the target tissue through the circulation system. Several of these systems were developed on a silicone elastomer basis. The base material is polydimethylsiloxane-α,ω-diol, and the gelling agent is usually tri- or tetraalkoxysilane, alkyl–amino–silane, and related compounds. The gelling process of these materials usually is catalyzed by organo-tin compounds[1–5] After gelation these materials remain in the silicone elastomer and can also penetrate through the human skin. However, these compounds are dangerous, they can be harmful to health. The second objective of the present work was to develop a practical process for these transdermal devices. The industrial process should ensure the long-term stability of the oligomer–gelling agent mixture, and yet permit rapid network formation.

In the present work we have studied some gelling agent and some amines having initiating effects on the network formation. The compounds

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Table I The Effect of Crosslinking Agent on the Gelling Time

Crosslinking Agent	"Skin Over" Time (min)	Gelling Time (min)
TES	60	200
TES-28	50	120
TES-40	35	90

were selected according to their optimal effect on both the gelling and the evaporation time.

EXPERIMENTAL AND RESULTS

Materials

The oligomer used was a product of the SZILOR Ltd. Hungary, with a code of R-5 (5000 mPa s viscosity). As gelling agent, freshly distilled tetraethoxysilane and two commercial products (from Wacker Chemie, Germany, TES-28 and TES 40) were used. TES-28 is 97% purity tetraethoxysilane for industrial use; TES-40 contains prehydrolyzed tetraethoxysilane. The product contains oligomers with 1–9 monomer residues; the average formula according to the Wacker catalogue is $Si(OC_2H_5)_{2.33}O_{0.835}$. The initiators investigated were from different firms but all of high purity. The investigations were carried out at 25 °C.

Selection of Gelling Agents

The polydimethylsiloxane-α,ω-diol with well-characterized viscosity (5000 mPa s) were homogenized with gelling agents. The gelling agents contained 96% alkoxy-silane [distilled tetraethoxysilane (TES), technical grade tetraethoxysilane (TES 28), or prehydrolyzed tetraethoxysilane (TES 40)] as crosslinking compounds, and 4% dibutyl-tin-dilaurate as the initiator. The samples were prepared in 1 mm-thick films at 25°C. We have measured the "skin over" time and the gelling time (see Table I).

The data in Table I indicate that the shortest gelling time can be reached with TES-40.

Measurement of the Initiator Effect of Amines

The initiator effect of amines has been studied in a subsequent experiment. Five milliliters of each amine have been poured into a closed vessel to saturate the airspace for 20 min at 25°C. A 0.1-mm thin layer has been made from the silicone oligomer, containing 5% crosslinking agent. This sample was put into the vessel containing the amine saturated airspace. The "skin over" time and gelling time obtained are presented in Table II.

The diffusion coefficients of the amines were determined by the following method. In the experimental apparatus (see Fig. 1) we have separated the liquid and gas phase with a silicone mem-

Table II Effect of Initializing Compound on the Gelling Time

Initiator	Diffusion Coefficient (D)	pK_b [8]	Solubility in the Silicone Oligomer (g/g)	"Skin Over" Time (min)	Gelling Time (min)
Ammonium	$7.7\ 10^{-6}$	4.81	4	—	—
Methylamine	$1.4\ 10^{-4}$	3.38	50	1	3
Ethylamine	$1.2\ 10^{-4}$	3.25	33	3	6
Butylamine	$5.7\ 10^{-5}$	3.4	45	2	6
Propylamine	$2.2\ 10^{-4}$	3.41	117	2	4
Hexylamine	$2\ 10^{-5}$	3.44	2.9	12	30
Cyclohexylamine	$1.9\ 10^{-5}$	3.36	3.4	12	23
i-Propylamine	$2.4\ 10^{-4}$	3.37	50	3	6
i-Butylamine	$1.4\ 10^{-4}$	3.4	28.6	5	8
i-Pentylamine	$4.2\ 10^{-5}$	3.15	17.8	3	7
Dimethylamine	$3.7\ 10^{-5}$	3.23	16	1	5
Dibutylamine	$6\ 10^{-5}$	2.69	4	5	>30
Pyrrolidine	$5.1\ 10^{-5}$	2.73	71	1	6
Piperidine	$2.4\ 10^{-5}$	2.78	25	2	7
Morfoline	$9.4\ 10^{-6}$	5.67	9	25	>30
Triethylamine	$7.9\ 10^{-5}$	3.13	6.1	20	>30

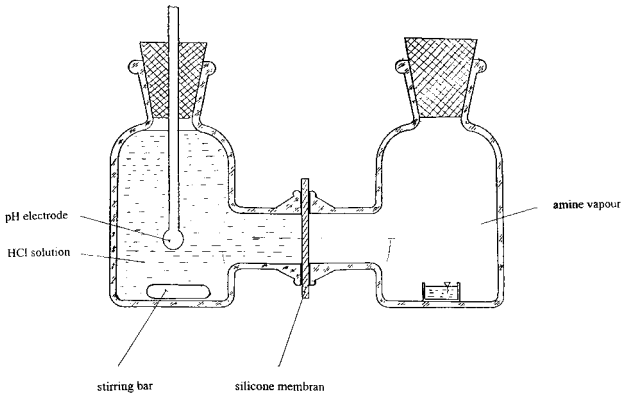

Figure 1 Apparatus for determination of the diffusion coefficient of the amine in the silicone membrane.

brane made from R-5 oligomer. The continously stirred liquid phase contained 0.001*M* HCl. We have measured the pH-change of the liquid phase. In this system, a plot of pH versus t gave a straight line, as described in ref. 6. Extrapolating the line to the x-axis gave the time lag, t_l. The diffusion constant D was then calculated[7] from the following equation:

$$D = \frac{l^2}{6t_l} \qquad (1)$$

where l is the membrane thickness and t_l is the time lag.

The result of this experiment shows that the increasing basicity of the amine reduces the "skin over" and gelling time of silicone oligomers. This behavior is understandable, considering the know mechanism of the networking process.

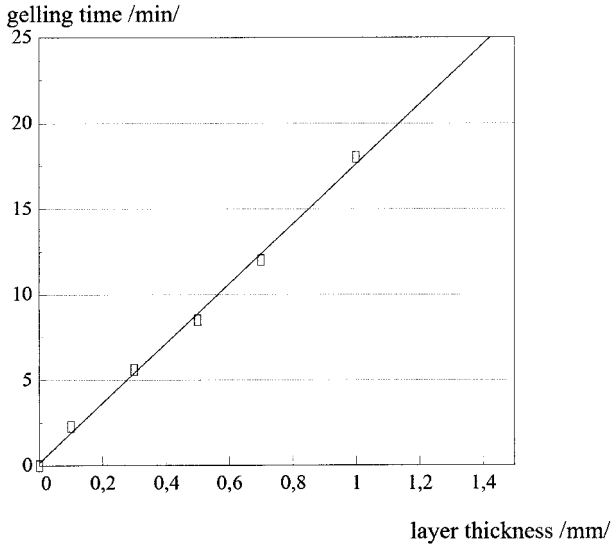

Figure 2 Relationship between the gelling time and layer thickness.

Table III Initiator Content in the Elastomer After Gelation

Airing Time (h)	Average Piperidine Content	
	mol/g Elastomer	mg/g Elastomer
0	$9.32 \cdot 10^{-5}$	8.57
1	$3.38 \cdot 10^{-5}$	2.87
2	0	0

The gelling of condensing-type siloxanes proceeds according to eq. (2) below, where "B" is a basic catalyst:

$$\equiv\text{Si—OH} + \text{B} \rightarrow \equiv\text{Si—O}^- + \text{HB}^+ \equiv\text{Si—O}^- + \equiv\text{Si—O—C}_2\text{H}_5 \rightarrow \equiv\text{Si—O—Si}\equiv + {}^-\text{OC}_2\text{H}_5\ \text{HB}^+ + {}^-\text{OC}_2\text{H}_5 \rightarrow \text{HOC}_2\text{H}_5 + \text{B} \qquad (2)$$

So it is not surprising that the gelling time will be shorter for amines with increasing basicity.

Not only the basicity but the solubility and the diffusibility of the silicone oligomer have significant effects on the networking process. Butylamine has the same "skin over" but longer gelling time in the oligomer as the propylamine, in spite of its lower solubility.

Piperidine has nearly the same basicity as pyrrolidine, but in spite of its lower solubility and diffusibility it has a longer "skin over" and gelling time. Only the triethylamine is an exception because it is a strong base and its solubility is the same as that of piperidine. The behavior of this tertiary amine, however, can be explain by considering its steric bulk, which prevents it from reacting with the Si—OH groups. Thus, the type of the amine has a great significance.

Thus, simultaneous use of TES-40 and piperidine has resulted in an optimal procedure of gelling silicone elastomers.

Relationship Between Layer Thickness and Gelling Time

In the following, the relationship between the layer thickness and the gelling time has been measured.

We have made some 5% TES-40 containing silicone oligomer (R-5) layer with different (0.1, 0.3,

Table IV The Type of Used Catalysts

Catalyst	Gelling Agent	Initiator
1. T-47	Silica-esther (*)	Organo-tin compound
2. BCA-31	Amine type (*)	Dibutyl-tin-dilaurate
3. BD-30	Neutral, oxim type (*)	Dibutyl-tin-dilaurate
4.	Prehydrolyzed tetraethoxysilane (TES-40)	Piperidine

0.5, 0.7, and 1.0 mm) thickness. The gelling time of the resulting samples were measured at 25°C in an air space saturated with piperidine vapor.

The relationship between the layers thickness and gelling time obtained is shown in Figure 2. Knowing the thickness of the oligomer layer the gelling time can be calculated using eq. (3) below. Using a linear least square fit the following equation was obtained with a regression coefficient of 0.9986:

$$t = 0.148 + 17.32 \cdot l \qquad (3)$$

Here, t is the gelling time at 25°C, and l is the siloxane oligomers layer thickness.

Measure of Amines Removing Time

The period needed to remove the initiator by airing after crosslinking was studied an follows: D = 20-mm discs were cut from the elastomer left on air hourly and were put to 10.00 cm^3 0.1M HCl solution for 1 h to extract the amine. The remaining acid content was titrated with 0.1M NaOH solution with phenolphtalein indicator. Results are summarized in Table III.

The data show that 2 h after networking process no initiator has been left. With increasing the airing intensity the airing time may be shorter (see Table IV), where (*) is the commercial available catalyst, respectively, TES-40 in the presence of 5%. Tests films with a 1-mm thickness were prepared, and after an aging period of 7 days discs with a diameter of 2 cm and a surface area of 3.14 cm^2 were cut out. Each test was made with five parallel samples.

Following a mass measurement with a 4 decimal point accuracy using an analytical balance, the samples were placed into solvents with different polarity (toluene, ethyl acetate, n-butanol, ethanol, and distilled water) and their mass was measured after 24, 48, and 72 h. The volume of the absorbed solvent was calculated using eq. (4):

$$V = \frac{m_{sw} - m_d}{V_d \cdot \delta_s} \cdot 100 \qquad (4)$$

where V is the relative volume of the solvent taken up (that is, the percentage increase in volume of the sample compared to that of the initial sample), m_{sw} is the mass of the sample in a given solvent after soaking for a given period, m_d is the mass of the "dry" sample, $_s$ is the density of a given solvent, and V_d is the volume of the "dry" sample.[9] The results can be seen in Table V.

Thermoanalitical Study of the Elastomers

To the thermoanalytical tests the silicone elastomer membranes were cut into pieces of about 1 $\times$ 1 mm. One hundred milligrams from these samples were tested in a derivatograph-type MOM OD2 using the simultaneous method of thermogravimetric analysis, differential thermogravimetry, or differential thermal analysis (TG, DTG,

Table V Solvent Uptake of Silicone Elastomers Made with the Use of Different Catalysts

	Solvent Uptake of Silicone Elastomers (%)				
Catalyst	Toluene	Ethyl Acetate	n-Butanol	Ethanol	Distilled Water
1.	197.2	100.5	1	2	0
2.	197.2	101.3	1	2	0
3.	198.0	100.0	1	2	0
4.	197.6	100.5	1	1.8	0

Table VI Thermoanalytical Data of Silicone Elastomers Cured with a Conventional Catalyst, T-47 (Sample 1), and a Gas-Phase Catalyst (Sample 2)

Step	A	B				C	
Parameters	Δm_{ev} (%)	T_{offset} (°C)	T_{max} (°C)	T_{DTA} (°C)	Δm_a (%)	T_{offset} (°C)	T_{max} (°C)
Sample 1	1.5	—	—	—	—	280	360
Sample 2	2.5	280	325	320	3.0	330	420

DTA, respectively). As reference material aluminium oxide was used in the same quantity as the sample. Recordings were made by means of platinum sample holders in static atmosphere with a heating up rate of 5°C per minute. The same test method was used to make the derivatograms of base polymers.[10]

The decomposition of the samples can be divided into three different steps (see Table VI). The first procedure (A), wich can be observed in both cases, is the evaporation of the volatile materials, which are absorbed on the surface, and those components have a low degree of polymerization. The observed weight loss was at approximately l (m/m)% higher in the case of sample 2. compared to sample 1, indicating the existence of short-chain oligomers of the dimethylsioxane. In the case of sample 2, a second process (B) can be observed on the thermoanalytical curves, due to the oxidative degradation of the polymer.[11] This is probably induced by small traces of the catalyst remaining after preparation. This weight change is reflected on the DTA curve with an exothermic heat effect. The third step is the depolymerization (C) of the samples, which can be seen on the thermoanalytical curves of the two samples. This takes place at a higher temperature in the case of sample 2 compared to sample 1.

CONCLUSIONS

We have developed a new method for crosslinking silicone oligomers. This process is suitable for the production of silicone elastomers for medical use. By use of this new method[12] we can mix the silicone oligomer and the other ingredients and store this mixture for a long time. Network formation starts only when the initiator vapor is in contact with the mixture. The gelling time can be changed by using different type of initiators. After network formation the initiator evaporates from the silicone elastomer.

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