A New Method for the Determination of a Hydrosilanization Inhibitor Applied to Measurements during Curing of a Silicone Elastomer

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ABSTRACT: A new method for the quantitative determination of the hydrosilylation inhibitor 1-ethynyl-1-cyclohexanol in a poly(dimethyl siloxane) matrix is presented. The method is based on headspace gas chromatography directly from the semisolid sample without solvent addition. The method was found to be both selective and sensitive. The relative standard deviation of the method was estimated to be 6%. The semisolid silicone sample was weighed directly in a headspace autosampler vial. After sample equilibration at 90°C for 1 h, the gas phase was injected into a gas chromatography system with a nonpolar methyl silicone capillary column. The inhibitor was detected with a flame ionization detector. The standard addition procedure was used for quantification. Recovery data on the inhibitor from the silicone during curing suggests that the inhibitor reacts with the silicone hydride crosslinker in the presence of the platinum catalyst to become part of the polymer network. This implies that the inhibitor will not migrate out from the silicone elastomer, which is a great advantage particularly for silicone elastomers used for medical devices or controlled drug release applications. © 2001 John Wiley & Sons, Inc. J Appl Polym Sci 79: 2349–2353, 2001

Key words: drug delivery; controlled drug release; poly(dimethyl siloxane); crosslinking; headspace gas chromatography

INTRODUCTION

Medical grades of silicone elastomers are found in many pharmaceutical and medical device applications.[1] For controlled drug release products the active drug substance has generally been incorporated into the silicone preelastomer followed by a curing step giving the final silicone matrix-based products.[2,3] Poly(dimethyl siloxane) polymers can be cured by peroxides such as benzoylperoxide. A second commonly used crosslinking mechanism is hydrosilylation or hydrosilation. The advantage of this curing process is that no by-products are produced.[4] Hydrosilylation crosslinking is performed by an addition reaction between methylvinyl siloxane and methylhydrogen siloxane groups with platinum as catalyst (Fig. 1).

To increase the shelf life, and to allow sufficient processing time for making an effective mix and storing the mixed material prior to curing, the manufacturer adds an inhibitor to the formulation. Different types of compounds containing an acetylenic group have been successfully used for this purpose.[5] As the silicone material is heated, this inhibition effect is lost or strongly reduced, and the curing reaction progresses rapidly.

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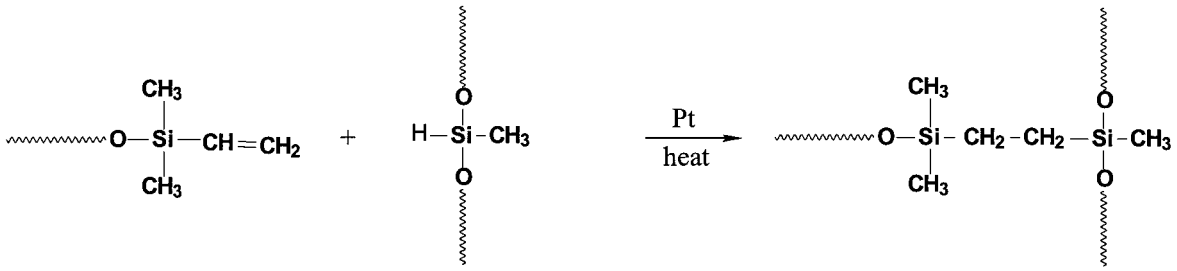

Figure 1 Curing of poly(dimethyl silicone) with the hydrosilylation reaction.

Q7-4735 is used, involving mixing on a two-roll mill followed by extrusion and curing in molds, it was found necessary to characterize the curing components in the silicone material.

The starting material consists of two parts of silicone preelastomers, Part A and Part B. Both parts are identical with regard to the main polymer composition, but they differ in the components for the crosslinking reaction. Part A contains the platinum catalyst, while Part B contains the silicone hydride crosslinker and the hydrosilylation inhibitor. The Pt content in the catalyst was quantified by atomic emission spectroscopy (ICP-AES). The silicone vinyl content in both Part A and Part B was measured with ^{1}H-NMR, and the silicone hydride amount was determined with both ^{1}H-NMR and infrared spectroscopy IR. No suitable method was found in the literature for the determination of the inhibitor in the silicone matrix. On the other hand, indirect methods were found where the curing rate was measured by, for example, rheometry, DSC, DMA, and IR.[6–9] However, these indirect measurements reflect not only the content of the curing components but also the presence of any substance that can poison the curing process, for example, amines, sulfur, nitrogen oxide, organotin compounds, and carbon monoxide.[10] Therefore, it was considered necessary to measure the content of the inhibitor itself. Different attempts to determine the inhibitor content by spectroscopy (NMR and IR) failed, probably because of the rather low amount of inhibitor in the silicone material. During the characterization by gas chromatography of oligomers in the Silastic® material, we found that the inhibitor present in Part B, 1-ethynyl-1-cyclohexanol (ETCH) eluted at a rather low temperature from the column. From this observation, we concluded that it should be possible to develop a headspace gas chromatography method.

In this article, we present a new method for the quantitative analysis of ETCH in Silastic® Q7-4735. In addition, we suggest a probable reaction path for the inhibitor during crosslinking of the silicone material.

EXPERIMENTAL

Samples and Chemicals

Different batches of the silicone preelastomer Silastic® Q7-4735 were obtained from Dow Corning, Sophia Antipolis Cedex, France. These samples were received in kits consisting of Part A, which contained the Pt catalyst, and Part B, which contained the crosslinker and inhibitor, 1-ethynyl-1-cyclohexanol (ETCH). The samples were received over a period of 1 year. As a reference substance, 1-ethynyl-1-cyclohexanol, purum quality, manufactured by Fluka Chemie AG, Switzerland, was used. In the system suitability test, octamethylcyclotetrasiloxane (D4) of 98% purity, from ABCR, Karlsruhe, Germany, was used.

Equipment

A headspace autosampler, Perkin-Elmer HS40, was coupled to a Hewlett Packard gas chromatograph, model 6890A, with a split/splitless injector and a flame ionization detector. The analogous signal from the flame ionization detector was processed by a Millennium 2020 chromatography data system from Waters. The capillary column (30 m $\times$ 0.32 mm) used was DB1 from J&W coated with 1 μm poly(dimethyl siloxane). For the identification of the unknown peaks in the GC chromatogram, a mass selective detector Model 5972A from Hewlett Packard replaced the flame ionization detector. The two parts of silicone material were mixed with a bench-top two-roll mixer (pasta blender), Atlas model 150, Marcato OMC.

Procedure

Approximately 10 g of sample were thoroughly mixed on the two-roll mixer. For each analysis, 1.00 $\pm$ 0.01 g of sample was placed in each of two 20-mL headspace vials. Ethanol (50 μL) was added to the first vial and 50 μL of a standard solution of ETCH (10 mg/mL) dissolved in ethanol

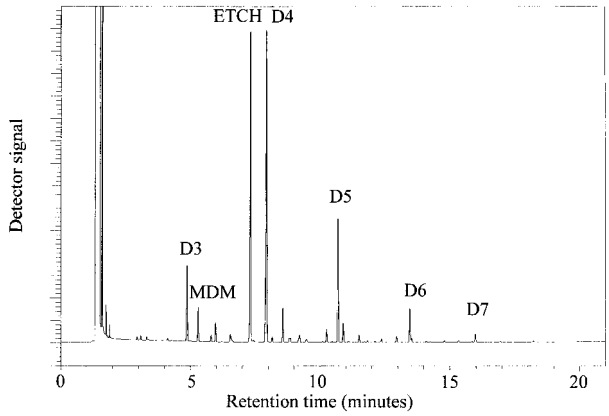

Figure 2 HS-GC chromatogram of Silastic Q7-4735 Part B, showing the inhibitor peak (ETCH) at approximately 7.5 min. D3–D7 show the peaks for the cyclic dimethyl siloxane oligomers, and MDM is the peak of the short linear oligomer octamethyltrisiloxane. Sample equilibrium for 60 min at 90°C.

was added to the second vial. After being sealed, the vials were put into the headspace autosampler. The headspace autosampler was set to a sample equilibrium temperature of 90°C for 60 min prior to injection into the gas chromatograph. The sampling needle and the transfer liner were set to 120°C and the applied pressure time was 1.0 min, the injection time 0.06 min and the needle withdrawl time 0.1 min. The gas chromatograph was programmed with an injection port temperature of 150°C and a detector temperature of 250°C. The column oven was set at 50°C for 1 min, and the temperature was then raised by 10°C/min to 250°C where it was kept constant for 1 min. The rate of flow of the helium carrier gas was approximately 2 mL/min. The peak areas for ETCH were determined for the sample with and without standard addition. The retention time for ETCH was approximately 8 min. A standard addition plot was constructed, and the amount of ETCH was calculated.

Prior to the analysis of the inhibitor, a system suitability test was performed to verify that the headspace gas chromatographic system had the expected performance. Fifty microliters of a solution of ETCH (0.5 mg/mL) and the cyclic silicone oligomer, D4 (0.3 mg/mL), was transferred to a headspace vial. After the vial has been sealed, an analysis of the mixture was performed according to the conditions for the silicone material described above except that the equilibration time was reduced to 10 min.

RESULTS

Measurement of the gas phase of the silicone sample takes advantage of the relative high vapor pressure of ETCH. The GC column used mainly separates substances according to their vapor pressures. It can be seen in a typical chromatogram from a sample without standard addition (Fig. 2) that the ETCH peak is one of the first eluting larger peaks. The figure also shows that other volatile substances are present in the sample. To identify these peaks, the mass selective detector was used. The interpretations of the mass spectra show a positive identification for 1-ethynyl-1-cyclohexanol for the peak at approximately 8 min. All other peaks were found to be different species of silicone compounds. The largest peaks were interpreted as being linear and cyclic oligomers of dimethylsiloxane, while many of the smaller peaks were related to the methyl silicone hydride crosslinker. For comparison, Figure 3 shows a chromatogram of Part A, which contains the platinum catalyst dissolved in low molecular mass vinyl-containing silicone oil. No ethanol was added to this sample. In this chromatogram, only the short linear and cyclic oligomers of poly(dimethyl siloxanes) can be found, apart from the first peak, which was related to the vinyl-containing silicone oil. No peak was eluted at the retention time for ETCH. Moreover, the mass spectrum of the ETCH peak from Part B was found to be free from any silicone compounds, i.e., the chromatographic method completely separates ETCH from other volatile compounds present in the sample.

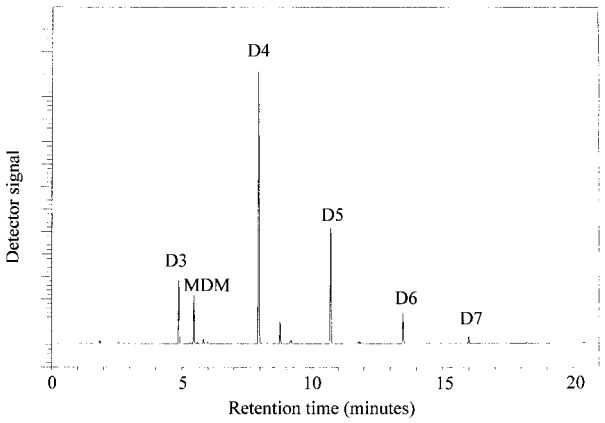

Figure 3 HS-GC chromatogram of Silastic Q7-4735 Part A showing the peaks for the cyclic dimethyl siloxane oligomers D3–D7, and MDM is the peak of the short linear oligomer octamethyltrisiloxane. Sample equilibrium for 60 min at 90°C.

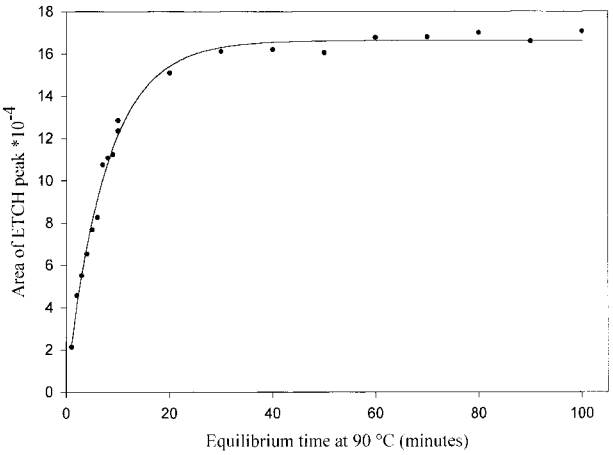

Figure 4 Peak area for ETCH in Silastic Q7-4735 Part B without standard addition vs. for sample equilibrium time at 90°C.

The time for a volatile solute to equilibrate between the solid phase and the gas phase is normally very long for solid samples. Attempts were, therefore, initially made to dissolve the semisolid silicone sample in different solvents. However, it was found that the sensitivity to ETCH became low using this approach. In addition, the procedure was very time-consuming, as the silicone material required a long time to dissolve. An investigation was, therefore, carried out to determine the time required for ETCH to equilibrate between the solid and gas phase using the sample as it is. After a few initial experiments with different equilibrium temperatures, the sample equilibration temperature was set to +90°C. This temperature was chosen as a compromise between different effects. To ensure sufficient sensitivity for ETCH, the temperature should be as high as possible. On the other hand, to avoid degradation of ETCH the equilibrium temperature should be as low as possible. Also, the higher the temperature, the higher volatile silicone oligomers would be injected into the column, and this would result in column bleeding, and in the worst case changes in the column performance. As shown in Figure 4, it was found that the peak area for ETCH reaches a maximum value within approximately 60 min. In addition, the figure also shows that the peak area was constant over the period 60–100 min, i.e., these seems to be no degradation of ETCH in the sample matrix consisting of reactive vinyl and hydride groups.

The precision of the method was estimated from duplicate analyses. Twelve different samples were analyzed on 12 different occasions. The relative standard deviation was estimated to be 6%. The contents of ETCH in these samples were found to be in the range of 0.4 to 0.6 mg/g. The linearity of the method was examined by making several standard additions to a sample with increasing concentrations of ETCH. Figure 5 shows a graph where four standard additions have been made to one sample. A good linear relationship was found within the examined concentration range that covers an ETCH content up to at least 1%.

The headspace method was also used to monitor the amount of ETCH in the sample during the crosslinking reaction, i.e., the addition reaction between vinyl and hydride groups. It was found that ETCH was stable in the headspace vial at 90°C both in Part B alone and also in Part A with separately added ETCH in the presence of platinum. In addition, by measuring the area for the cyclic oligomer D4 in the samples, it was found that the relationship between the area for ETCH and the area for D4 was constant over the investigated thermostat period of 2–100 min. This means that D4 could be used as an internal standard for ETCH. This observation was used when the mixture of Part A and Part B was analyzed for relative ETCH content.

Figure 6 shows that the ETCH content rapidly decreased in the sample at an equilibration temperature of 90°C as the silicone crosslinked. Because this effect is not seen when Part A (with added ETCH) and Part B are analyzed separately, the probable reason for the loss seen in the mixture of Part A and Part B is that ETCH reacts with the silicone hydride with platinum as the catalyst in the same way as in the silicone vinyl–silicone hydride addition reaction. Thus, ETCH

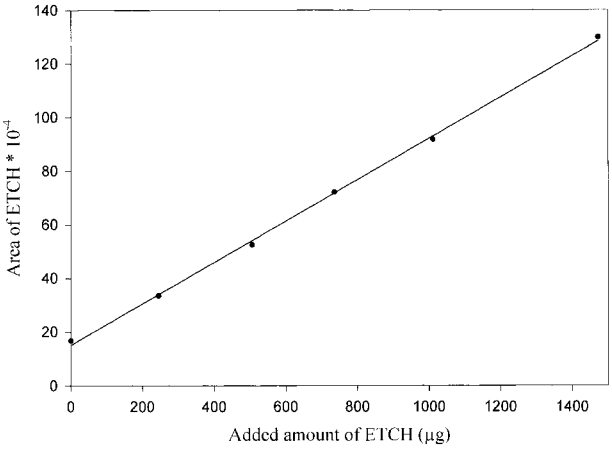

Figure 5 Peak area for ETCH with different amounts of standard additions to the sample. Sample equilibrium for 60 min at 90°C.

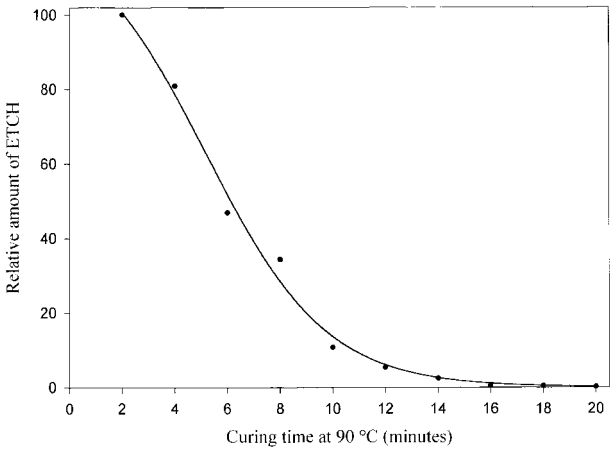

Figure 6 Relative amount of ETCH in mixture of Part A and Part B vs. time of curing at 90°C vs. equilibrium time, expressed as peak area for ETCH divided by peak area of the cyclic oligomer of dimethyl siloxane, D4.

becomes incorporated into the silicone matrix on curing.

DISCUSSION

The method for the quantitative determination of the hydrosilylation inhibitor 1-ethynyl-1-cyclohexanol in Silastic® Q7-4735 described in this article was found to be both sensitive and selective. The relative standard deviation of the method was estimated to be 6%. This reflects the sum of the variations in, for example, weighing, volume of added standard, and the final headspace chromatographic determination. The disadvantage of the rather long equilibration time of 1 h for the semisolid silicone material prior to injection is easily overcome due to the very simple and easy sample preparation and the use of automatic headspace equipment. In addition, no time has to be spent on dissolving the sample, which would be quite time-consuming for this type of high molecular mass polymer. Furthermore, there is, of course, an advantage in using an almost solvent-free method from an environmental point of view.

Quantification methods for the other components in the crosslinking system, platinum catalyst, silicone hydride, and silicone vinyl groups are well known,[11] but a suitable specific quantification method for the inhibitor has been lacking. This new method for measurement of the curing inhibitor can be used for better characterization of the silicone preelastomers, as the amount of this inhibitor substance has a great influence on the curing characteristics of the silicone material. Measurements of similar volatile inhibitors in silicone materials can probably be made with the same headspace technique, perhaps with other instrumental settings.

The curing of the silicone material described in this article was performed in a gas-tight system. However, on a production scale with a time lag from mixing on a two-roll mill to curing in molds, some part of the inhibitor will be lost by evaporation. Our conclusion is that the inhibitor reacts with the crosslinker methyl silicone hydride in the presence of platinum. The same type of reaction has been proposed earlier in an addition reaction between acetylene and trichlorosilane in the presence of a transition metal.[12] Therefore, the inhibitor remaining in the final silicone elastomer is probably trapped in the silicone network as it reacts with the multifunctional crosslinker. In conclusion, it is unlikely that there will be any migration of the inhibitor from the silicone elastomer, which is of great importance when the silicone elastomer is used in any medical device or drug delivery system.

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