

DEVELOPMENT OF A NEW SILICONE BASE TRANSDERMAL SYSTEM

III. Study of thermal properties of silicone elastomers containing liquid ingredients

Ö. Wagner¹, G. Kenessey² and G. Liptay¹

¹Department of Inorganic Chemistry, Technical University of Budapest, Szt. Gellért tér 4
H-1521 Budapest

²MOL Hungarian Oil and Gas Co., LPG Division, P.O. Box 22, H-1502 Budapest, Hungary

Abstract

In present work we have investigated the commonly used base silicone elastomers namely cured poly-dimethyl-siloxanes and the change of the inner polarity of silicone elastomers containing various amounts of polar liquid ingredients and trifunctional silicone additives. It was shown that the polarity of the inside of the matrix is related to the diffusion properties of model substances and thermal properties of silicone elastomers. The ingredients used have changed the matrix framework, that was influenced by the type of trifunctional additive too. These properties show large dependence on the timing of the measurement. Measurements carried out after 48 hour of the production of the polymer showed reproducible properties, indicating that the final structure of the polymer has been formed.

These results show that the ingredients influence the properties of the silicone matrices considerably, thus the characteristics of the drug release of pharmaceutical forms can be varied too.

Keywords: diffusion coefficient in the silicone elastomers, liquid ingredients, poly-dimethyl-siloxane elastomers, trifunctional silicone additives

Introduction

As the result of pharmaceutical technology research a new drug type, the Transdermal Therapeutic System (TTS), emerged in pharmaceutical technology in the early 1970's. This new drug type releases its active ingredient through the patient's skin approaching a rather uniform blood level. In addition, since the active ingredient moves with the blood stream directly into the targeted organ, the effective dose can be lower than that in the traditional drug types [1–3]. Several forms of TTSS have been developed during the recent years [4–6], which may be divided into two major groups. In the first case the optimal degree of release of the active ingredient is provided by the plaster base and the plaster structure together, and in the second case by a special microporous or non-porous membrane. In the present work the objective was to select silicone elastomers that will allow the development of a new TTS with the optimal characteristics. It is known, that silicone elastomers are hydrophobic and impermeable to ions. It is however, important from technological point

of view to measure the effect of different liquid additives on this hydrophobic property. In this case we can make polymer films be able to deliver polar drugs.

Materials and methods

The silicone oligomers R-1, R-5, R-18, R-38 (the number used in the product code indicates the viscosity of the oligomer with Pa.s) and the poly-dimethyl-siloxane oil /M 350/ (Szilor Kft, Budapest, Hungary) have been selected for the test. The catalyst used for networking process was T-47 (Wacker Chemie GmbH, München, Germany). It contains polyalkoxy-silane as the cross-linking compound and organic tin compound as the cross-linking initiator. The T-47 was mixed in a quantity of 5% into the oligomer and/or oligomer-additive mixtures, then the mixtures were cross-linked at 25°C by spreading them on Teflon plates at a thickness of 0.4 and 1.0 mm. The dry glycerine and propylene glycol used were Ph Hg VII. degree, the ethylene glycol was analytical purity (Reanal Finechemical Factory, Budapest, Hungary) and the polyethylene glycole (PEG 400) was PLURIOL E 400 (BASF, Ludwigshafen, Germany). The silicone oil (M 350) used has 350 mPa.s viscosity.

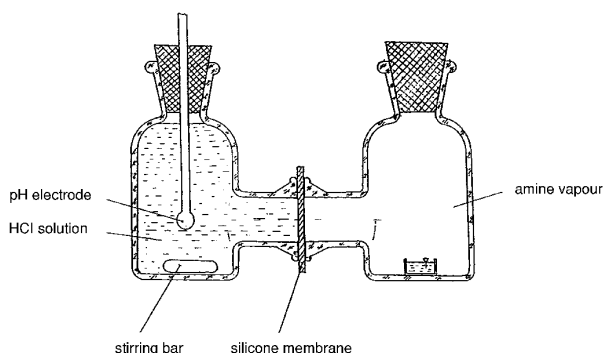


Fig. 1 Apparatus for determination the diffusion coefficient of ethyl amine in the silicone membrane

The diffusion coefficients of the model-substance ethyl amine in the silicone elastomer membranes were determined. We have separated the liquid and gas phase in the experimental apparatus (Fig. 1) with the investigated silicone membrane. The aqueous phase stirred continuously have consisted of a 0.001 M HCl solution. We have measured the pH-change of the liquid phase. In this system, a plot of pH vs. t gave a straight line as described in [7]. Extrapolating the line to the X-axis gave the time-lag, t_1 . The diffusion coefficient (D) was then calculated [8] from the following Eq. (2), (where: l is the membrane thickness, t_1 is the time-lag):

$$D = \frac{l^2}{6t_1} \quad (2)$$

The data of the parallel samples were averaged, and later on these averaged data are shown. Deviation of the parallel samples has not in a single case exceeded 3%.

To the thermoanalytical tests the silicone elastomer membranes were cut into pieces of about 1×1 mm. 100 mg from these samples were tested in a derivatograph type MOM OD2 using the simultaneous method (TG, DTG, DTA). As reference material α -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.

Thermoanalytical study

As it has been stated in our study mentioned above, the R-1 and R-5 samples have two exothermic events. The mass reduction of 2–2.5% observed until the first decomposition event is due to the exit of the small amount of volatile components absorbed on the surface and/or contained by the matrix. At 295°C a significant mass reduction of 8% was observed and this was followed at 350°C by the thermic degra-

Table 1 Thermoanalytical data of the elastomers

Additives	Concentration/%	$\Delta m/\%$	
		I/	II/
Glycerine	3	1.0	10.0
	5	4.0	9.0
	10	5.5	9.5
PEG 400	3	2.5	12.5
	5	3.0	14.5
	10	5.0	32.0
Propylene glycol	3	1.0	3.0
	5	1.5	4.5
	10	3.0	8.5
Glycerine	10		
MTS	5	5.0	–
PEG 400	10		
MTS	5	5.0	–
Propylene glycol	10		
MTS	5	4.5	47.0
Glycerine	10		
GF 91	5	5.5	25.0
PEG 400	10		
GF 91	5	5.0	44.0
Propylene glycol	10		
GF 91	5	3.5	44.5

dation of the matrix. The recordings of samples made from R-18 and R-38 did not show the first thermic event observed in the previous samples, only the continuous mass reduction due to the exit of volatile components (5.75 and 4.25%) and then the exothermic mass reduction due to the degradation of the structure at 364 and at 360°C [9].

The thermal decomposition of the additive containing samples (Table 1) starts with the release of the non-bonded and physically adsorbed additive (I). The mass loss of this procedure increases with the increasing concentration of the additives. This first step is followed by the thermal oxidation (II).

By adding glycerine at 3, 5 and 10% to the base elastomers the appearance of a new step for thermobalance was observed between 80 and 220°C (I). The size of mass reduction increased when the additives were added in larger amounts, but each particular mass reduction was always below the actual concentration value. At the same time the mass reduction observed for base elastomers increased by about 1.5 to 2%. The sum of partial processes I and II amounted approximately to the sum of the concentration of the additives used and that of the mass reduction observed during the testing of base elastomers. On the basis of these results it can be concluded that glycerine at 1.5 to 2% can be incorporated into the matrix structure and quantities greater than this is linked only with very weak interactions.

The sum of the mass changes observed in step I and II is around the amount of the additive used with the exception of polyethylene glycol 400, where the step II. led to 3–4 times larger mass change than expected probably due to an oxidative process.

In the case of 5% MTS and 10% glycerine containing sample the thermal oxidation has been reduced and only a thermal degradation follows the evaporation of the volatile and absorbed materials. Although the thermal decomposition scheme of the 5% GF 91 and 10% glycerine containing sample is similar to that of the sample containing only 10% glycerine, the mass changes corresponding to step I. and II. increase from 4.5 to 5.5 % and from 10.0 to 25.0 % (m/m) respectively.

In the case of 5% MTS and 10% polyethylene glycol 400 containing sample the initial mass change remained 5% (m/m), however the amount of the thermal oxidation is negligible and only the thermal degradation occurs on the thermal curves. The peak maximum corresponding to the thermal decomposition shifted down to 290°C in the case of GF 91 containing sample comparing to that of the sample containing only polyethylene glycol 400 (340°C) and polyethylene glycol 400 and MTS (330°C).

In the case of 5% MTS or GF 91 and 10% propylene glycol containing samples the starting mass loss is slightly higher than in the 10% propylene glycol containing sample. The mass change corresponding to thermal oxidation increases up to 44.5–47.0% (m/m) and shifted down to 175–250°C. In the case of the GF 91 containing sample an endothermic effect occurs on the DTA curve having a maximum at 60°C.

Investigation of diffusion coefficients

The results of the investigation of the diffusion coefficients supported the results of thermoanalytical study (Table 2). The diffusion properties of ethyl amine did not change in the presence of polydimethyl-siloxane oil. The polarity of the silicone elastomer is the same than the polarity of the silicone oil containing elastomer.

Table 2 Diffusion coefficients of ethyl amine in various amount ingredients containing silicone elastomers

Sample	Diffusion coefficient $D/\text{mm}^2 \text{s}^{-1}$
R5	$6.7 \cdot 10^{-5}$
+3% M 350	$6.3 \cdot 10^{-5}$
+5% M 350	$6.2 \cdot 10^{-5}$
+10% M 350	$7.2 \cdot 10^{-5}$
+3% propylene glycol	$6.3 \cdot 10^{-5}$
+5% propylene glycol	$6.2 \cdot 10^{-5}$
+10% propylene glycol	$5.6 \cdot 10^{-5}$
+3% glycerine	$7.0 \cdot 10^{-5}$
+5% glycerine	$7.7 \cdot 10^{-5}$
+10% glycerine	$8.3 \cdot 10^{-5}$
+3% PEG 400	$1.1 \cdot 10^{-4}$
+5% PEG 400	$1.3 \cdot 10^{-4}$
+10% PEG 400	$1.7 \cdot 10^{-4}$
+10% Propylene glycol + 5% MTS	$2.5 \cdot 10^{-5}$
+10% Glycerine + 5% MTS	$6.4 \cdot 10^{-5}$
+10% PEG 400 + 5% MTS	$8.7 \cdot 10^{-5}$
+10% Propylene glycol + 5% GF 91	$4.1 \cdot 10^{-5}$
+10% Glycerine + 5% GF 91	$5.8 \cdot 10^{-5}$
+10% PEG 400 + GF 91	$2.8 \cdot 10^{-5}$

The diffusion coefficient in the PEG 400 containing elastomer is larger than in the base elastomer and increases with the increasing concentration of the ingredient. The large polar polymer stretches the apolar structure of the elastomer thus the polar amine can diffuse across the matrix more easily. The curing process in presence of MTS produced a more compact structure and this resulted in a smaller diffusion coefficient. The polar macromolecule sorted out from the apolar group containing elastomer structure and this process resulted a decreased diffusion coefficient.

The glycerine built into the structure of the silicone elastomer and the presence of physically bonded glycerine increased the value of the ethyl amines diffusion coefficient. The networking process in the presence of MTS resulted a compact structure and the amine has the same diffusion coefficient in this elastomer than in the base elastomer. The physically bonded glycerine diffused from the polar aminoethyl-aminopropyl-group of the GF 91 into the elastomer. This process resulted a homogeneous, opalic elastomer and the amine has a slightly decreased diffusion coefficient in this matrix.

Elastomer with propylene glycol built into the matrix structure reveals for ethyl amine a nearly equal diffusion coefficient compared to the value obtained in the base

elastomer. Use of trifunctional additives resulted in a significant decrease of the ethyl amines diffusion coefficient.

Conclusions

The amount of the additive built into the structure of elastomer may be suggested on the basis of the study for the solvent uptake which had been previously investigated [10]. Another investigation was concerning the diffusion coefficient and the mass changes observed during thermal decomposition. In case of glycerine 1.5–2% of additive may covalent be integrated into the poly-dimethyl-siloxane chain, however, in case of polyethylene glycol 400 these values are in the range 2.0–5.0 % respectively.

Because the amount of the chemically bonded ingredient is lower in case of glycerine, we suggest that only one hydroxyl group may react with the poly-dimethyl-siloxane chain. The low number of OH group in polyethylene glycol led to a larger amount of ingredient bonded. The highest level of chemical absorption is observed in the case of propylene glycol. We suggest that only one hydroxyl group is bonded in the case of glycerine. The elastomer containing less polar groups reveal lower diffusion properties for ethyl amine as compared to elastomers containing glycerine.

The use of trifunctional silane additives results in a change of the matrix's structure. The use of apolar methyltrimethoxy silane caused a more compact matrix structure, but in the case of GF 91 resulted a homogeneous dispersion of the ingredients.

These tests could support our original assumption that not only the viscosity of the oligomers, but the time elapsed between preparation and testing, namely the time necessary for the matrix structure to reach practically an equilibrium, or in other words the final development of the matrix structure, and also the additive applied influences the polarity characteristics of a silicone elastomer matrix. The polar ingredients used in the tests were integrated both chemically and physically in the inside of the matrix structure, significantly modifying its characteristics.

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