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A New Method for Diffusion Measurement in Polymeric Films Based on a Stacked Sheet Concept

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Purpose. To develop and evaluate a simple, yet well defined, method to measure diffusion in semi-solids, i.e. polymeric materials.
Method. The method was based on a concept where equivalent discs of polymeric films were cut and stacked on top of each other. The diffusion process was allowed to proceed unidimensionaly through the stack of films perpendicular to the film surface. After an appropriate time, the stack was analysed disc by disc with respect to solute content and from the concentration profile so obtained the diffusion coefficient was calculated.
Results. An all-in-one device was developed, manufactured in stainless-steel, that cuts circular discs and stores each one successively in a "stack" in the cell compartment.
Conclusions. Data from a silicone based system shows that the method, although simple, is accurate and reproducible.

KEY WORDS: diffusion measurements; semi-solids; polymer matrixes.

INTRODUCTION

In many applications it is important to have precise information about the diffusion process in dense materials like polymeric films and matrices. This is essentially equivalent to a knowledge of the diffusion coefficient in the material. Normally the measurement of diffusion coefficients in films is performed indirectly. The polymer film is placed so as to separate a liquid solution of the solute in question from the corresponding solvent. The change in concentration on the solution and on the solvent side of the film, respectively, is monitored as a function of time and this change is used to calculate the diffusion coefficient of solute in the polymer membrane. The technique described, although simple, has several drawbacks. For instance, the calculations are based on the assumption of an equilibrium between the surface of the film and the solution in contact with it. The solubility of the solute in the film is normally different from that in the liquid and a distribution is set up at the liquid/membrane interface that "distorts" the concentration gradient in the membrane in an unknown way. Furthermore, no matter how carefully the stirring is arranged, there will always be a thin layer of liquid on both sides of the film with a noticeable concentration gradient that also contributes in the regulation of the overall flow rate. Hence this indirect technique is less suited for an absolute determination of diffusion coefficients. In the past, specific methods, such as photobleaching (1) have been used to overcome these inherent difficulties of the membrane permeation technique. Various optical methods based on refractive index or light absorption or light emission have also been utilised (2,3). They require, however, non-opaque materials and specific properties of the solute (fluorescence, strong light absorption, etc.). The present paper describes a fairly general, yet simple, method by which the diffusion coefficient can be determined in solid and semisolid materials in the form of a film.

GENERAL PRINCIPLE

The principle of the method is the following. From a homogeneous sheet of film a number of equal circular discs are punched out. One of them is "loaded" with the solute for which the diffusion coefficient is to be determined. The non-loaded discs are stacked on top of the loaded one. In order to give good contact between successive discs the entire "sandwich" is pressed together inside a metal cylinder. This device is allowed to stand at constant temperature for a sufficient time to allow the solute to diffuse from the loaded disc a certain distance into the stack. When the experiment is finished, the stack is pushed out of the cylinder and each disc is analysed for solute content. Since the thickness of each disc is known, this gives for discrete points in the diffusion direction the concentration profile in absolute units. For the geometry in question the mathematical form of the concentration profile is well known for the continuous case (4) and hence the diffusion coefficient can easily be calculated by standard techniques assuming that the discrete experimental data fit the continuous solution. The method described is especially suited for the study of slow diffusion transport in fairly dense materials. In certain aspects it is similar to previously published techniques for the measurement of diffusion in gel slabs (5) and dye penetration into plastic films (6). Penetration studies into human skin have also been performed by a somewhat similar principle (7), although no quantitative evaluation of diffusion coefficients were performed. The advantage of using pre-cut film or sheet discs in a stacked configuration over using a homogeneous block, which is sliced after the diffusion process, is quite obvious, since uniform slices with known geometry are not easily accomplished due to deformation in the slicing procedure. A monolithic stainless steel cell will be described, which allows both the punching and the storage of the stack. Some typical results will also be presented for the diffusion of the hormone estradiol in an elastomer.

THEORY

The geometry of the stacked disc system, as described above, corresponds to unidimensional semiinfinite free diffusion from an infinitely thin initial source. For this geometry the mathematical solution of Fick's second law is well known and becomes fairly simple if the diffusion coefficient, D, can be assumed to be independent of concentration and of position in the film (4). This should be a very appropriate assumption in most experimental studies and is certainly valid for the experiments discussed later in this paper. If the position coordi-

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nate (perpendicular to the disc surface) is denoted x, with $x \geq 0$, the initial conditions for the solute concentration distribution in the discs, $c(x,t)$ are given by

$$c(0,0) = C_0$$

$$c(x,0) = 0, \quad x > 0$$

and the solution of Fick's second law becomes (4)

$$c(x,t) = C_0 \mathrm{erfc}\left\{\frac{x}{2\sqrt{Dt}}\right\} \tag{1}$$

From an experiment with the stacked disc system one obtains after analysis of the disc contents a set $\{c_i\}$ of discrete values $c(x_i,t)$ where "i" denotes the disc number and "t" the duration of the experiment. The value of D and C_0 can then be obtained by fitting Equation (1) by a least squares procedure to the data set $\{c_i\}$, minimising the sum of residuals. Standard mathematical and calculation software, such as MATLAB® or MS EXCEL®, can be employed for fitting the theoretical profile to the experimental data. Results for two experiments obtained under identical conditions, except for the thickness of the discs, are presented in Figures 2 and 3. The deviation of experimental points from the fitted curve is also shown. Obviously the experimental points follow the fitted curve—Equation (1)—very closely with an average deviation of only a few per cent relative to the value of C_0. Equation (1) for the concentration distribution holds as long as C_0 can be regarded as a constant. This requires of course a sufficiently dense "source" of diffusion material at $x = 0$. In a standard polymeric system C_0 could be regarded as the solubility. In the more complex cases presented here as illustrations, it is sufficient to treat C_0 as an integration constant. From the form of Equation (1) it is obvious that as long as C_0 remains constant—for all x and t combinations—the actual value of C_0 does not affect the value of the "form" parameter D. In accord with all similar methods for the treatment of diffusion data (see e.g. (8)) it is essential that the fitting procedure is designed in such a way that the c-values for large values of x approach a proper "baseline". For the case with initially empty discs this means that the values should approach zero within experimental error.

MATERIALS AND METHODS

Diffusion Cell

The diffusion cell was constructed from stainless steel and with cylindrical symmetry, which greatly simplifies its manufacturing, see Fig. 1. The following parts can be identified: A bottom part, B, that supports the stack; a cylinder, C, with a sharp cutting edge to cut the film into properly sized discs that remain inside the cylinder; a piston, P, that runs within the cylinder and by which the discs are pressed firmly together; a top, T, to fit on the piston top, and finally a fixture, F, to hold the device in place. This fixture is provided with a top screw, S, to allow a slight pressure to be applied. The ring, R, in the top part is included to guide the pressure applied to the top plate, T. The O-rings allow appropriate decoupling of the force on the piston from that on the cylinder. The cylinder, with the piston kept inside, is used as a tool for cutting successive elastomer discs. Once cut, the disc is left inside the cylinder. During cutting, a moderate pressure is applied "by hand" on the piston to ensure good contact between successive discs along the total surface area. The design is thus mechanically very simple and can easily be machined in a lathe with straightforward tool settings. The piston, P, measures in our device 25 mm in diameter. The wall thickness of the cylinder is of the order of 4 mm. The height of the cylinder and the piston allow a total thickness of compressed discs of the order of 10 mm. This thickness can be changed by shifting to a thicker ring, R. The dimensions given can of course be varied within certain limits. It is essential for the precision of the measurements, however, that the volume of each disc is large enough to allow a sufficient analysis precision for the solute concentration determination. Furthermore, the discs should have a sufficient area to allow a proper smoothing of spatial variations in the film properties.

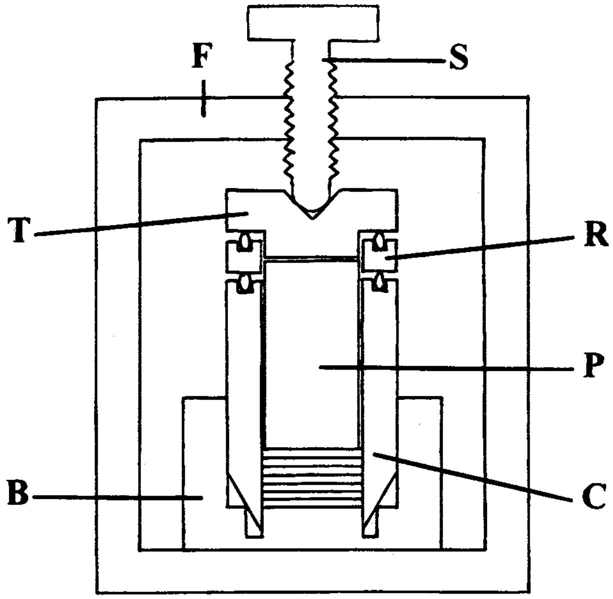

Fig. 1. Idealised machine drawing of the cell. For description of the parts refer to the main text.

Preparation of Elastomer

The silicone elastomer samples, kindly provided by Pharmacia Pharmaceuticals, Uppsala, Sweden, were divided into two parts (pre-elastomers). Part A contained PDMS and the polymerisation catalyst, and part B contained PDMS, a crosslinking agent and a reaction inhibitor. Apart from the components indicated, both parts contained silica. Part A and part B of each elastomer were carefully blended together, in some cases manually using a glass bottle and a glass plate, in the other cases using a two-roll roller-mill. In each case blending was achieved in a controlled and reproducible manner with respect to total time and numbers of mixing (material turnovers). The curing was done, in the case of elastomer mixed manually, by placing the elastomer in an aluminium block at room temperature and then placing the molding block between two preheated iron blocks, all kept in an oven at 200°C for 150 seconds. The elastomer was kept in the molding block for another 15 minutes to allow for a rapid postcure process to come to equilibrium. In the cases where the elastomer was blended in the roller-mill it was cured by means of a hydraulic press between two stainless-steel plates. In the hydraulic press the curing elastomer was kept under pressure for 90 seconds at a temperature of 120°C, whereafter the cured sheet was promptly removed from the hot steel plates. A sample of PDMS membrane with a silica content of 3% (w/w) was made by Dow Corning©, Valbonne, France, and was used as provided. Prior to use in the diffusion experiments, the elastomer sheets were conditioned at a specified humidity of approximately 60% RH and 100% RH, respectively, and at 25°C.

Measurement and Analysis

Discs were cut from the conditioned elastomer sheets as described. The last disc was loaded with the diffusant, in this case estradiol. To ensure an "infinite" source condition, this estradiol loaded disc contained an estradiol suspension giving an overall concentration in the disc much above the expected solubility of estradiol in the elastomer phase. The equipment, mounted with the stack of discs inside, was stored in a hygrostat, at a controlled temperature, for an appropriate time and was then dismantled. Each disc was weighed and the thickness measured, before being placed in the extraction medium. The extraction was allowed to proceed for at least 12 hrs in a test tube. The extract was removed from the test tube and poured into a new one. The volatile extraction medium was evaporated by means of flowing nitrogen gas and at a slightly raised temperature. The remaining substances, estradiol, the internal standard and some extracted silicone fluids were then dissolved in an eluent medium suited for chromatographic analysis and centrifuged. The supernatant was carefully removed and placed in a small vial adequate for the HPLC-sampler. The concentration of estradiol in each elastomer disc was calculated from the chromatographic data. An estimation of the approximate maximum sum of all errors was made by calculating the variance in the C_0-value calculated from twenty-two separate runs, all on the same elastomer/penetrant system. For a confidence level of 95% the estimated variation in C_0 was ± 0,5 μg/g, which for a value $C_0 = 10$ or higher, cf. table 1, gives an error of 5% or less. This confidence interval, in absolute units, was taken to hold for each analytically determined solute concentration and indicated in Figure 2 and 3 as errorbars. The errors arising from position measurements are well below 1% and can be left out of consideration.

RESULTS AND DISCUSSION

Data from two diffusion experiments with the equipment described, selected from a number of similar ones, are presented in Figures 2 and 3. Obviously the experimental points agree quite well with the curve fitted according to Equation (1). The two experiments were performed under identical conditions except that the discs for the experiment in Figure 2 were approximately twice as thick as those for the experiment in Figure 3. The fitted curve in Figure 2 gave $C_0 = 13.9$ μg/g and $D = 4.3_3 \cdot 10^{-12}$ m²/s and that in figure 3, a $C_0 = 14.3$ μg/g and

Table I. Experimental Data for Some Elastomer-Solute Systems Investigated

Elastomer	Condition	$D_{app} \cdot 10^{12}$/ m^2 sec^{-1}	C_{0app}/μg g^{-1} (elastomer)
PDMS 3%[b]	60% RH	10.3	9
Q7-4735	60% RH	4.0	20
Q7-4735	97% RH	4.4[a]	14[a]
Q7-4765	60% RH	0.9	52

Note: See the main text for details.
[a] See Fig. 2 and 3.
[b] Provided by Dow Corning©, Valbonne, France, silica content 3% (w/w).

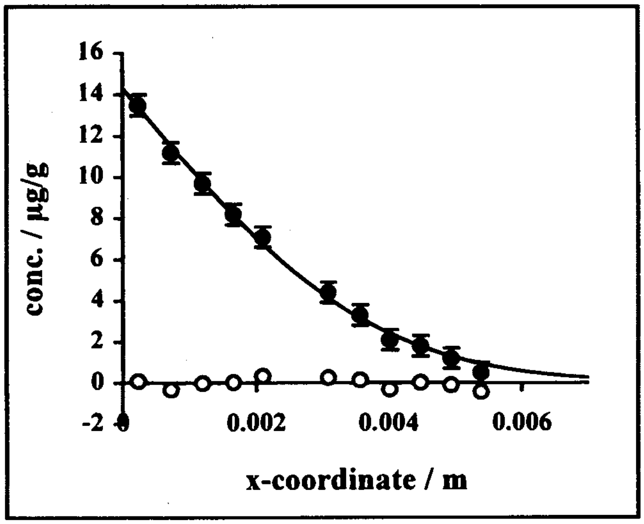

Fig. 2. Concentration profile of estradiol in elastomer (Q7-4735) after diffusing for 949980 seconds (11 days) in a stack of thin sheets, approximately 0.5 mm each, at 25°C and 97% relative humidity. The axis of ordinates express the concentration of estradiol within the elastomer as μg estradiol per g elastomer. Experimental data shown as ●, data fitted according to equation (1) as —, and the deviation between experimental and fitted data denoted by ○.

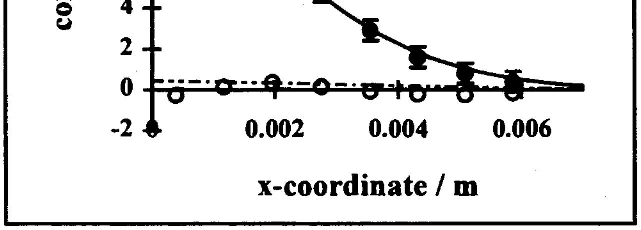

Fig. 3. Concentration profile of estradiol in elastomer (Q7-4735) after diffusing for 949980 seconds (11 days) in a stack of thicker sheets, approximately 0.8 mm each, at 25°C and 97% relative humidity. The axis of ordinates express the concentration of estradiol within the elastomer as μg estradiol per g elastomer. Experimental data shown as ●, data fitted according to equation (1) as —, and the deviation between experimental and fitted data denoted by ○. Shown is also the difference between the fitted data in figure 2 and figure 3, -----.

$D = 4.5_0 \cdot 10^{-12}$ m²/s. Thus the values of C_0 and D in the two experiments agree to better than 2% which must be considered as a very good result. This result also indicates that doubling the number of disc interfaces per unit length in the diffusion direction does not affect the resulting value of D within experimental error. Hence there does not seem to be any boundary effect introduced by the disc surfaces, which further validates the method. As an example of the applicability of the method, the diffusion coefficient, D, and the integration parameter (apparent solubility), C_0, of estradiol in an elastomer have been determined for three different elastomer samples, differing as to the content of silica. Samples Q7-4735 and Q7-4765 had silica contents of approximately 24 % (w/w) and 37 % (w/w), respectively, both values being slightly overestimated due to analytical difficulties. A third sample, provided by Dow Corning©, Valbonne, France, had a silica content of 3% (w/w). The sample Q7-4735 was also tested for effects of humidity as a parameter of storage conditions. The results are presented in Table I. Figures 2 and 3 correspond to sample Q7-4735 at 97% relative humidity (RH). From these results it is obvious that for well defined conditions the reproducibility of both D and C_0 is very good. Furthermore, variations in experimental conditions, like relative humidity and silica content of the elastomer, lead to values of D and C_0 that can be related to these experimental conditions. Increasing RH from 60% to 97% increases D only slightly whereas C_0 is decreased by 30%. If, however, the relative humidity is kept constant whereas the silica content is increased from 24% to 37%, the apparent diffusion coefficient, i.e. the D-value calculated from equation (1), drops by a factor of four, and C_0 increases almost by the same factor. This shows that the method can be used to monitor material properties.

The literature concerning measurements of diffusion coefficients of estradiol in silicone elastomers is sparse. Bloch et al (9) has presented data on diffusion coefficients of estradiol in Silastic 382® (Dow Corning©) and at 25°C obtained values ranging from $1.75 \cdot 10^{-13}$ to $1.15 \cdot 10^{-12}$ m² sec⁻¹. These values were obtained by two different methods, a time-lag method and a sorption kinetics method. Like the method described here, both these methods measures diffusion in a non-steady-state situation, thereby giving apparent ("effective") values of D. Neither of these techniques are considered to be as reliable as ours. In a paper by Kincl et al (10) permeation of estradiol through a silicone elastomer, Siliastic 372® (Dow Corning©), was studied. Recalculation of their results gives $1.2 \cdot 10^{-10}$ m² sec⁻¹ as an approximate average value of D at 37°C, which is very close to what we have found for a PDMS membrane with a silica content of 3% (w/w) at 40°C. Data simulations based on experimental release data from vaginal silicone rings loaded with estradiol have been performed by Nilsson (11). The diffusion coefficient that rendered the best fit to the experimental data was $1.22 \cdot 10^{-11}$ m² sec⁻¹ and this is in fair agreement with the coefficient we got for the elastomer with 3% (w/w) silica filler. The elastomer and estradiol system is by no means a strict two-component system. As already pointed out the elastomer includes different amounts of silica. A reasonable assumption is that silica can act as an adsorption medium, and retard the overall estradiol mobility, thus decreasing the apparent diffusion coefficient. In a following study, the effect of specific system properties such as the silica content of the elastomer will be analysed in more detail. In complex systems it is likely that the simple Equation (1) is no longer valid. For instance, there could be a position dependence of D due to concentration variation or matrix swelling. In the system for which data are given here, however, Equation (1) applies, as noted above, within error of measurement. Apart from Equation (1) differential expressions have also been tried for the evaluation of D, but for obvious numerical reasons they scatter somewhat more than data obtained by Equation (1), although they give fairly similar average values of D. For the geometry chosen, one may then conclude that the curve fitting calculations described give the best results.

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