Evidence that pores are the primary conductive pathway in human skin.

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For many chemicals, the outermost layer of human skin, called the stratum corneum (SC), acts as the primary barrier to dermal absorption. The specific diffusion pathways through the SC for different types of chemicals is a matter of ongoing debate. (1) Research has shown that the permeation rate of polar compounds through human skin is correlated with the electrical resistance across the skin. Other research has shown that the permeation rate of polar compounds through two pieces of human SC in contact with each other is much slower than is predicted by simply doubling the thickness of a single piece of SC. (1, 2) In contrast, permeation rate of nonpolar compounds through two pieces of SC is equal to half the rate through one piece of SC. (1, 2, 3) This has led to the hypothesis that permeation of polar compounds through human SC occurs primarily through pores in the skin, such as those created by hair follicles and sweat glands. If the hypothesis is true, then when two pieces of stratum corneum are put in contact with each other, it is unlikely that their pores will line up with each other. Each piece of skin occludes the pores of the other, resulting in much reduced diffusion rates.

This work seeks to examine the "pore diffusion" hypothesis with impedance spectroscopy measurements. Electrical conduction through the skin occurs by movement of ions, which are likely to use the same pathways as polar compounds. If electrical conduction through human SC occurs in a homogeneous fashion, then the impedance across two pieces of SC should be the same regardless of whether they are in contact or separated by a gap filled with electrolyte.

Split thickness human cadaver skin collected within 24 h postmortem and frozen immediately was acquired from NDRI (Philadelphia, PA) and kept frozen at less than -60°C until use. The impedance across two pieces skin mounted in a diffusion-type cell was measured both with the pieces in direct contact and with the pieces separated by 1.5 cm of electrolyte solution. The measurements were made at 32°C, which is the physiological temperature of human skin. The electrolyte, 10 g LiCl:100 mL water has a low electrical resistivity and a relative humidity of 90%. (4,5) The working and reference electrodes were sintered Ag/AgCl exposed directly to the electrolyte. A region of skin 1.5 cm in diameter was exposed to the electrolyte. The impedance was measured with a Gamry PCI4/300 potentiostat/galvanostat/impedance analyzer. Measurements were taken at the open circuit potential with a 10 mV (root-mean-square) probe voltage ranging in frequency from 300 kHz to 1 Hz with 10 frequencies per decade.

The impedance data were fit with a model circuit consisting of three segments in series, which is shown in Figure 1. The first segment was a resistor accounting for the solution resistance. The second and third segments were each a resistor in parallel with a constant phase element, which represented the resistive and capacitive characteristics of the skin. It was assumed that the two pieces of skin had identical characteristics, so the elements of the second and third segments had identical parameters.

The data analysis showed that the resistance across the two skin pieces increased by approximately a factor of 10 when they were in contact with each other relative to when they were separated by an electrolyte gap. The resistance results are summarized in Figure 2. The constant phase element properties, which are not shown here, also changed depending on whether the two pieces of skin were in contact. This cannot be explained by homogeneous electrical conduction through the skin, and supports the hypothesis that electrical conduction occurs primarily through pores in human skin.

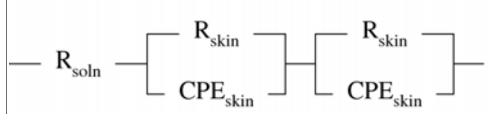

Figure 1. The model circuit used for analyzing the impedance data. "R" denotes resistors, and CPE denotes constant phase elements.

First Sequence	Donor	SC-SC (k Ω)	SC-sol-SC (k Ω)	Ratio
SC-SC	G	28.5	1.5	19
SC-SC	G	22.5	2.5	9
SC-SC	G	17.5	2	8.8
SC-sol-SC	G	10	1	10
SC-sol-SC	K	3.45	0.35	9.9
SC-sol-SC	K	2.25	0.2	11.25

Figure 2. A summary of the resistance across two pieces of skin that are touching (SC-SC) or separated by solution (SC-sol-SC). Different letters in the "Donor" column denote different cadaver skin sources.

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