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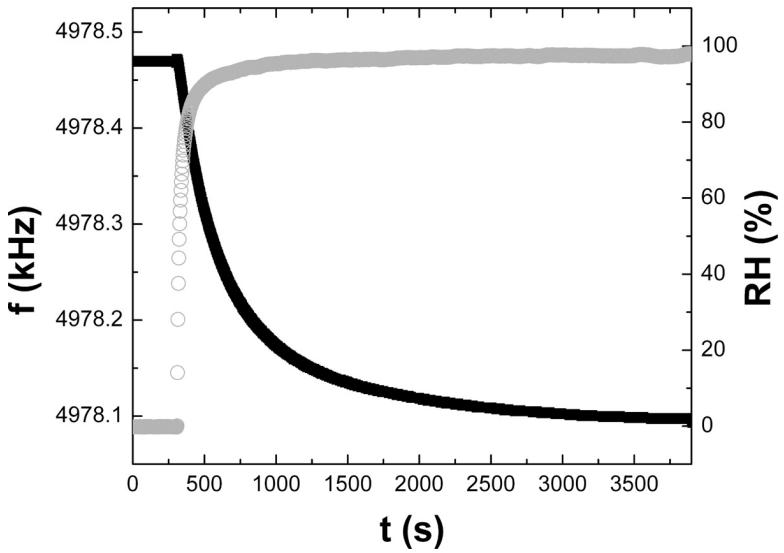

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Permeability of Model Stratum Corneum Lipid Membrane Measured Using Quartz Crystal Microbalance

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The stratum corneum (SC) is the outermost layer of the epidermis. Stacked intercellular lipid membranes found in the SC play a crucial role in regulating water transport through the skin. Despite the importance of this role of the SC lipid membranes, only a few studies have presented quantitative methods to measure the permeability of water in SC lipid membranes. In this work, we present a new method to determine the water permeability of a model SC lipid membrane using a quartz crystal microbalance (QCM). We investigate a model SC lipid membrane comprising an equimolar mixture of brain ceramide (CER), cholesterol (CHO), and palmitic acid (PA), and use QCM to determine the diffusivity (D), solubility (S,) and permeability (P) of water vapor in the model SC lipid membrane.

Introduction

The stratum corneum (SC) is the outermost layer of the epidermis. The SC has a brick-and-mortar-like structure where bricks represent flattened dead cells known as corneocytes and mortar represent intercellular lipid membranes.[1−3] Unlike most biomembranes, the intercellular lipid membranes found in the SC contain hardly any phospholipids. Instead, the three major components of the SC lipid membranes are free fatty acids, ceramides, and cholesterol. These lipids are organized in nearly perfect multilamellar arrays in between corneocytes.[4] It is widely believed that the intercellular SC lipid membranes, the only continuous element of the complex structures that make up the SC, play a crucial role in regulating the loss of water from the skin.[2]

A number of studies have focused on studying the phase behavior of SC lipid membranes using X-ray scattering techniques as well as spectroscopic methods such as Fourier transform infrared (FT-IR) and NMR.[5−7] These techniques provide rich information on the phase behavior and molecular organization of the SC lipid membranes under different conditions. Very few studies, however, have directly correlated the phase behavior of SC lipid membranes with their permeability to water. Methods to determine the water permeability of lipid membranes have focused primarily on phospholipid bilayer membranes. These methods include monitoring the size change of vesicles upon application of osmotic shock and detecting the release of fluorescent molecules either from lipid vesicles or through black lipid membranes.[8,9] These approaches can provide quantitative information on the water permeability of lipid membranes; however, it is difficult to use SC lipid molecules to form either black lipid membranes or unilamellar lipid vesicles with precisely controlled physicochemical properties. Alternatively, studies have shown that permeability measurements can be made on an intact SC.[1,10,11] This approach tends to suffer from a large sample-to-sample variability, and it is difficult to understand the role of SC lipid membranes in determining the permeability of skin due to the complex nature of the SC. Indeed, it is important to develop a technique that enables determination of the water permeability of SC lipid membranes.

In this study, we present a new approach to determine the water permeability of a model SC lipid membrane using a quartz crystal microbalance (QCM). The QCM method has been used to determine the permeability of various gases such as water and oxygen through polymer thin films and membranes.[12−15] The QCM measures the changes in mass per unit area by measuring the shifts in the frequency of a quartz resonator due to absorption and diffusion of the permeating species such as water in the

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(1) Blank, I. H.; Moloney, J.; Emslie, A. G.; Simon, I.; Apt, C. *J. Invest. Dermatol.* **1984**, *82*, 188–194.
(2) Mouritsen, O. G. *Life - As a Matter of Fat: The Emerging Science of Lipidomics*; Springer: Berlin, 2005.
(3) Scheuple, R. J.; Blank, I. H. *Physiol. Rev.* 1971, 51, 702.
(4) Fatouros, D. G.; Groenink, H. W. M.; de Graaff, A. M.; van Aelst, A. C.; Koerten, H. K.; Bouwstra, J. A. *Eur. J. Pharm. Sci.* **2006**, *29*, 160–170.
(5) Chen, X.; Kwak, S. J.; Lafleur, M.; Bloom, M.; Kitson, N.; Thewalt, J. *Langmuir* **2007**, *23*, 5548–5556.
(6) Mendelsohn, R.; Rerek, M. E.; Moore, D. J. *Phys. Chem. Chem. Phys.* **2000**, *2*, 4651–4657.
(7) Rowat, A. C.; Kitson, N.; Thewalt, J. L. *Int. J. Pharm.* **2006**, *307*, 225–231.
(8) Fettiplace, R.; Haydon, D. A. *Physiol. Rev.* **1980**, *60*, 510–550.
(9) de la Maza, A.; Lopez, O.; Coderch, L.; Parra, J. L. *Int. J. Pharm.* **1998**, *171*, 63–74.
(10) Michniak-Mikolajczak, B. B.; Barry, B. W.; Waller, I. L. *Int. J. Pharm.* **1986**, *31*, 247–259.
(11) Scheuple, R. J. *J. Invest. Dermatol.* 1967, 48, 79.
(12) Oliveira, N. S.; Dorgan, J.; Coutinho, J. A. P.; Ferreira, A.; Daridon, J. L.; Marrucho, I. M. *J. Polym. Sci., Part B: Polym. Phys.* **2006**, *44*, 1010–1019.
(13) Vogt, B. D.; Soles, C. L.; Lee, H. J.; Lin, E. K.; Wu, W. *Polymer* **2005**, *46*, 1635–1642.
(14) Smith, A. L.; Ashcraft, J. N.; Hammond, P. T. *Thermochim. Acta* **2006**, *450*, 118–125.
(15) Vogt, B. D.; Soles, C. L.; Lee, H. J.; Lin, E. K.; Wu, W. L. *Langmuir* **2004**, *20*, 1453–1458.

membrane. Permeability is defined as

$$P = \frac{J \cdot l}{\Delta p} = D \cdot S \quad (1)$$

where J, l, and Δp are flux (gas flow rate across membrane per unit area), film thickness, and partial pressure difference across the membrane, respectively.[16] The study of water permeation into membranes involves both the kinetics of the permeation process, represented by diffusivity (D), and the equilibrium uptake, solubility (S). These two parameters, D and S, can be obtained from a mass uptake experiment by using QCM. Our setup also allows precise control over the humidity in the sample chamber; thus it is possible to study the effect of relative humidity on the physical properties of the model SC lipid membrane. This study demonstrates the use of QCM in determining the moisture permeability of a model SC lipid membrane. The direct measurement of permeability using QCM, when combined with spectroscopic methods and X-ray scattering, will be a powerful tool to characterize physical properties of SC lipid membranes of different compositions.

Experimental Section

Materials. Brain ceramide (CER; Porcine) in powder form was purchased from Avanti Polar Lipids. Palmitic acid (PA), cholesterol (CHO), hexane, and ethanol were purchased from Sigma Aldrich. Quartz crystals with gold electrodes were purchased from Masscal Scientific Instruments.

Deposition of Model SC Membranes. Model SC lipid membranes were deposited and annealed on quartz crystals using a procedure described previously.[17] Briefly, an equimolar mixture of CER, PA, and CHO was dissolved in a mixture of hexane and ethanol (2:1 in volume ratio) at 4.5 mg/mL. An airbrush (Precision Aire) was used to apply a thin layer of model SC membrane onto substrates. Deposited model SC lipid membrane was dried under vacuum overnight and was annealed at 70 °C for 10 min.

Grazing Incidence Small-Angle X-ray Scattering (GISAXS) of Lipid Membranes. X-ray studies were performed at the G1 beamline station at the Cornell High Energy Synchrotron Source (CHESS). The wavelength of the X-rays was 0.1239 nm, and the sample-to-detector distance was calibrated with silver behenate (first-order scattering vector q of 1.076 nm^{-1} (with $q = 4\pi \sin\theta/\lambda$, where 2θ is the scattering angle and λ is the wavelength). Slit collimation was used to achieve a resulting beam spot that was approximately 0.2 mm in height and 0.4 mm in width (the z- and y-axes, respectively). A home-built slow-scan charge-coupled device (CCD)-based X-ray detector was used for data collection.

Permeability Measurement Using QCM. A Masscal G1 QCM was used for the permeability measurement.[13] The temperature of the sample chamber was maintained at 30 °C for all our measurements. In a typical measurement, lipid membranes were subjected to dry nitrogen purge for at least 30 min. After drying the lipid membranes, the relative humidity of the QCM chamber was increased to ~100% by flowing in a stream of humidified nitrogen from an external relative humidity generator into the chamber at 10 cm^3 (STP)/min. The relative humidity within the QCM chamber could be precisely controlled by varying the ratio of dry and fully humidified nitrogen streams using two mass flow controllers. The mass uptake due to water sorption was monitored as a function of time at 30 °C at 3 s intervals. The mass of absorbed gas, due to absorption and diffusion of water in the model SC membrane, is determined from the shift in the resonant frequency, Δf, by the Sauerbrey equation:[18]

$$\Delta f = \frac{-2f_0^2 \Delta m}{A\sqrt{\rho_q \mu_q}} = -C \cdot \frac{\Delta m}{A} \quad (2)$$

where f_0 is the fundamental frequency of the crystal, Δm is the mass of the adsorbed gas; $\mu_q = 2.95 \times 10^{11}$ g cm^{-1} s^{-2} and F_q = 2.65 g cm^{-3} are the shear modulus and the density of quartz, respectively; and A is the area of a geometrically flat surface of an electrode on a major face of the crystal. Thus the shift in the resonant frequency is directly proportional to mass uptake per unit area. A bare gold electrode coated quartz crystal was subjected to humidity changes from 0 to ~100% as a control; the shift in frequency due to moisture condensation was negligible.

Results and Discussion

SC lipid membranes consist of three major components: ceramides, cholesterol, and free fatty acids. We use a model system that comprises CER, CHO, and PA in an equimolar ratio.[5,19,20] CER contains ceramide 2 (NS), which is the major component of the ceramide classes found in the SC. This model system has been extensively studied as a model SC lipid membrane system, and its phase behavior has been characterized by different techniques. However, the tail lengths of the ceramides and free fatty acids in the actual SC are much longer than those of lipids used in this study; this model does not fully reproduce the lamellar spacings observed in lipid extracts from the SC. It nevertheless provides a well-characterized system that can provide important insight; thus we use this model system to show the versatility of the QCM method for making permeability measurement. The lipid membrane is deposited onto a substrate using a spray-method.[17] The deposited lipid is dried under vacuum and annealed at 70 °C. The orientation of lipid molecules in the thermally annealed samples is characterized by GISAXS, as shown in Figure 1. Three primary periodic spacings were found at 4.29, 3.45, and 3.27 nm, along with several higher order reflections. These diffraction patterns show that several phases coexist, as has been observed by a previous study, in which an X-ray diffraction experiment was performed on dispersions of CER, CHO, and PA mixtures.[20] The 3.45 nm peak is much less intense than the other two, indicating that there is less of the phase that exhibits a periodic spacing of 3.45 nm in the lipid membrane. These lipids are highly oriented and form lamellar stacks that are parallel to the substrate, as indicated by the strong anisotropic scattering in the q_z direction. However, because of the significant difference in lipid membrane preparation procedure and conditions of X-ray scattering experiments, the lipid membrane structure observed in this study differs from those reported in the previous study;[20] the X-ray scattering data reported in this study was taken from dry thin films, whereas the scattering data in the previous report was taken from suspensions of lipid mixtures.

From eq 1, the permeability of the model SC lipid membrane can be determined by separately measuring the solubility (S) and diffusivity (D) of the lipid membrane to water. These two important properties can be determined by measuring the water uptake of the model SC lipid membrane as a function of time. From the saturation value of such a plot, solubility ($S \equiv$ volume of gaseous water at standard temperature and pressure (STP)/(volume of lipid membrane·vapor pressure)[16]) is determined,

(16) Mulder, M. *Basic Principles of Membrane Technology*., 2nd ed.; Kluwer Academic Publishers: Dordrecht, 1996.
(17) de Jager, M.; Groenink, W.; van der Spek, J.; Janmaat, C.; Gooris, G.; Ponec, M.; Bouwstra, J. *Biochim. Biophys. Acta, Biomembr.* **2006**, *1758*, 636–644.
(18) Sauerbrey, G. *Z. Phys.* **1959**, *155*, 206.
(19) Arseneault, M.; Lafleur, M. *Biophys. J.* **2007**, *92*, 99–114.
(20) Bouwstra, J. A.; Thewalt, J.; Gooris, G. S.; Kitson, N. *Biochemistry* **1997**, *36*, 7717–7725.

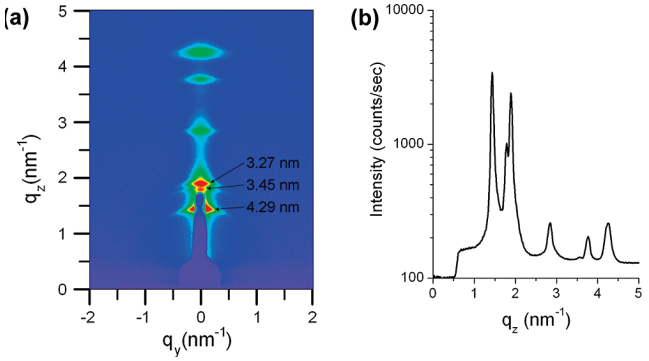

Figure 1. GISAXS profile of model SC lipid membrane. The membrane was spray coated onto a substrate and annealed at 70 °C for 10 min.

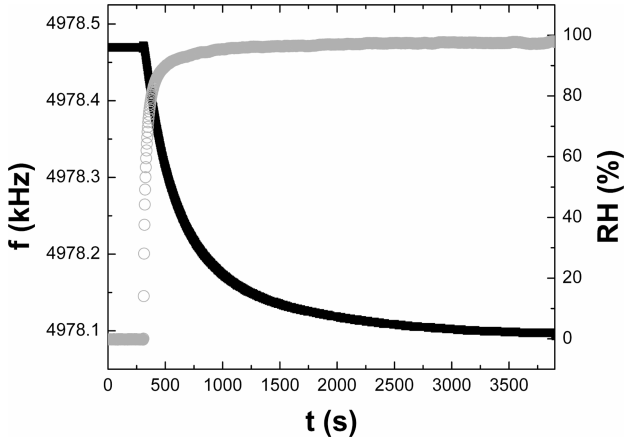

Figure 2. Changes in resonant frequency of model SC lipid membrane-coated quartz crystal and relative humidity in the QCM chamber as a function of time. Filled squares and open circles represent frequency and relative humidity, respectively. Nitrogen stream saturated with water vapor (relative humidity ~ 100%) was introduced at $t = 300$ s. Little change in frequency was observed after 4000 s.

and, from the temporal evolution of mass uptake, D is determined. The model SC lipid membrane is deposited onto an AT-cut quartz crystal with gold electrodes with a fundamental resonant frequency of 5 MHz (see Experimental Section for details). The sample chamber is purged with dry nitrogen for more than an hour to completely remove water from the lipid membrane, and then a nitrogen stream saturated with water vapor is introduced into the chamber. The temperature of the chamber is set at 30 °C to mimic the temperature of SC in vivo. It takes over 3000 s for water absorption to reach a plateau value, whereas the relative humidity in the QCM chamber typically reaches the equilibrium value in less than 100 s, as shown in Figure 2. The delay is caused by slow diffusion of water vapor into the model SC lipid membrane. As the lipid membrane absorbs water, the resonant frequency shifts to lower values, indicating changes in the mass (Figure 2). The mass uptake as a function of time then is converted from Figure 2 by using the Sauerbrey equation (eq 2) and is plotted in Figure 3. The solubility (S) of water in the lipid membrane is defined as the volume of water vapor at standard temperature and pressure (STP) per unit volume of lipid membrane in equilibrium with a unit partial pressure of water vapor. We determine S from the saturation value in the mass uptake curve in Figure 3a. Some studies have shown that QCM-based measurement may deviate from the Sauerbrey relationship (eq 2), because of the softening of the samples on the quartz crystals. We believe that such deviation is minimal since we are estimating the changes in mass by monitoring only the fundamental frequency, which tends to have small deviation even when samples are highly swollen with water vapor.[21]

We determine the diffusivity (D) of water vapor in the lipid membrane by modeling the process as a one-dimensional diffusion of water into a slab, as described by the following equation:[22]

$$\frac{m_t - m_0}{m_\infty - m_0} = 1 - \sum_{n=0}^{\infty} \frac{8}{(2n+1)^2 \pi^2} \exp\left[\frac{-D(2n+1)^2 \pi^2 t}{l^2}\right] \quad (3)$$

where, m_∞, m_0, and m_t are the mass of the film plus the sorbate (water) at time $= \infty$, 0, and t, respectively. l and t are thickness of the membrane and time, respectively. Equation 3 can be simplified by taking the first term of the series on the right-hand side (RHS) of the equation:[23]

$$-\frac{1}{\pi^2} \ln\left[\frac{(m_\infty - m_t)\pi^2}{8(m_\infty - m_0)}\right] = \frac{D}{l^2} t \quad (4)$$

This equation applies for a sorption range between 35 and 85%. The water sorption of the model SC fit to eq 4 is shown in Figure 3b, where the diffusivity can be obtained from the slope of the curve. The thickness of the lipid membrane (l) is independently determined by the shift in the resonant frequency of the quartz crystal due to the deposition of the lipid membrane. Typical thickness of the deposited lipid membranes is ~2−4 μm.

Solubility (S), diffusivity (D), and permeability (P) determined from QCM measurements are summarized in Table 1. Equivalent parameters reported in previous studies using different model systems and measurement methods are also summarized in Table 1. For the ease of comparison, S and P obtained in this study have been converted to equilibrium moisture content ($m_{H_2O}/m_{dry\ sample}$) and flux of water vapor (J; using eq 1), respectively. All parameters measured on the model SC lipid membrane using the QCM method are comparable to or smaller than the equivalent parameters measured on an intact SC or a model SC lipid membrane of different compositions. Similar values for D through dehydrated SC have been reported in previous studies using a gravimetric microbalance technique (Table 1).[10,11] However, depending on the model system and the method of measurement, significantly different values of diffusivity also have been reported.[24] The equilibrium moisture content ($m_{H_2O}/m_{dry\ sample}$) in the model SC lipid membrane is ~0.015 g/cm^3, whereas the values obtained for an intact SC range from 0.06 to 0.42 g/cm^3.[1,10] The value of flux (J) converted from the average value of P is approximately 1.27 μmol/(cm^2·h), which is significantly smaller than the value measured using different methods with an intact SC or a model SC lipid membrane deposited atop porous membranes.[25−27] It is interesting to note

(21) Vogt, B. D.; Lin, E. K.; Wu, W. L.; White, C. C. *J. Phys. Chem. B* **2004**, *108*, 12685–12690.
(22) Crank, J. *The Mathematics of Diffusion*; Oxford University Press: Oxford, United Kingdom, 1979.
(23) Hernandez, R. J.; Gavara, R. *J. Polym. Sci., Part B: Polym. Phys.* **1994**, *32*, 2367–2374.
(24) Packer, K. J.; Sellwood, T. C. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 1592–1606.
(25) Abraham, W.; Downing, D. T. *J. Invest. Dermatol.* **1989**, *93*, 809–813.
(26) Potts, R. O.; Francoeur, M. L. *J. Invest. Dermatol.* **1991**, *96*, 495–499.
(27) Johnson, M. E.; Blankschtein, D.; Langer, R. *J. Pharm. Sci.* **1997**, *86*, 1162–1172.

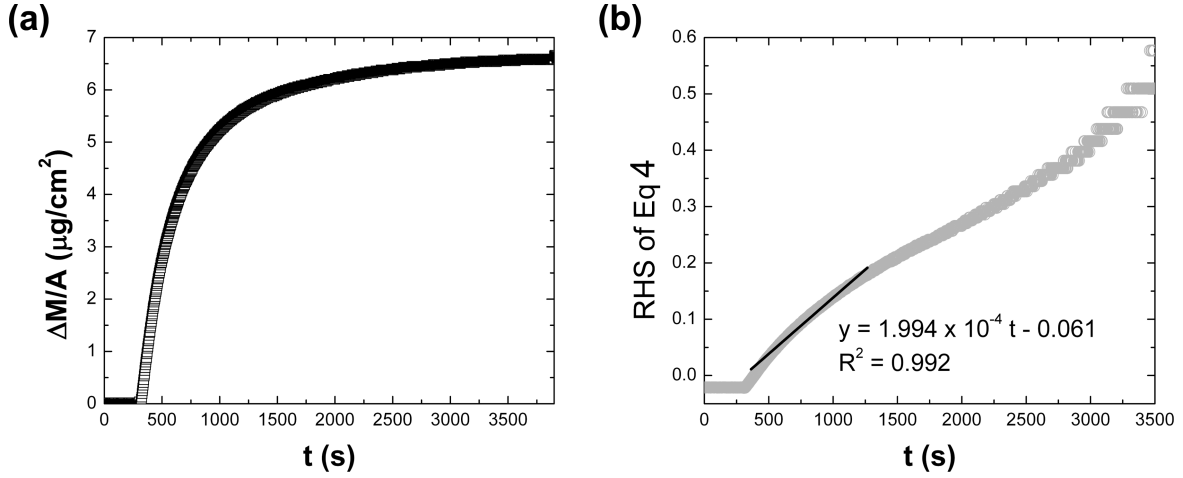

Figure 3. (a) Water vapor uptake as a function of time based on the Sauerbrey equation. (b) Determination of diffusivity of water in a model SC lipid membrane using eq 4. The straight line in panel b was obtained from the sorption range between 35 and 85%.

Table 1. Solubility, Diffusivity and Permeability of the Model SC Lipid Membrane Determined Using QCM and Relevant Parameters in Previous Reports

	measurement method	$m_{H2O}/m_{dry\ sample}$ (g/g)	S (cm^3(STP)/cm^3·cm Hg)	D (10^{-10} cm^2/s)	P (Barrer)[g]	J (μmol/(cm^2·h))
model SC lipid membrane (CER:CHO:PA = 1:1:1 molar ratio)[a]	QCM	0.015 ± 0.001	6.89 ± 0.74	0.39 ± 0.07	2.66 ± 0.19	1.27
human SC[b]	gravimetric microbalance	0.06−0.12		0.15−.32		
human SC[c]	gravimetric microbalance			~1		
human SC[d]	diffusion cell	0.08−0.42		2.50−9.57		11−55
polyvinylidene chloride[e]					0.5	
Candelilla wax[f]					2.98 ± 0.40	

[a] Experiments were performed in triplicate and the error for each average represents standard deviation. Measurements were measured by increasing the relative humidity from 0 to ~100%. [b] Reference 10. [c] Reference 11. [d] Reference 1. [e] Reference 35. [f] Reference 28. [g] 1 barrer = 10^{-10} [cm^3(STP)·cm]/[cm^2·s·cmHg].

that, while the permeability for the model SC lipid membrane is higher than that for poly(vinylidene chloride) films (Saran), it is very close to that of a wax film (Table 1). This is likely due to the similarity in the chemical structure of the compounds that constitute the model SC lipid membrane and the wax film.[28]

Caution must be taken in directly comparing the values obtained in the previous studies with our results since the measurement method and the model systems used in the previous reports are very different from the one used in the current study (Table 1). While our model membrane comprises equimolar mixture of CER, CHO, and PA, the previous studies mostly use excised SC from different subjects comprising complex structure of corneocytes and intercellular lipid membranes. Since the lipid membrane makes up only 5 wt % of the SC,[3] the large saturation concentration of water reported for the SC is likely due to the absorption of water by corneocytes, which accounts for 95 wt % of the SC.[29] The SC is also known to contain a high content of natural moisturizing factors (NMFs), which aid water binding and diffusion in the tissue.[30] In contrast, because of the high degree of order in the lipid bilayers, as illustrated by the X-ray diffraction pattern in Figure 1, the diffusivity and solubility of the model SC lipid membrane are expected to be lower than those of the lipid membranes in the intact SC. Therefore, it is not surprising that the values of permeability reported here are lower than those for the SC.[25−27] In this respect, our approach provides a unique opportunity to study the diffusivity, solubility, and permeability of water in the SC lipid membranes without the complication of having other SC components such as corneocytes and NMFs. This is important as the results based on an excised SC tend to be highly dependent on the source of the tissue and the measurement method, resulting in large sample-to-sample variability and complicating the interpretation of data.[1,11,17]

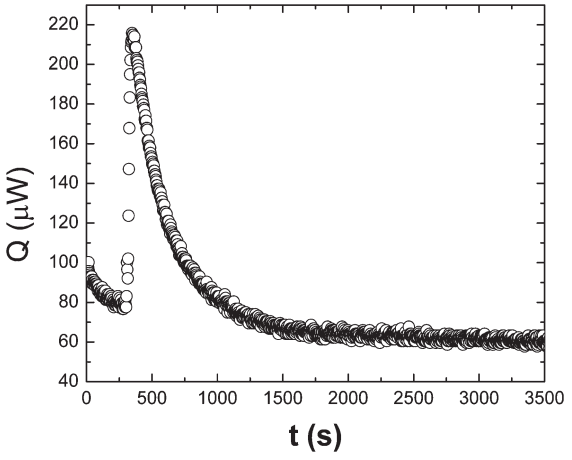

Figure 4. Heat of sorption measured using an HCC. The relative humidity in the chamber was increased from 0 to ~100% after the SC lipid membrane was purged with dry nitrogen for 3 h. A baseline, based on user-defined points, was established before integrating the thermal power signal to estimate the heat of sorption using Origin 6.0.[34]

In addition to the permeability of the SC lipid membrane to water vapor, we are also able to measure the heat of water

(28) Donhowe, I. G.; Fennema, O. *J. Am. Oil Chem. Soc.* **1993**, *70*, 867–873.
(29) Menon, G. K.; Elias, P. M. *Skin Pharmacol.* **1997**, *10*, 235–246.
(30) Quattrone, A. J.; Laden, K. *J. Soc. Cosmet. Chem.* **1976**, *27*, 607–623.

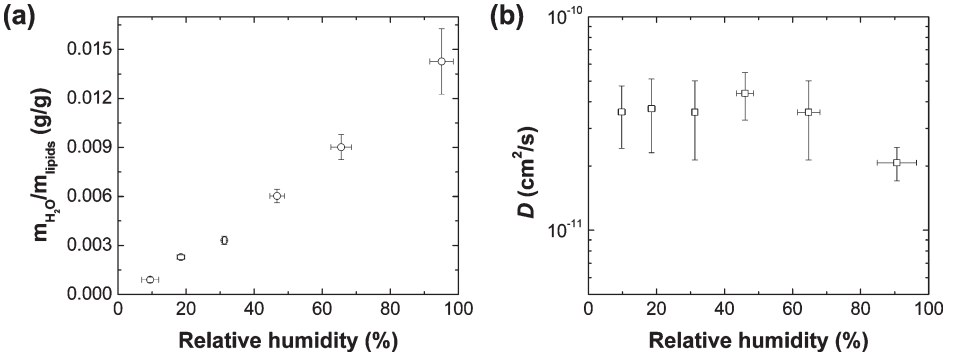

Figure 5. (a) Water sorption isotherm and (b) water diffusivity in the model SC lipid membrane as a function of relative humidity.

sorption by using a QCM equipped with a heat conduction calorimeter (HCC).[31] A typical example of an HCC curve is shown in Figure 4. Heat of water vapor sorption by the model SC lipid membrane was determined to be -33 ± 15 kJ/mol. This value is in a good agreement with the heat of condensation of water at room temperature (-40.65 kJ/mol), indicating that the intermolecular interaction of water molecules with the accessible functional groups on lipid molecules is similar to that among water molecules.[3,32] This value is also quite close to the values for the heat of water absorption reported for different polymer thin films.[14,32]

The physical properties of SC are quite sensitive to the changes in the relative humidity of the environment.[1,33] Studies, for example, have shown that the permeability of an excised SC to water changes as a function of humidity.[1] Our approach allows investigation of changes in the properties of the model SC lipid membrane as a function of relative humidity ($p_{H_2O}/p_{H_2O,sat} \times 100$ (%), where p_{H_2O} and $p_{H_2O,sat}$ denote partial pressure of water in air and vapor pressure of water at a given temperature, respectively). The relative humidity in the QCM sample chamber was gradually increased from 0 to ~100% in a stepwise-manner, and the moisture uptake by the lipid membrane was measured. The water sorption isotherm (equilibrium moisture content, $m_{H_2O}/m_{dry\ sample}$) as a function of relative humidity is shown in Figure 5a. The amount of water in the model SC lipid membrane increases with the relative humidity and shows a linear relationship. This is an indication that the gaseous water is being dissolved into the model SC lipid membrane following Henry's law.[32] While a direct comparison cannot be made, a number of previous studies also showed that the equilibrium moisture content in an intact SC increased with increased relative humidity.[1] In addition to the sorption isotherm, the diffusivity of water in the model SC lipid membrane is determined by fitting water uptake curves during step increases in relative humidity to eq 4. Unlike water uptake at equilibrium, the diffusivity, which is the kinetic parameter defining permeability, showed relatively small changes in response to changes in relative humidity, as shown in Figure 5b. A small decrease in D is observed at a high relative humidity above 90%. Interestingly, a previous study on water permeation across an intact SC also showed a similar trend.[1] It was reported that the diffusivity of water is constant over a wide range of relative humidity but shows a small decrease above 90% relative humidity. Our results suggest that the changes in the permeability of the SC lipid membranes in varying humidity are mainly due to the changes in the solubility of water rather than the mobility (diffusivity) of water molecules in the membranes.

In summary, we have described a new method for measuring the water permeability of a model SC lipid membrane using a QCM. Quantitative information on the diffusivity (D), solubility (S), and permeability (P) of the model SC lipid membrane to water vapor are determined. The approach enables reliable measurement of the water permeability of a model SC lipid membrane with an unprecedented precision. It should now be straightforward to use SC lipid membrane systems of different compositions to measure the permeability using the QCM method. In addition, it is possible to test the effect of various additives that are included in personal care products such as soaps and cosmetics on the permeability of SC lipid membranes. The combination of the QCM-based method and spectroscopic techniques such as NMR and FTIR should provide a unique opportunity in correlating the phase behavior of SC lipid membranes with the macroscopic permeability of SC lipid membranes.

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(31) Smith, A. L.; Shirazi, H. M. *Thermochim. Acta* **2005**, *432*, 202–211.
(32) Smith, A. L.; Mulligan, R. B.; Shirazi, H. M. *J. Polym. Sci. Part. B: Polym. Phys.* **2004**, *42*, 3893–3906.
(33) Wildnaue, Rh.; Bothwell, J. W.; Douglass, A. B. *J. Invest. Dermatol.* 1971, 56, 72.
(34) Smith, A. L.; Shirazi, H. M.; Mulligan, S. R. *Biochim. Biophys. Acta, Protein Struct. Mol. Enzymol.* **2002**, *1594*, 150–159.
(35) Brandrup, J.; Immergut, E. H. *Polymer Handbook*, 2nd ed.; John Wiley & Sons, Inc.: New York, 1966.