REPORT NUMBER 1

THE PERMEABILITY OF THE SKIN TO GASES

ANNUAL REPORT

BY

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Summary

This summary covers the work done on the project during the first year period 1 June 1969 - 1 June 1970. [Army project number 2N061102B71D; grant number DAHC 19-69-G-0018].

I. Introduction

The purpose of this work is to determine the permeability of the intact human epidermis to gases and vapors. The transport properties of the unhydrated stratum corneum are virtually unknown. By measuring the sorption and diffusion rates of homologous series of selected gases and vapors we hope to be able to establish the mechanism of gas or vapor phase diffusion through the skin. A specific aim of this work is to measure the effect of hydration on the permeability of gases. The effect of hydration is important because the interior surface of the skin's barrier layer is normally hydrated and even small amounts of moisture can significantly alter the physical structure of this tissue.

II. Research Rationale

As emphasized in the original grant application, diffusion data on stratum corneum could be obtained from two independent kinds of experiments, i.e. permeation measurements and sorption measurements.
The former requires an intact sheet of tissue or membrane which is used as a diaphragm between two chambers, one containing the vapor whose rate of diffusion through the membrane is to be measured. Analyses of the rate of permeation lead to a value for the diffusion constant D and for the solubility S. Sorption measurements do not require an intact membrane, these experiments require only pieces of tissue which are suspended from the arm of a sensitive microbalance into a concentration of vapor. Sorption measurements also yield values for D and S. But it is in the comparison between these two sets of values that significant information is obtained.

During the first year sorption measurements were made on the series of linear alkanes and alcohols. Permeation measurements of a limited nature were made on many of these same substances using their infrared absorption as an analytical technique. Final and more precise measurements of permeation will be made using a vacuum manifold and a quartz crystal microbalance technique; progress in the construction and use of this apparatus is described.

III. Results

A. Gas Permeation by Infrared Absorption

The IR absorption bands near 2970-2930 cm\(^{-1}\) of the alkanes and those near 1032-1052 for the alcohols were made the basis of their concentration measurement.
Steady state penetration rates of the linear alkanes (from $C_4 - C_{10}$) and of $H_2O$, methanol, and ethanol were measured through epidermal membranes. From these data diffusion constants and permeability constants were computed.

**Discussion**

The permeability of alkanes increases with the number of methylene groups in the molecule from 0.01 cm hr$^{-1}$ for butane to 0.2 cm hr$^{-1}$ for decane. Permeation rates of alkanes with three of few methylene groups were too small to be measured with this technique. The corresponding alcohols ($C_1 - C_3$) had higher permeabilities. Water vapor penetrated faster than any of the alcohols or alkanes.

The infrared (IR) technique was useful to get an approximate idea of the permeability of the gases. But it was not sensitive enough to measure the penetration rates of all the alkanes and alcohols, and this comparison is crucial.

**B. Gas Sorption**

(1) Sorption rates of alkane vapors ($C_3 - C_{16}$) and alcohol vapors ($C_1 - C_{10}$) were measured. Diffusion constants corresponding to the initial rate of sorption were computed. These were greater for the alkanes than for the corresponding alcohol from ($C_1 - C_{10}$) but were very similar beyond $C_{11}$. The alkane diffusion constants were inversely proportional to the square root of the molecular weight.
(2) The solubility of each gas or vapor in dry stratum corneum was measured from the amount of gas sorbed at equilibrium. Alcohols were many times more soluble than the corresponding alkanes between \((C_1 - C_{10})\); the higher members of both series tended to converge toward similar solubilities. The solubility of the alkanes increased exponentially with an increasing number of methylene groups; alkanes with less than three methylene groups were not measurably sorbed by the tissue.

(3) The sorption isotherm of pentane \((30^\circ C)\) a representative alkane, was obtained. It was approximately linear up to a pentane mole fraction of 0.5 but then increased more rapidly at higher mole fractions. Henry's law is a poor approximation to vapor solubilities at saturation for stratum corneum.

(4) Sorption and desorption curves were measured for representative members of each homologous series. These curves were not superimposable thus showing that the diffusion constants for the vapors actually are functions of concentration.

(5) There is evidence that continued contact with alkane or alcohol vapors increases the effective surface area of the stratum corneum. Solubilities obtained after long contact with these vapors were three times higher than those measured initially.

Discussion

From the present data there is no evidence that vapor diffusion involves transport through holes in the tissue. The evidence ob-
tained suggests that substances applied as vapors must dissolve into the tissue per se. in order to penetrate. Their diffusion constants are from one to two orders of magnitude lower than for the same substances applied as liquids. Whether the same conclusion applies to gases (i.e. non-condensable at room temperature) remains to be seen. The gases and the insoluble alkanes penetrate too slowly to be measured by the IR technique; their rates will be obtained with the aid of our new quartz crystal oscillator technique. (See below).

C. Gas Permeation Measured by the Quartz Sorption Detector

For precise measurements of diffusion rates of gases through epidermis a high vacuum manifold was needed. This system consists essentially of a diaphragm - diffusion cell suitable for epidermal membranes, a vacuum apparatus for evacuating this cell and for supplying test gases and a quartz crystal sorption detector for measuring their rate of accumulation in the receptor portion of the diffusion cell. This apparatus has now been constructed and has been successfully tested using the known diffusion behavior of water.
Foreword

This report covers the first year's work on the project.

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FERMEABILITY OF THE SKIN TO CASES

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Measurement of vapor transport by IR absorption

Epidermal membranes, carrying the intact stratum corneum were fitted as diaphragms separating two halves of a diffusion chamber. The donor half contained an isolated reservoir with a few ml of the test liquid part of which vaporized and thus served as constant vapor supply to the membrane. The receptor half of the system was a one meter, folded path IR absorption cell. This cell was fitted with a fan which assured thorough and rapid mixing of the vapor which diffused through the membrane.

Theory and Mathematical Formulae

The permeability of the membrane to the particular vapor was obtained from the rate at which the absorbancy of the gas in the IR gas cell increased. The increase in absorbancy was related to the corresponding increase in concentration by previous calibration of the individual gases using their published vapor pressures. (See Table I, Columns 1 - 4). The equations derived below show the relationship between these units and the standard permeability parameters.
Basic assumptions

We consider the system to be a case of diffusion through a plane sheet or membrane of thickness $\delta$ and diffusion coefficient $D$, whose surfaces, $x = 0$ and $x = \delta$, are maintained at constant concentrations $C_1$ and $C_2$ respectively. At steady state, integration of the one dimensional diffusion equation leads to a constant rate of transfer across all sections of the membrane given by:

$$J_s = \frac{D(C_1 - C_2)}{\delta} \quad (1)$$

In our case the surface concentrations $C_1$ and $C_2$ are not known but only the vapor pressure $P_1$ and $P_2$ on the two sides of the membrane. The rate of transfer in the steady state becomes:

$$J_s = \frac{P(P_1 - P_2)}{\delta} \quad (2)$$

and $P$ is referred to as the permeability constant. If the diffusion constant $D$ is constant, i.e. not dependent on concentration as it might be if the tissue gradually degraded on contact with the vapor, and if the vapor sorption isotherm is linear, then equations (1) and (2) are equivalent. The linear isotherm may be written

$$C = \frac{S P}{RT} \quad (3)$$

where $C$ is the surface concentration of the vapor on the
membrane in equilibrium with an external vapor pressure $p$, and $S$ is the solubility. Using all three equations we may write

$$\mathcal{J}_s = \frac{DS(p_i - p)}{RT \delta} \quad (4)$$

Instead of using vapor pressures one may use external vapor concentrations and remove the RT factor since $P_0 C_0 = RT$, where $C_0$ refers to external vapor concentration on the $x = 0$ side of the membrane. We have

$$\mathcal{J}_s = \frac{DS(C_0 - C_s)}{\delta} = k_p \Delta C \quad (5)$$

where our new permeability constant $k_p = \frac{DS}{\delta}$.

Analysis of the data

Vapor flux through the membrane of area $A$ will increase the concentration of the gas in the receptor (initially zero) in accord with equation (5). The flux by definition is the number of moles of substance, $n$, crossing a square cm of membrane per unit time or

$$\mathcal{J}_s = \frac{1}{A} \frac{dn_s}{dt} = k_p \Delta C_s \quad (6)$$

Relating $n_s$ to concentration, $C_s = \frac{n_s}{V}$ where $V$ is the receptor volume, and relating $C_s$ to the corresponding absorbancy
As = kcl we may rewrite equation (6) in the form
\[ J_s = \frac{V}{Ak} \frac{dA_s}{dt} = k_p \Delta C_s \quad (7a) \]

The right hand side of equation (7) can be simplified further since \( \Delta C = C_o - C_6 = C_o \) since the experiment can be terminated before \( C_6 \) is significant compared with \( C_o \). Also since
\[ C_o = \frac{A_o}{kl} \]
where \( k = \) absorbancy index and \( l = \) light path length of gas cell, we have:
\[ J_s = \frac{V}{Ak} \frac{dA_s}{dt} = k_p \frac{A_o}{kl} \quad (7b) \]
or
\[ k_p = \frac{V}{A_s A} \frac{dA_s}{dt} = f \frac{dA_s}{dt} \quad (8) \]
The permeability constant \( k_p \) apart from the factor \( f \) can be obtained directly from the slope of the linear portion of the \( A_s \) vs. \( t \) curve. Values of \( f \) for specific vapors are listed in Table I, column 5.

Other numerical constants are:
\[ A = \text{area of exposed membrane} = 3.43 \text{ cm}^2 \]
\[ V = \text{volume of receptor chamber} = 1,020 \text{ cm}^3 \]
\[ l = \text{path length of gas cell} = 100 \text{ cm} \]
Experimental Results

Data obtained for vapor penetration by the infrared absorption technique is listed in Table I, columns 6, 7, and 8. Not all the simple alcohols and alkanes could be run owing to the insensitivity of the method in these cases. The sensitivity of the technique is determined by the absorbance of the gas at its normal saturated vapor pressure and the rate at which it penetrates. The product of absorbance, vapor pressure and rate of penetration is reflected in the magnitude of $\frac{dA}{dt}$, e.g. (8). The average values of $\frac{dA}{dt}$ obtained for the various vapors are given in column (6) i.e. by the slope of the $A_s$ vs $t$ plot = $m$. (See the example in Figure 1). When this number was greater than 0.01 units of absorbancy per hour, measurements could satisfactorily be made in a reasonable amount of time. When $m < 0.01$ measurements were correspondingly more lengthy, and less precise. From column (6) it can be seen that several of the determinations fall into the marginal class. For the alcohols only methanol and ethanol could be measured and for the alkanes only those between butane and decane.
Figure 1 - Rate of decrease of the I. R. Transmission of the folded path 1 meter gas cell. Two experiments are plotted corresponding to D$_2$O ($\gamma$ = 1434 cm$^{-1}$) and decane ($\gamma$ = 2930 cm$^{-1}$) permeation.
<table>
<thead>
<tr>
<th>GAS</th>
<th>( C^0(25^\circ C) ) (mg/cc)</th>
<th>( \nu ) (cm(^{-1}))</th>
<th>( \Lambda^0_{k=0^1} ) (l=1cm)</th>
<th>k (cm(^2)/mg)</th>
<th>( f = V ) (100 A(^0)-A)</th>
<th>m (1/hr)</th>
<th>k_p (cm/hr)</th>
<th>J_s = k_p \Delta C_s = k_p C^0 (mg/cm(^2)/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D(_2)O</td>
<td>0.023</td>
<td>1434</td>
<td>0.0117</td>
<td>0.508</td>
<td>254</td>
<td>0.015</td>
<td>3.8</td>
<td>0.087</td>
</tr>
<tr>
<td>MeOH</td>
<td>0.214</td>
<td>1032</td>
<td>1.10</td>
<td>5.14</td>
<td>2.70</td>
<td>0.10</td>
<td>0.27</td>
<td>0.058</td>
</tr>
<tr>
<td>EtOH</td>
<td>0.145</td>
<td>1052</td>
<td>0.257</td>
<td>1.76</td>
<td>11.6</td>
<td>0.0015</td>
<td>0.02</td>
<td>0.0029</td>
</tr>
<tr>
<td>C(_4)H(_10)</td>
<td>2.38</td>
<td>2969</td>
<td>5.80</td>
<td>2.44</td>
<td>0.514</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C(_5)H(_12)</td>
<td>2.02</td>
<td>2965</td>
<td>6.29</td>
<td>3.26</td>
<td>0.452</td>
<td>0.022</td>
<td>0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>C(_6)H(_14)</td>
<td>0.675</td>
<td>2969</td>
<td>2.53</td>
<td>3.75</td>
<td>1.18</td>
<td>0.016</td>
<td>0.02</td>
<td>0.014</td>
</tr>
<tr>
<td>C(_7)H(_16)</td>
<td>0.238</td>
<td>2969</td>
<td>0.843</td>
<td>3.54</td>
<td>3.53</td>
<td>0.018</td>
<td>0.06</td>
<td>0.014</td>
</tr>
<tr>
<td>C(_8)H(_18)</td>
<td>0.814</td>
<td>2933</td>
<td>0.401</td>
<td>4.94</td>
<td>7.42</td>
<td>0.016</td>
<td>0.12</td>
<td>0.010</td>
</tr>
<tr>
<td>C(_9)H(_20)</td>
<td>0.0308</td>
<td>2933</td>
<td>0.165</td>
<td>5.36</td>
<td>18.05</td>
<td>0.007</td>
<td>0.13</td>
<td>0.004</td>
</tr>
<tr>
<td>C(_{10})H(_22)</td>
<td>0.0133</td>
<td>2930</td>
<td>0.0462</td>
<td>3.48</td>
<td>64.3</td>
<td>0.0035</td>
<td>0.20</td>
<td>0.003</td>
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<tr>
<td>CCl(_4)</td>
<td>0.95</td>
<td>7.94</td>
<td>8.83</td>
<td>9.30</td>
<td>0.337</td>
<td>0.10</td>
<td>0.03</td>
<td>0.028</td>
</tr>
</tbody>
</table>

(1) (2) (3) (4) (5) (6) (7) (8)
Discussion of Results

Magnitude of Permeability Constant

The measured permeability constants for the alcohol and alkane vapors are given in Table I column (7). This is the parameter $k_p = \frac{DS}{\delta}$ which is defined by equation (5). The first thing one notices about these numbers is their generally large values compared to corresponding solution phase permeability constants for the same molecules dissolved in water. For example, in the following table it can be seen that for methanol and ethanol the gas phase $k_p$'s are respectively 500 and 25 times larger than the corresponding values obtained in aqueous solution.

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Gas Phase</th>
<th>$k_p$ (cm hr$^{-1}$) S</th>
<th>$k_p$ (cm hr$^{-1}$) $K_m$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_2O$</td>
<td></td>
<td>3.8</td>
<td>2560</td>
</tr>
<tr>
<td>MeOH</td>
<td></td>
<td>0.27</td>
<td>260</td>
</tr>
<tr>
<td>ETOH</td>
<td></td>
<td>0.02</td>
<td>140</td>
</tr>
</tbody>
</table>

The $k_p$ for water is 8000 times greater in the gas phase than it is for the liquid. From the definition of $k_p$ it is clear that gas phase permeabilities are characterized by a much larger diffusion constant D or a much larger solubility $S$ or both. (As shown below, after gas sorption data is presented, the factor responsible is the solubility $S$ which is much greater...
than its corresponding equivalent, mean analyzing solution permeability).

B. Changes in \( k_p \) with the chemical nature of the gas

The main purpose of measuring the gas permeabilities by the IR method was to get some estimate of their permeabilities which would help in the design and planning of a more suitable experimental method. From Table I it is clear that one cannot assess the role of functional groups on the permeability of these vapors using this method. The main reason is that corresponding acids and alcohols cannot be compared - the method is too insensitive for the alcohols with carbon number greater than \( C_3 \) and for the alkanes less than \( C_4 \). The discussion of this question must be postponed until data is obtained with the much more sensitive Quartz crystal oscillator technique.

Progress in this area is discussed below.

Measurement of Vapor Sorption

It is clear from the foregoing discussion that independent measurements of \( D \) and \( S \) are necessary in order to interpret the observed permeability constant which depends upon both parameters, e.g. eq (5). This was foreseen in the original
experimental protocol which emphasized that independent de-
terminations of the solubility of the gas in the tissue could
be made gravimetrically by gas sorption techniques.

The method is simply to suspend a known amount of tissue
from the beam of a microbalance into a known vapor pressure
of the gas and measure the amount absorbed at equilibrium.
In addition, the value of the diffusion constant can be ob-
tained by analyzing the rate of gas sorption. Thus D and S
can both be obtained in a single experiment. It should be
emphasized that the diffusion constant obtained in this way
is an average value if D depends on concentration. Also
this D represents true diffusion through the tissue whereas
the one computed from permeability measurements by the re-
lation \( k_p = \frac{D S}{6} \) may not be. The reason is that if holes
exist in the membrane, the flux of gas through it will be
greater than if they do not. If the flux is greater for this
reason, then the measured permeability constant and the value
of D computed from it will be higher. The presence of holes
in the tissue does not affect sorption or desorption measure-
ments since they depend on the rate at which gas molecules
actually chemically bonded in the tissue move. It is there-
fore very useful to measure the diffusion constant both ways
and see if they are comparable. If they agree one can be cer-
tain that if holes do exist they are too small or too few to
appreciably enhance permeability.
The Cahn balance shown in Figure 2 was used for the sorption experiments. The glass jacketed vessel on the left is the water controlled constant temperature "air bath" into which the sample is suspended. A small quantity of liquid in the bottom furnishes a constant source of vapor.

Theory and Mathematical Formula

For the case of sorption and desorption by a membrane of thickness $t$, where $M_t$ denotes the total amount of diffusing substance which has entered the sheet at time $t$, and $M_\infty$ the corresponding quantity after infinite time, it can be shown: (Crank p 45)

$$\frac{M_t}{M_\infty} = 1 - \frac{D}{\pi^2} \sum_{n=0}^{\infty} \exp\left(-\frac{D(2n+1)^2\pi^2 t}{\delta^2}\right)$$

(9)

The corresponding solution useful for small times is

$$\frac{M_t}{M_\infty} = 4\left(\frac{Dt}{\delta^2}\right)^{1/2} \left\{ \frac{\pi^{-1}}{\sqrt{2\pi}} + 2 \sum_{n=1}^{\infty} \frac{(-1)^n \exp\left(-\frac{n\pi^2}{2Dt}\right)}{\sqrt{n\pi}} \right\}$$

(10)

The application of either equation is based on the assumption that the uptake is a diffusion process controlled by a constant diffusion coefficient $D$ and that immediately the concentration at each surface of the membrane attains a constant equilibrium value. The membrane is considered to be initially free of vapor. From eq (9) the value of $t/\delta^2$ for which $M_t/M_\infty = 1/2$
Figure 2 - Vapor sorption apparatus.
is given by

\[
\left\{ \frac{t}{l^2} \right\}_w = -\frac{1}{\pi^2 D} \ln \left\{ \frac{\pi^2}{16} - \frac{1}{9} \left( \frac{\pi^2}{16} \right)^9 \right\} \tag{11}
\]

approximately, the error being about 0.001 percent.

Thus we have:

\[
D = \frac{0.049}{\left\{ \frac{t}{l^2} \right\}_w} \tag{12}
\]

and so, if the half time of a sorption process is observed experimentally, the value of the diffusion constant (assumed to be constant) can be simply determined from eq (12).

It is also possible to deduce an average diffusion coefficient (or the true one if D is constant) from the initial gradient of the sorption curve when plotted against the square root of time. From eq (10) at early times when the error function term can be neglected we have

\[
\frac{M_t}{M_\infty} = \frac{4}{\pi^2} \left( \frac{D \tau}{l^2} \right)^\frac{1}{2} \tag{13}
\]

If the initial gradient \( \frac{dM_t}{dt} \) is observed the diffusion constant is

\[
D = \frac{\pi^2 l^2}{16} \frac{m^2}{M_\infty^2} \tag{14}
\]

The average thickness of the stratum corneum membrane is approximately 8 \( \mu \) so (14) becomes

\[
D = 1.26 \times 10^{-7} \left( \frac{m}{M_\infty} \right)^2 \text{ cm}^2 \text{ mm}^{-1} \tag{15}
\]
Experimental Results on Vapor Sorption

Rationale for experiments

One of the main purposes of measuring diffusion coefficients by both permeability and sorption techniques is to learn whether there is appreciable transport through "holes" or micropores in stratum corneum. If such gas phase diffusion does exist then a comparison of the diffusion coefficients obtained by the two different techniques should reveal it. The reason is, as mentioned above; v. s. p 9, that rapid transport through "holes" increases the permeability constant but has no effect on a sorption experiment. Therefore the diffusion constant $D$ computed from the permeability constant by the expression:

$$ k_p = \frac{D S}{\delta} \quad (5) $$

will be correspondingly higher than that computed by the sorption expressions: eqs (12) or (14). In order to compute $D$ from (5) Solubility $S$ must be measured and of course $\delta$ must be known. However, both methods of analysis involve $\delta$ so that for a relative comparison only the value of $S$ is required. $S$, the so-called solubility of the gas in the tissue, is the ratio of the density of the gas within the surface regions of the tissue in equilibrium with the external vapor to...
the density of that external vapor, thus $S = \frac{C_m}{C_0} = \frac{RTC_m}{P_o}$

$C_m$ is that effective surface concentration which is presumed to arise very rapidly just within the surface of the tissue once the vapor is brought into contact with it. After a long time the tissue will reach equilibrium or close enough to it so that $C_m$ will represent the concentration for the entire tissue and not just the surface regions.

**Nature of the Sorption Isotherm**

As indicated in the discussion on page 2 one of the basic assumptions underlying the general validity of eqs. (4) or (5) is the presumed linearity of the vapor-tissue isotherm. This assumption turns out to be quite untrue for stratum corneum regardless of whether an alkane or an alcohol or $H_2O$ is the specific vapor. It is therefore imperative to know how this non-ideal situation limits the usefulness of our equations and modifies the interpretation of the data.

First it is clear that the purpose of utilizing the isotherm in the diffusion eqs (2) - (5) is simply to relate external vapor concentration, $C^0$ to internal concentration, $C^0_m$. The assumed linearity of the isotherm simply makes eq (5) simpler than it otherwise might be. For example if the isotherm were quadratic in $p$ instead of linear in $p$, i.e. CRT = $S(p + sp^2)$,
<table>
<thead>
<tr>
<th>Alkane</th>
<th>F\textsuperscript{O25\textdegree} \textdegree (Torr)</th>
<th>Vapor Density CO\textsuperscript{O}(mg/cc)</th>
<th>M(\infty) (mg)</th>
<th>M(\infty) (corrected) (mg)</th>
<th>C(t) m (mg/cc)</th>
<th>S=cm \text{co}</th>
<th>S_{\text{max}}=1000 \text{co}</th>
<th>% Coverage \text{S} \text{100}</th>
</tr>
</thead>
<tbody>
<tr>
<td>C\textsubscript{1}</td>
<td>760.0</td>
<td>0.656</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C\textsubscript{2}</td>
<td>760.0</td>
<td>1.23</td>
<td>0.188</td>
<td>0.058</td>
<td>2.6</td>
<td>1.5</td>
<td>[250]</td>
<td>1.0</td>
</tr>
<tr>
<td>C\textsubscript{3}</td>
<td>760.0</td>
<td>1.81</td>
<td>0.163</td>
<td>0.054</td>
<td>2.4</td>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C\textsubscript{4}</td>
<td>760.0</td>
<td>2.38</td>
<td>0.425</td>
<td>0.14</td>
<td>6.2</td>
<td>2.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C\textsubscript{5}</td>
<td>520.0</td>
<td>2.02</td>
<td>1.459</td>
<td>0.49</td>
<td>21.8</td>
<td>10.8</td>
<td>310</td>
<td>3.5</td>
</tr>
<tr>
<td>C\textsubscript{6}</td>
<td>145</td>
<td>0.673</td>
<td>1.174</td>
<td>0.39</td>
<td>17.3</td>
<td>26.7</td>
<td>977</td>
<td>2.7</td>
</tr>
<tr>
<td>C\textsubscript{7}</td>
<td>44</td>
<td>0.238</td>
<td>1.157</td>
<td>0.38</td>
<td>16.9</td>
<td>71.0</td>
<td>2.87x10\textsuperscript{3}</td>
<td>2.5</td>
</tr>
<tr>
<td>C\textsubscript{8}</td>
<td>14.5</td>
<td>0.0814</td>
<td>1.157</td>
<td>0.38</td>
<td>16.9</td>
<td>208</td>
<td>8.65x10\textsuperscript{3}</td>
<td>2.4</td>
</tr>
<tr>
<td>C\textsubscript{9}</td>
<td>4.47</td>
<td>0.0306</td>
<td>1.050</td>
<td>0.35</td>
<td>15.6</td>
<td>510</td>
<td>2.33x10\textsuperscript{4}</td>
<td>2.2</td>
</tr>
<tr>
<td>C\textsubscript{10}</td>
<td>1.78</td>
<td>0.136</td>
<td>0.849</td>
<td>0.28</td>
<td>12.5</td>
<td>920</td>
<td>5.49x10\textsuperscript{4}</td>
<td>1.7</td>
</tr>
<tr>
<td>C\textsubscript{11}</td>
<td>0.403</td>
<td>0.0034</td>
<td>0.803</td>
<td>0.27</td>
<td>12.0</td>
<td>3530</td>
<td>2.18x10\textsuperscript{5}</td>
<td>1.6</td>
</tr>
<tr>
<td>C\textsubscript{12}</td>
<td>0.0305</td>
<td>0.000033</td>
<td>0.172</td>
<td>0.057</td>
<td>2.5</td>
<td>7580</td>
<td>2.32x10\textsuperscript{6}</td>
<td>0.3</td>
</tr>
<tr>
<td>C\textsubscript{16}</td>
<td>0.0040</td>
<td>0.000049</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.58x10\textsuperscript{7}</td>
<td></td>
</tr>
</tbody>
</table>

(1) (2) (3) (4) (5) (6) (7) (8)
eq. (5) would become

\[ J_s = \frac{D \delta}{\delta} \left\{ \left[ (C_s^2 + C_s^2) - (C_s - \alpha C_s^2) \right] \right\} \]

If this isotherm were experimentally established one could still relate the external vapor concentration to the internal concentration, and compute \( D \). Thus the important quantity is \( C_m \) which is always simply related to \( D \) through equation (1)

\[ J_s = \frac{D (C_m^0 - C_m^0)}{\delta} \]

Experimental Example - The pentane isotherm

Sorption data for pentane at 25°C are listed in Table II. Pentane sorption onto dry stratum corneum was studied as a function of pentane partial pressure. The partial pressure was controlled by using solutions of pentane in hexadecane, the latter being essentially non-volatile. Raoult's Law gives:

\[ p_C = p_C^0 N_C \]

where \( p_C^0 \) is the vapor pressure of pure pentane and \( N_C \) the mole fraction of pentane in the hexadecane-pentane solution. Three representative sorption curves are shown in Figure 3: these correspond to experiments #3 and #8 and #10 in Table II. From these curves and from the Tabular data several facts emerge:
Figure 3 - Typical pentane sorption curves corresponding to experiments #3, #8 and #10 in Table VI. Note the increasing uncertainty in the determination of $M_\infty$ as the concentration increases.
1) Pentane sorption deviates from an ideal Langmuir type isotherm as higher concentrations are used. (Shown by the increasing slope of the "horizontal" part of the sorption curve.)

2) Equilibrium is achieved faster for low pentane concentrations.

3) The sorption isotherm is not linear $M_\infty$ does not increase in proportion to pentane mole fraction (For example pentane sorption increases on the ratio from 1/9/16.5 while the mole fraction ratios increase from 0.22/0.86/1.0 for the three cases shown).

The isotherm itself constructed from all the values of $M_\infty$ in Table II is shown in Figure 4. It is clear that a linear approximation to the isotherm is very inaccurate beyond a mole fraction of 0.5. The value of the solubility computed from the slope of this line would seriously underestimate the actual concentration of pentane, $C_m$, corresponding to any external vapor pressure greater than that produced by a 0.5 mole fraction pentane solution. For example the $C_m$ corresponding to pure pentane is approximately 30.8 mg/cc and not 8.6 mg/cc which is the Henry's Law or linear isotherm prediction.
PENTANE ISOTHERM AT 30°C.

\[ C_m = \frac{S \cdot \frac{p}{RT}}{N_c} = 2.42 \text{ mg/cc SN}_c \]

Slope = 2.42 S

8.60 = ""

\[ S = 3.55 \text{ mg/cc} \]

\[ C_m = 8.60N_c \]

Figure 4 - Isotherm for pentane at 30°C. Constructed from the data given in Table VI.
### Table III

**Sorption Data on Alcohols**

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>$P_{30^\circ C}$ (Torr)</th>
<th>$C_0$ (mg/cc)</th>
<th>$M_{180}$ min (mg)</th>
<th>$M^*$ (mg)</th>
<th>$C_m(180)$ min</th>
<th>$S_{cm}$ (mg)</th>
<th>$S_{max}$ (1000 mg)</th>
<th>% Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_2O$</td>
<td>31.8</td>
<td>0.033</td>
<td>1.90</td>
<td>3.00</td>
<td>84.6</td>
<td>2560</td>
<td>4.34x10^4</td>
<td>5.9</td>
</tr>
<tr>
<td>$C_1$</td>
<td>160</td>
<td>0.271</td>
<td>1.60</td>
<td>2.00</td>
<td>71.3</td>
<td>263</td>
<td>3.71x10^3</td>
<td>7.1</td>
</tr>
<tr>
<td>$C_2$</td>
<td>78.1</td>
<td>0.190</td>
<td>0.60</td>
<td>0.88</td>
<td>26.7</td>
<td>141</td>
<td>5.44x10^3</td>
<td>2.6</td>
</tr>
<tr>
<td>$C_3$</td>
<td>27.6</td>
<td>0.0875</td>
<td>0.24</td>
<td>0.46</td>
<td>10.7</td>
<td>121</td>
<td>9.19x10^3</td>
<td>1.32</td>
</tr>
<tr>
<td>$C_4$</td>
<td>10.0</td>
<td>0.392</td>
<td>0.17</td>
<td>0.34</td>
<td>7.57</td>
<td>193</td>
<td>2.07x10^4</td>
<td>0.93</td>
</tr>
<tr>
<td>$C_5$</td>
<td>3.59</td>
<td>0.0167</td>
<td>0.12</td>
<td>0.28</td>
<td>5.34</td>
<td>320</td>
<td>4.90x10^4</td>
<td>0.65</td>
</tr>
<tr>
<td>$C_6$</td>
<td>1.55</td>
<td>0.00836</td>
<td>0.10</td>
<td>0.26</td>
<td>4.45</td>
<td>532</td>
<td>9.84x10^4</td>
<td>0.54</td>
</tr>
<tr>
<td>$C_7$</td>
<td>0.543</td>
<td>0.00334</td>
<td>0.12</td>
<td>0.24</td>
<td>5.34</td>
<td>1600</td>
<td>2.47x10^5</td>
<td>0.65</td>
</tr>
<tr>
<td>$C_8$</td>
<td>0.263</td>
<td>0.00181</td>
<td>0.09</td>
<td>0.23</td>
<td>4.00</td>
<td>2210</td>
<td>4.57x10^5</td>
<td>0.48</td>
</tr>
<tr>
<td>$C_9$</td>
<td>0.134</td>
<td>0.00102</td>
<td>0.06</td>
<td>0.14</td>
<td>2.67</td>
<td>2620</td>
<td>8.12x10^5</td>
<td>0.32</td>
</tr>
<tr>
<td>$C_{10}$</td>
<td>0.071</td>
<td>0.00059</td>
<td>0.02</td>
<td>0.06</td>
<td>0.89</td>
<td>1500</td>
<td>1.41x10^6</td>
<td>0.11</td>
</tr>
</tbody>
</table>

**Notes:**

- $T$issue weight = 29.90 mg.
- *$CO-C_4$, M taken at 10 hr.*
- **$C_5-C_10$, M taken under 24 hr.**
Values for alkanes and alcohols

Sorption data for the simple alkanes from C₁ - C₁₄ and for the corresponding alcohols from C₁ - C₁₀ are collected in Tables II and III. The principal experimental quantity is the amount of substance absorbed at equilibrium $M_\infty$, given in column (4) in both tables. As the sorption curves in Figure 3 show $M_\infty$ values for the higher external vapor densities are more indefinite than those corresponding to lower vapor densities. True equilibrium is probably not reached 180 min. or even in 24 hours in some cases, particularly for water and the alcohols. But the error is not large and the $C_m$ values obtained from the measured uptakes of vapor are reasonably close to the presumably higher actual equilibrium values.

The measured $C_m$ values in column (5) in both Tables after conversion to moles/cc instead of mg/cc have been plotted in Figure 5. Low molecular weight alcohols (including H₂O) are sorbed in much greater quantity than the corresponding alkanes. This is not due to a higher vapor pressure since the first three alkanes are gases at room temperature and were applied at partial pressures of 760 Torr. It is due to the larger affinity of the alcohols for the tissue due to the presence of the polar OH group. This is made clear below in the discussion of the gas solubility.
Figure 5 - Solubility of the alcohols (○) and alkanes (●) vs. the carbon number. The concentration of the vapor in the tissue at equilibrium $C_m$ is given in moles/cc.
The solubility of the alkanes and alcohols

The measured solubilities of the gases are given in Tables II and III column (6) and are plotted in Figure 6. These are the ratio of the actual membrane concentration $C_m$ in equilibrium with the vapor over the pure liquid to the vapor concentration, i.e. $\frac{C_m}{C}$ for $N = 1.00$. (In terms of Figure 3 this is the last point on the isotherm and corresponds to the vapor concentration used in the permeability studies). Several interesting findings can be noted:

1. The solubility of the alkanes is less by a factor of from 10 - 100 than that of the alcohols between $C_3$ - $C_9$.
2. The disparity in solubility is very much greater for the low molecular weight molecules and is less pronounced for the high molecular weight members of the series.
3. The solubility of the alkanes appears to be determined between $C_3$ - $C_9$ by the number of $\text{CH}_2$ groups. Each methylene unit confers 600 cals on the free energy of desorption. The linear relationship between log $S$ and $n$ intercepts the ordinates for $S = 0$ between $n = 2$ and 3. This suggests that 3 methylene groups are required in order to have appreciable absorption of the alkane by the tissue.
4. The solubility of the alcohols is appreciably enhanced by the presence of the OH group. From the slope of the
SOLUBILITY OF THE ALCOHOLS AND ALKANES

\[ \log S = n \left( \frac{0.42}{2.3RT} \right) + \frac{5.95}{23RT} \]

\[ \log S = n \left( \frac{0.60}{2.3RT} \right) + \frac{1.72}{23RT} \]

Figure 6 - Log S vs. carbon number "n" for the alcohols (O) and alkanes (●).
log plot the OH group may be seen to increase the free energy of desorption by 5.95 and 1.72 = 7.87 k. cal over the alkanes. For the lower molecular weight members of the series the increased stabilization is several times larger. The diminishing effectiveness of the polar group as \( n \) increases might be due to a lessened capacity of the molecule to make effective polar bonds as it is drawn into a more non-polar membrane environment.

(5) Too much weight probably should not be given to the apparent turning over of the solubility for the high alcohols. (More work needs to be done on these larger molecules. Their diffusion rates are extremely small and there is a greater probability that equilibrium was not attained).

(6) The \( \% \) coverage \( = \frac{\nu_{\text{S}}}{S_{\text{max}}} \) is seen to be the order of one percent for most of the vapors. This number actually compares the density of the molecules in the tissue to the density of the molecules in their respective pure liquid states. It is roughly equal to (but different from) the weight percent sorption.
Discussion of Results

Diffusion Constants from Sorption Experiments

Diffusion data obtained from the sorption experiments are listed in Tables IV and V. In all cases the tissue was dried thoroughly with dry air before exposing it to the test vapor. Temperature was controlled to ± 0.1°C using the constant temperature air bath shown in Figure 2. Representative sorption curves are shown in Figure 7. Those for the alkanes are more nearly of the Fickian or ideal type than are those for the alcohols. Sorption curves for both are linear in the initial stages when $M(t)$ is plotted against $t^{1/2}$ (the time for $M_\infty$ to reach $M_\infty$). For the alkanes the linear region extends over 60% of $M$ while for the alcohols a figure of 40% is more typical. Above the linear portions both absorption and desorption curves for the alkanes are concave to the abscissa axis. This was not always true for the alcohols as shown in Figure 7.

Utilizing the initial portions of the sorption curves and equation (15) the diffusion constants given in Table IV and V were obtained. For both alcohols and alkanes there is a decrease in the diffusion constant as molecular weight increases. The two series are graphed in Figure 8, the curves show that the alkane diffusion constants are substantially higher than the corresponding alcohols over most of the range. The separation between the two groups becomes
Figure 7 - Typical sorption curve for butanol. Many of the alcohols but none of the alkanes exhibited this non-Fickian behavior.
<table>
<thead>
<tr>
<th>Molecule</th>
<th>$D 	imes 10^{11}$</th>
<th>$S$</th>
<th>$k_p = \frac{D S}{\delta}$</th>
<th>$J_s = k_p \Delta C_b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_1$</td>
<td>1.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_2$</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_3$</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_4$</td>
<td>7.62</td>
<td>13.7</td>
<td>104</td>
<td>2.6</td>
</tr>
<tr>
<td>$C_5$</td>
<td>8.49</td>
<td>9.3</td>
<td>79</td>
<td>10.8</td>
</tr>
<tr>
<td>$C_6$</td>
<td>9.28</td>
<td>8.7</td>
<td>80.7</td>
<td>26.7</td>
</tr>
<tr>
<td>$C_7$</td>
<td>10.78</td>
<td>7.0</td>
<td>72.1</td>
<td>71.0</td>
</tr>
<tr>
<td>$C_8$</td>
<td>10.68</td>
<td>6.2</td>
<td>66.3</td>
<td>208.0</td>
</tr>
<tr>
<td>$C_9$</td>
<td>11.32</td>
<td>4.5</td>
<td>51.0</td>
<td>510.0</td>
</tr>
<tr>
<td>$C_{10}$</td>
<td>11.93</td>
<td>1.9</td>
<td>22.6</td>
<td>1.450.0*</td>
</tr>
<tr>
<td>$C_{11}$</td>
<td>12.5</td>
<td>1.6</td>
<td>20</td>
<td>3530.0</td>
</tr>
<tr>
<td>$C_{14}$</td>
<td>18.1</td>
<td>0.27</td>
<td>3.8</td>
<td>7580.0</td>
</tr>
</tbody>
</table>

Note:

(1) Diffusion constants computed from initial rates according to:
    
    $$ D = \frac{\pi d^2 \rho_m}{16 \ M_b} = 2.1 \times 10^{-9} \frac{\text{m}^2}{\text{cm}^2 \text{sec}} @ 25^\circ C $$
    
    $$ \delta = 8.0 \times 10^{-4} \text{cm} $$

(2) $M_\infty$ values were asymptotic values.

(3) $k_p = \frac{DS}{\delta} = 4.5 \times 10^6 \text{DKm (cm hr}^{-1})$

(4) $J_s = k_p \Delta C_b \text{ (mg cm}^{-2} \text{ hr}^{-1})$
DIFFUSION CONSTANTS OF ALIPHATIC VAPORS

Figure 8 - Diffusion constants for the alcohols (○) and alkanes (●) corresponding to the data in Tables II and III.
### TABLE V

Diffusion Data For The Alcohols From Sorption Experiments

<table>
<thead>
<tr>
<th>Molecule</th>
<th>$D \times 10^6$</th>
<th>$S$</th>
<th>$k_p = \frac{D S}{\delta}$</th>
<th>$J_b = k_p \Delta C_s$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2O</td>
<td>9.8</td>
<td>2,560</td>
<td>1.17</td>
<td>0.037</td>
</tr>
<tr>
<td>C1</td>
<td>4.0</td>
<td>263</td>
<td>0.048</td>
<td>0.013</td>
</tr>
<tr>
<td>C2</td>
<td>3.4</td>
<td>141</td>
<td>0.022</td>
<td>0.042</td>
</tr>
<tr>
<td>C3</td>
<td>2.6</td>
<td>121</td>
<td>0.014</td>
<td>0.0012</td>
</tr>
<tr>
<td>C4</td>
<td>1.8</td>
<td>193</td>
<td>0.016</td>
<td>0.00062</td>
</tr>
<tr>
<td>C5</td>
<td>3.0</td>
<td>320</td>
<td>0.043</td>
<td>0.00072</td>
</tr>
<tr>
<td>C6</td>
<td>5.0</td>
<td>530</td>
<td>0.12</td>
<td>0.0010</td>
</tr>
<tr>
<td>C7</td>
<td>1.6</td>
<td>1,600</td>
<td>0.11</td>
<td>0.00036</td>
</tr>
<tr>
<td>C8</td>
<td>0.41</td>
<td>2,210</td>
<td>0.041</td>
<td>0.000074</td>
</tr>
<tr>
<td>C9</td>
<td>0.40</td>
<td>2,620</td>
<td>0.047</td>
<td>0.000048</td>
</tr>
<tr>
<td>C10</td>
<td>0.59</td>
<td>1,500</td>
<td>0.040</td>
<td>0.000024</td>
</tr>
</tbody>
</table>

**Note:**

1. Diffusion constants were computed from initial rates according to
   \[
   \frac{\pi \delta^2 m^2}{16 M_0} = 2 \times 10^{-9} \text{ m}^2 \text{sec}^{-1} \text{ at } 25^\circ \text{C; } \delta = 8.0 \mu \text{m}.
   \]

2. $M_{\infty}$ values were taken at arbitrary times always greater than 180 min.

3. $k_p = \frac{D S}{\delta} = 4.5 \times 10^{-6} \text{ cm/hr}$

4. $J_b = k_p \Delta C_s \text{ (mg cm}^{-2} \text{ hr}^{-1})$
less as the molecular weight increases. This is to be expected as the relative importance of the hydroxy group must become less with increasing molecular weight. From the solubility data e.g. Figure 6, a similar inference can be drawn - the solubility of the two groups tends to coincide as the molecular weight increases. One might speculate that beyond C\textsubscript{11} or C\textsubscript{12} the presence of a single hydroxy group does not matter in the diffusion and solubility behavior of these molecules within the stratum corneum.

The trend of decreasing diffusivity with increasing molecular weight shown for the alkanes in Figure 8, suggests an inverse square root dependence on molecular weight. The alkane data is replotted in Figure 9 vs. \( \frac{1}{\sqrt{M}} \) and there does appear to be a linear correlation. Obviously a plot of D vs. \( \frac{1}{\sqrt{V}} \) where V is the molecular volume would also be linear. This empirical correlation between D and \( \frac{1}{\sqrt{M}} \) cannot tell us much about the mechanism of diffusion since it can be observed both in the free diffusion of gases (Graham’s Law of Diffusion) as well as in bulk diffusion in solids. But it does support the credibility and accuracy of the measured data.
Figure 9 - Alkane diffusion constants plotted vs. $\frac{1}{\sqrt{M}} x 10$
Concentration Dependence of D

It has been assumed up to now that D is a constant (at a particular temperature) and as such is independent of the concentration of the external vapor. As it turns out D is not constant but appears to increase with concentration. On the basis of a rather limited amount of experimental data it appears that the increase in the value of D with concentration is greatest for H₂O and the alcohols and least for the alkanes. The formulae which have been used to compute D yield an average diffusion constant D values of which from a series of experiments using different vapor concentrations can be used to obtain D₀, the diffusion coefficient at zero concentration. This technique is fortunately not required for our purpose which is to compare the diffusion coefficients obtained by sorption with those from permeation data. All that is required is that the diffusion constants obtained either way correspond to identical vapor concentrations. The vapor pressures employed in our permeation measurements were the saturated vapor pressures, i.e., those in equilibrium with the pure liquid at a given temperature. Consequently the diffusion constants measured from sorption experiments must correspond to these same saturated vapor pressures. Since it is always possible in a sorption experiment to measure D as a function of external vapor concentration this is not a serious limitation.
Diffusion constants corresponding to various constant concentrations of pentane are listed in Table VI. Ignoring the first experiment which was probably inaccurate owing to the small weight changes involved, it can be seen that D appears very nearly constant over the full concentration range. Whether D is computed from the half time for sorption (eq 12) or from the initial sorption gradient (eqs. 14 - 15), the initial stages of the diffusion process rather than the latter are weighted more heavily. This means in effect that if D is not increased except at the very highest concentration it could deceptively appear to be constant in this series of determinations. A way of testing this possibility is to compare the diffusion constants obtained with sorption and desorption curves. Some typical results for pentane are given in the short table below and a comparison of a pair of sorption - desorption curves are given in Figure 10.
Figure 10 - Sorption and desorption curves for pentane. These curves are not superimposable and suggest unusual surface sorption.
## TABLE VI

Pentane Sorption Data @ 30°C

<table>
<thead>
<tr>
<th>#</th>
<th>N pentane</th>
<th>M∞ (mg)</th>
<th>Cm</th>
<th>tνa (min)</th>
<th>Dνa x10⁻¹⁰ cm² sec⁻¹</th>
<th>Dνa x10⁻¹⁰ cm² sec⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.065</td>
<td>0.0099</td>
<td>0.44</td>
<td>6.6</td>
<td>0.79</td>
<td>1.57</td>
</tr>
<tr>
<td>2</td>
<td>0.118</td>
<td>0.023</td>
<td>1.02</td>
<td>19.3</td>
<td>0.27</td>
<td>0.92</td>
</tr>
<tr>
<td>3</td>
<td>0.221</td>
<td>0.042</td>
<td>1.87</td>
<td>17.5</td>
<td>0.30</td>
<td>1.02</td>
</tr>
<tr>
<td>4</td>
<td>0.351</td>
<td>0.075</td>
<td>3.64</td>
<td>16.6</td>
<td>0.32</td>
<td>0.91</td>
</tr>
<tr>
<td>5</td>
<td>0.459</td>
<td>0.099</td>
<td>4.42</td>
<td>16.4</td>
<td>0.32</td>
<td>0.99</td>
</tr>
<tr>
<td>6</td>
<td>0.653</td>
<td>0.187</td>
<td>8.31</td>
<td>16.4</td>
<td>0.32</td>
<td>0.91</td>
</tr>
<tr>
<td>7</td>
<td>0.719</td>
<td>0.258</td>
<td>11.5</td>
<td>15.0</td>
<td>0.35</td>
<td>1.02</td>
</tr>
<tr>
<td>8</td>
<td>0.858</td>
<td>0.378</td>
<td>16.8</td>
<td>14.5</td>
<td>0.36</td>
<td>1.01</td>
</tr>
<tr>
<td>9</td>
<td>0.911</td>
<td>0.429</td>
<td>19.1</td>
<td>15.1</td>
<td>0.35</td>
<td>0.97</td>
</tr>
<tr>
<td>10</td>
<td>1.000</td>
<td>0.693</td>
<td>30.8</td>
<td>13.5</td>
<td>0.38</td>
<td>1.10</td>
</tr>
</tbody>
</table>

\[ M_\infty \] is the weight of pentane sorbed on 29.90 mg of dry stratum corneum computed from \( t_\nu \) values using formula (12).

\[ D_\nu \] computed from \( t_\nu \) values using formula (15).

\[ D_1 \] computed from initial rate using formula (15).

Pentane partial pressure at 30°C = 630 Torr.
SORPTION - DESORPTION DATA
FOR PENTANE a 30° C

<table>
<thead>
<tr>
<th>SORPTION</th>
<th>( D_t \alpha )</th>
<th>( D_l )</th>
<th>( t_{\chi_2} ) (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.34 x 10^{-10}</td>
<td>1.05 x 10^{-10}</td>
<td>15.5</td>
<td></td>
</tr>
<tr>
<td>0.39 x 10^{-10}</td>
<td>0.95 x 10^{-10}</td>
<td>13.5</td>
<td></td>
</tr>
</tbody>
</table>

| DESORPTION | 2.62 x 10^{-10} | | 2.0 |
| 3.50 x 10^{-10} | | | 1.5 |

The data show that the pentane diffusion constant may be from 8 - 10 times greater for a fully saturated membrane than for a moderately unsaturated one. Curve (1) is the sorption curve and curve (2) is the desorption curve. The desorption curve is replotted as curve (2A) in the standard sorption form to allow more meaningful comparison. The initial desorption process is clearly a far more rapid phenomenon. In 1.5 min. one half of the pentane has diffused out of the tissue. This same amount of pentane required 13.5 min. to enter the tissue. The most rapid part of the desorption is over with very early as the curves show. This behavior at high concentrations could obviously not be observed by the sorption method as the tissue is never fully saturated except at the end of the experiments.
Measurement of Gas and Vapor Transport with the Quartz Crystal Oscillator.

Introduction

For accurate measurements of the permeation of the less permeable gases and vapors a method more sensitive than our I. R. technique is needed. The ultimate objective is to be able to detect very small quantities of the test gas in relatively large concentrations of water vapor. This requirement arises due to the necessity of studying the effect of membrane hydration on the permeation of other gases. The selectivity afforded by the quartz oscillator technique, in principle, allows this to be done. The second year's report will contain the precise description of the final apparatus as well as the data gained from it. A short description of the progress being made is given below.

Details of Apparatus

The permeation apparatus which we have constructed and are currently testing consists of essentially three components: (1) a vacuum manifold, (2) a diaphragm diffusion cell and (3) a detector system.
(1) **Vacuum manifold**

A means of evacuating the diffusion cell and introducing gases is required. Since the sensitivity of the detector is high, a pump down to a good vacuum is necessary to clean the system even though it is possible during the measurements to work at higher pressures. The present system consists of a fore pump, in line-bakeable water trap, liquid nitrogen trap, McLeod gauge and assorted gas inlet and vapor inlet tubes.

(2) **Diaphragm-diffusion cell**

The cell is built around the membrane supports which consist of porous bronze plates fitted into brass sleeves. These plates are necessary to support the tissue against rupture caused by pressure changes. The brass sleeves fit into the main body of the diffusion cell through vacuum tight O-ring connections. A vacuum of $10^{-4}$ Torr has been attained. The diffusion cell itself is a heavy brass cylinder in two sections (donor and receptor) which rests in a saddle which permits the two parts to be tightened together thus enclosing the epidermal membrane.
(3) Detector System

A pair of quartz crystals fit into the detector portion of the diffusion cell. These are fitted into a brass insert which can be easily removed from the cell and yet can be refitted to make a vacuum tight seal. Each of these crystals must be delicately coated with a substrate to absorb the gas. This is done by a special spraying apparatus built around an artist's air brush. As the gas penetrates the membrane and enters the detector chamber it absorbs into the substrate coated on the quartz crystal. The natural frequency of the crystal changes and this signal is detected, converted to an analogue output and recorded.

The entire system has been working and the permeability of water has been measured with it. Some problems remain to be solved including leaks in the vacuum system, finding suitable, stable crystal coatings and keeping the membrane intact during dehydration.
List of References


Permeability of the skin to gases

A study of the permeability of human skin (epidermis and stratum corneum) to vapors and gases. Physical measurements include the determination of the solubility of homologous series of organic vapors, alkanes, alcohols, etc... in stratum corneum; the permeability of these substances through epidermis and the measurement of gas-tissue sorption rates and equilibria. Primary emphasis is placed upon the measurement of fundamental physical constants characteristic of the tissue and relevant to diffusion. These include gas and vapor solubilities, diffusion constants and activation energies for diffusion... The effect of hydration of the permeability of gases and vapors is studied. The mechanism of diffusion of gases through dry stratum corneum is discussed and compared with diffusion through hydrated tissue.
stratum corneum membrane permeability solubility of gases in skin hydration of stratum corneum diffusion of non-electrolytes through skin skin permeability sorption of vapors and gases by skin