Permeant Saturation and Regulation of Membrane Transport

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Synopsis

Studies have been made on the equilibrium sorption of p-toluene sulfonic acid by nylon 66. The sorption was found to vary strongly with concentration of sulfonic acid in aqueous phase, approaching a saturation concentration in nylon for high concentration in aqueous phase, similar to a Langmuir adsorption isotherm. It was also found to vary strongly with pH. These findings have been used to give simple conditions for the establishment of almost constant permeation rates through nylon film over extended periods of time.

INTRODUCTION

Permeation through macromolecular films is a process of considerable importance in the pharmaceutical sciences. From the more fundamental point of view, permeation through membranes or films presents a variety of physicochemical problems of general interest, the main point being the dynamic interaction between the mobile permeant and the fixed membrane matrix, often polymeric in nature. In recent years the dynamic aspects of membrane properties have attracted much attention. The present study is part of a more extensive investigation of the transport phenomena in macromolecular films and gels, especially for systems of potential pharmaceutical interest. Of special importance are mechanisms and arrangements by which a regulation of the transport rate could be achieved. In this paper it will be discussed how permeant saturation in the membrane phase provides conditions for such a regulation.

In some earlier work the permeation through nylon films was studied.[1] Nylon films are usually fairly impenetrable for most water-soluble substances. Nevertheless, the nylon structure, especially the NH_2- and $COOH-$ end groups, but also the amide linkages $-NH-CO-$ make some interaction with suitably chosen protolytes possible.[2,3] Under conditions where such an interaction is present permeation may sometimes be quite noticeable.[4] From these remarks it could be anticipated that protolytes would in general only be partially soluble in nylon membranes. Furthermore, the solubility—and hence the transport rate—could be expected to vary considerably with pH. This has also been found experimentally.

Classic permeability experiments give the product of the distribution coefficient k_d and the diffusion coefficient D, i.e., (k_dD), as the basic experimentally accessible parameter. If the parameter (k_dD) is found to vary with the conditions (pH, concentration, etc.), which was the case for the permeation of some aromatic sulfonic acids through nylon films, the explanation could be that either k_d or D
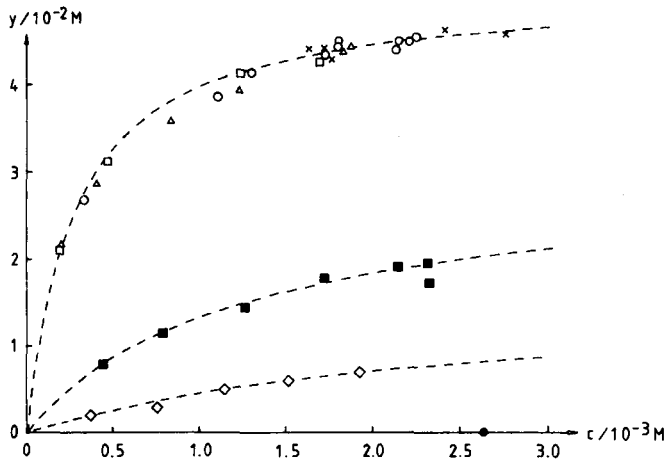
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Fig. 1. Equilibrium concentration of p-toluene sulfonic acid in nylon film (y) plotted vs. concentration in aqueous phase (c): ($\times$) pH 1.83; ($\square$) pH 2.33; ($\bigcirc$) pH 2.82; ($\triangle$) pH 3.75; ($\blacksquare$) pH 5.94; ($\diamond$) pH 7.13; ($\bullet$) pH 10.74.

or both varied. It will be shown in this work that most of the variation in permeability can be assigned to a variation in k_d, reflecting permeant saturation in the membrane phase. As a natural corollary of this finding, simple conditions can be given for the establishment of constant (or almost constant) permeation rates over extended periods of time.

EXPERIMENTAL

Chemicals

The chemicals used were of analytical grade. Granular nylon 66 was purchased from BDH Chemicals Ltd. The melting point was 250–256°C. The water used was freshly redistilled.
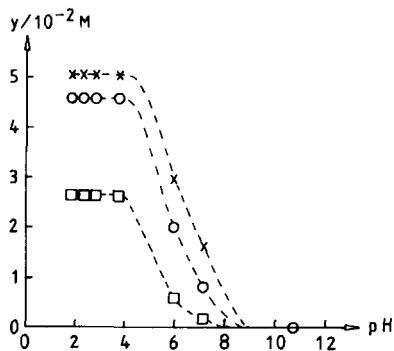

Fig. 2. pH dependence of equilibrium concentration of p-toluene sulfonic acid in nylon film for three concentrations in aqueous solution: ($\times$) infinitely high concentration; ($\bigcirc$) $2.6 \times 10^{-3}M$; ($\square$) $3.0 \times 10^{-4}M$.
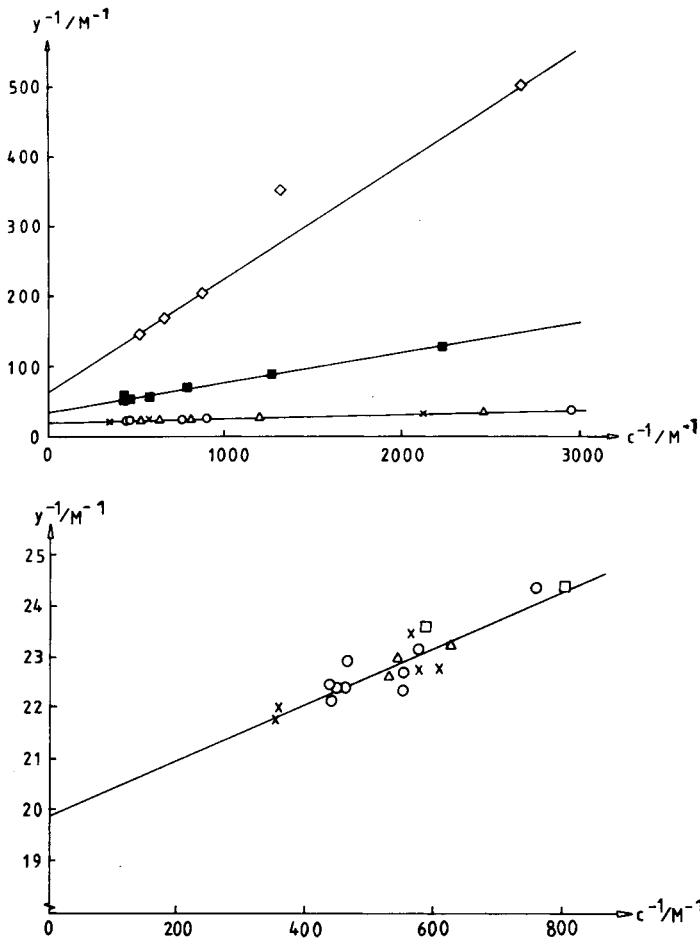
Fig. 3. (a) $1/y$ plotted vs. $1/c$ for sorption of p-toluene sulfonic acid by nylon film: (✕) pH 1.83; (O) pH 2.82; (△) pH 3.75; (■) pH 5.94; (◇) pH 7.13.   (b) Enlargement of Figure 3(a) showing data corresponding to the plateau values of Figure 2:   (✕) pH 1.83; (□) pH 2.33; (O) pH 2.82; (△) pH 3.75.

Methods

Nylon films were made by spraying a solution of nylon 66 in formic acid onto a rotating cylinder, as in an earlier work.[1,5]   The film thickness was determined from the absorbance of β-rays.

The permeation experiments were also performed by the same method as earlier.[1]   The membrane is clamped between two lucite blocks in which channels have been cut (the two blocks are mirror images of each other) to allow circulation of the two solutions for the continuous concentration determination (spectro-photometric).   The solutions are pumped and stirred in such a way as to assure homogeneous concentration (apart from obvious concentration changes in the circulation channels).

Partitioning studies were performed on nylon film at $25.0 \pm 0.5°C$.   The film was first washed in phosphate buffer solution pH 1.9 to remove any impurities,

TABLE I
Constants Calculated from the Langmuir Adsorption Isotherm for the Sorption of p-Toluene
Sulfonic Acid by Nylon Film at Different pH Values

pH	y_m	k'
1.83–3.75	5.03×10^{-2}	2.71×10^{-4}
5.95	2.93×10^{-2}	1.22×10^{-3}
7.13	1.60×10^{-2}	2.57×10^{-3}

and then in phosphate buffer of the same pH as used in the experiments. About
0.1 g nylon film was placed in a test tube containing 5.00 mL of p-toluene sulfonic
acid in phosphate buffer solution, $\mu = 0.1M$. This was stirred during 24 h.
Equilibrium was found to be reached after about 10 h. The amount partitioned
to the film was determined by measuring the absorbance of the solution spec-
trophotometrically before and after partitioning. The same films were used in
a series of studies, and between the experiments the films were washed in
phosphate buffer, pH 11, and then in phosphate buffer of the same pH that was
going to be used in the next experiment. At pH 11, the partitioning of p-toluene
sulfonic acid to nylon film is zero, and during the washing at pH 11 one could
observe that all solute was desorbed from the film. This observation is a support
for the attainment of equilibrium in the partitioning experiments.

RESULTS AND DISCUSSION

Some results from the equilibrium partitioning experiments of p-toluene
sulfonic acid in nylon film at different pH values are presented in Figure 1, where
it can be seen that there is no linear relationship between concentration in nylon
(y) and concentration in aqueous solution (c). Instead, the concentration of the
sulfonic acid in nylon is approaching an asymptotic value for high concentration
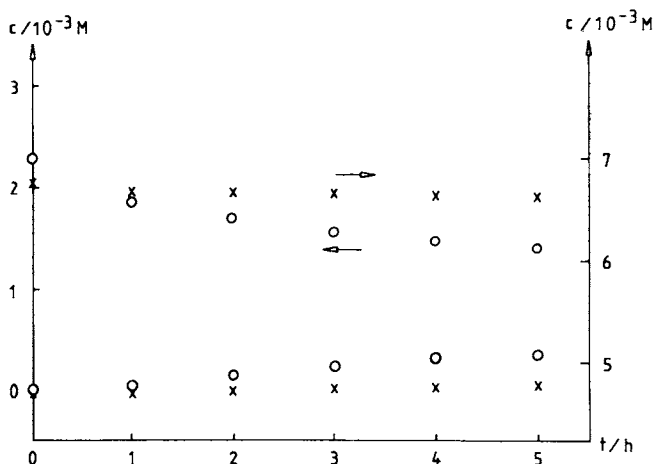in aqueous phase, similar to a Langmuir adsorption isotherm. Langmuir be-

Fig. 4. Permeation studies of p-toluene sulfonic acid, pH 3.43, through nylon film: ($\times$) film ini-
tially equilibrated with p-toluene sulfonic acid $4.71 \times 10^{-3}M$ in phosphate buffer, pH 3.43; ($\bigcirc$) film
initially equilibrated with phosphate buffer, pH 3.43.

TABLE II

Comparison of the Flux of p-Toluene Sulfonic Acid through Nylon Film Initially Equilibrated with p-Toluene Sulfonic Acid $(4.71 \times 10^{-3}M)$ in Phosphate Buffer Solution and through Nylon Film Initially Equilibrated with Phosphate Buffer Solution

Time (h)	From (×) in Fig. 4 (initially saturated film)		From (○) in Fig. 4 (film initially at zero concentration)	
	$-dC_1/dt$	dC_2/dt	$-dC_1/dt$	dC_2/dt
0–1	1×10^{-4}	1×10^{-5}	4×10^{-4}	4×10^{-5}
2–3	2×10^{-5}	2×10^{-5}	1×10^{-4}	1×10^{-4}

havior has earlier been reported for sorption in nylon.[6,7] Figure 1 also shows that the partitioning is strongly pH-dependent, reaching a maximum at pH values lower than about 3.8; see Figure 2, which is a plot of concentration in nylon vs. pH for three aqueous solution concentrations. A further lowering of pH below pH 3.8 makes no difference in partitioning behavior until such a low pH is reached that the films swell and disintegrate. At higher pH values the partitioning is lower, and finally reaches zero (at pH slightly lower than 11). In Figure 3(a) the data of Figure 1 are plotted as $1/y$ vs. $1/c$ according to the Langmuir relationship

$$1/y = 1/y_m + k'/(y_m c) \tag{1}$$

where y_m is the maximum concentration possible in nylon and k' is a constant. Within experimental accuracy the plots are all linear but slopes and intercepts vary with pH. Thus a Langmuir model for the partitioning seems to be appropriate. Data corresponding to the plateau levels in Figure 2 all fall on the same line [see Fig. 3(b)].

From the lines y_m and k' were determined (see Table I). The dashed lines in Figure 1 are calculated from (1) using the appropriate values of y_m and k' in
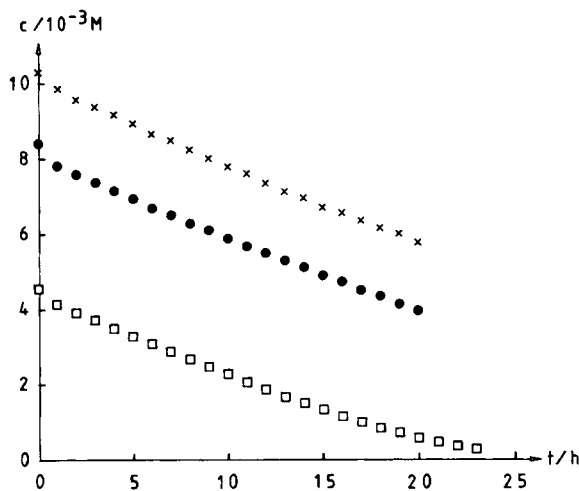

Fig. 5. Permeation studies of p-toluene sulfonic acid, pH 3.42 through nylon film. Initial concentration at one side of the film: (×) $1.03 \times 10^{-2}M$; (●) $8.21 \times 10^{-3}M$; (□) $4.52 \times 10^{-3}M$; sink condition at the other side.
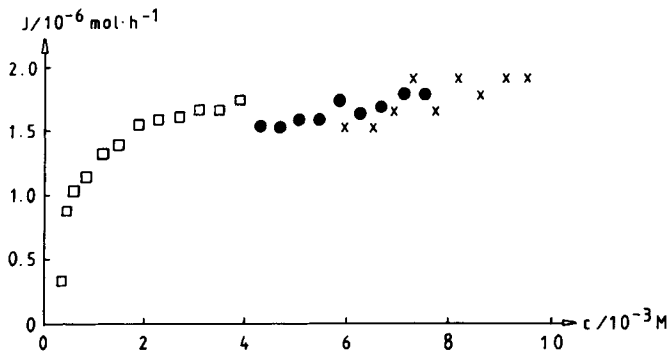
Fig. 6. Flux of p-toluene sulfonic acid through nylon film plotted vs. concentration at one side of the film for the permeation studies shown in Figure 5.

Table I. The considerable variation of y_m and k' with pH indicates that both the capability of the nylon film to accommodate the solute and the absorption kinetics change remarkably and, as seen from Figure 2, *in a nonlinear way* over the pH scale. At lower pH values the film structure "opens up" whereas at higher pH values it "closes."

Since it is the concentration gradient of solute in the membrane phase that acts as the driving force for permeation, it is obvious that these nonlinear absorption characteristics will have some interesting consequences for the possibility of regulating permeation flow.

In the first place the existence of an absorption (asymptotic) plateau for a given pH value (see Fig. 1) means that, *above a certain solute concentration in the aqueous phase (assuming sink conditions on the other side of the membrane), the permeation rate becomes constant.*

In the second place the nonlinear variation of the absorption with pH (see Fig. 2) means that *a relatively small change in the medium pH can bring about a considerable change in permeation rate.*

These two principles—as evidenced by our model system—could certainly have many practical applications, for instance, as to the design of encapsulated medicine. To illustrate these ideas, some model experiments have been made that clearly indicate the potentialities of the principles.
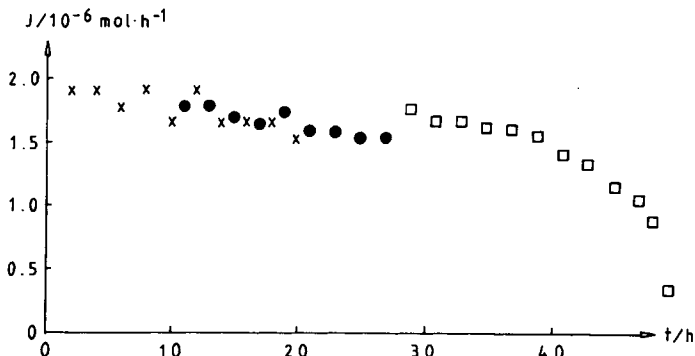

Fig. 7. Flux of p-toluene sulfonic acid through nylon film plotted vs. time for the three experiments shown in Figure 5 connected into one.

If the solute is first partitioned to the film at a concentration rather close to y_m, and then an even higher concentration is supplied to one side of the film, there will be only a very small concentration gradient in the film, although the concentration difference in the two aqueous solutions is quite large. As a result, the permeation rate will be very low [(×) in Fig. 4] compared to the situation with zero initial concentration at one side of the film and in the film, and the same concentration difference in aqueous solutions [(○) in Fig. 4]. These results are also further evidence of a saturation phenomena in the film. Table II shows that there is about a fivefold difference in flux between the two experiments.

Figure 5 shows the situation of rather high concentration (plateau region in Fig. 1) at one side of the film and sink condition at the other side. After initial partitioning of the film, very soon an almost linear change in concentration is obtained, corresponding to an almost constant concentration gradient and permeation rate in the film. The permeation rate does not fall appreciably until there is a rather low concentration in the aqueous phase [as seen from the later behavior of the (□) points in Fig. 5]. This could be seen more clearly in Figure 6, where the flux J is plotted vs. concentration in aqueous phase for the three experiments in Figure 5. If these experiments were connected into one, starting at time = 0 with a concentration of $1 \times 10^{-2}M$ on one side of the membrane and sink conditions on the other, a plot of flux vs. time would be as in Figure 7. Starting at this concentration, it would in the actual case be possible to have almost constant flux for about 40 h.

The three permeation studies are performed with three pieces of nylon film, prepared at two occasions, showing a rather good reproducibility of film preparation.

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