Science & skin permeation
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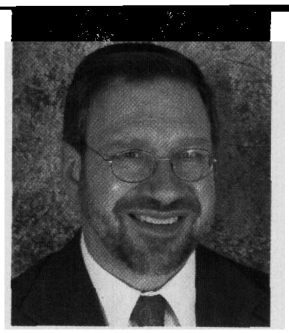


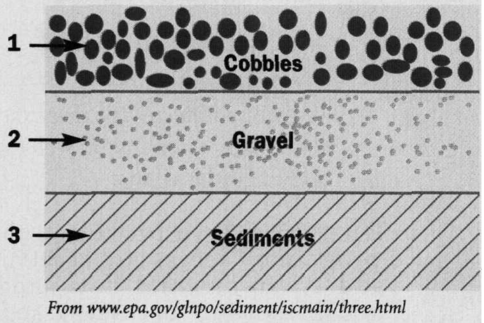
Science & Skin Permeation

Delivery of actives is related to larger scientific concepts developed by some of the greatest technical minds over the last century and a half. BY STEVE HERMAN

"You are 87 percent water; the other 13 percent keeps you from drowning."
—P. E. Morris

WITH ALL THE WATER in the human body, organization is required from many biochemical structures. The skin is a key component for holding it all together. The skin is not a solid barrier, and selected materials can move in and out under a variety of conditions. The literature on skin structure and function typically refers to illustrations such as Figure 1 to demonstrate the layers of the stratum, corneum, dermis, and epidermis. Well, not exactly—

FIGURE 1: STRATA



From www.epa.gov/glnpo/sediment/iscmain/three.html

FIGURE 2: MODEL OF STRATUM CORNEUM

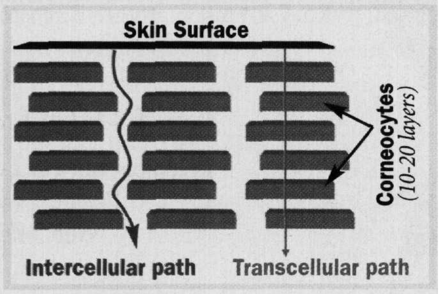


Figure 1 is from an EPA report on the proper disposal of sediment from dredging and quarries. Layer 1 is cobbles; layer 2 is gravel; layer 3 is sediment. Science is science, and the same principles governing percutaneous absorption or transepidermal water loss apply to the flow of liquids and pollutants in and out of layers of sediment.

Cosmetic or drug function is an example of materials interacting with a substrate. The underlying science of diffusion involves Chemistry 101 or Physics 101 topics such as osmotic pressure or Brownian motion. Since Einstein did not get his Nobel Prize for his relativity theory but for his work on the photoelectrical effect, with a boost from his mathematical analysis of Brownian movement, he is a good starting point for the study of diffusion.

Brownian motion is based on an observation by Robert Brown. In 1827, he found that small particles suspended in a fluid were in continuous movement. His discovery did not receive much attention until the turn of the 20th century, when scientists concluded that Brownian motion constituted a clear demonstration of the existence of molecules.

Quantitative analysis came in 1905, when Einstein stated the mathematical laws governing the movements of particles on the basis of the kinetic theory of heat. According to this theory, bodies of microscopically visible size suspended in a liquid will perform irregular thermal movements. Once Brownian motion could be treated by a mathematical model, many related scientific theories and applications were developed.

In the presentation speech for Einstein's Nobel prize[1], Professor S. Arrhenius, chairman of the Nobel Committee for Physics of the Royal Swedish Academy of Sciences, explained the importance of this work for the cosmetic industry:

"Throughout the first decade of this century, the so-called Brownian movement stimulated the keenest interest. In 1905, Einstein founded a kinetic theory to account for this movement by means of which he derived the chief properties of suspensions, i.e., liquids with solid particles suspended in them. This theory, based on classical mechanics...has grown into a large branch of science, colloid chemistry."

By 1905, thanks to Brown and Einstein, we have atoms

TABLE 1: PERCUTANEOUS ABSORPTION
Some influential parameters

Vehicle	Polarity Concentration Penetration enhancers pH
Compound	Molecular weight Water/lipid partition coefficient Ionization
Skin	Age, sex, race Anatomical site Temperature Hydration of SC Damage to SC
Application	Dose Duration Skin area in contact with vehicle

From http://altweb.jhsph.edu/science/pubs/ECVAM/ecvam13.htm

jiggling around in liquids. The permeation story goes back further, to Adolf Fick (1829-1901) in 1855[2]. Fick's two laws of diffusion are the basis of a vast range of scientific disciplines, from oceanography to skin permeation. Fick's laws are differential equations, but the first law can be stated without calculus as follows:

Flux (molecules per unit time)=

$$\frac{D \times A \times P}{T}$$

where D is the difference in concentration; A is the area; P is the permeability coefficient; and T is the thickness.

The second law concerns the time dependence related to change of concentration, and unfortunately appears in print as:

$$\frac{\partial C}{\partial t} = X \frac{\partial^2 C}{\partial x^2}$$

In English, it states that the greater the difference in concentration, the quicker the movement of material. Since mathematics is rearing its ugly head, there is room for one last relationship involving two big names in science, the Stokes-Einstein Equation:

$$D = \frac{kBT}{6\pi rn}$$

where the diffusion coefficient D is related to the size of the molecule (radius r); kB is the Boltzmann constant; T is the absolute temperature; and n is the viscosity of the liquid through which the molecule is diffusing. The diffusion coefficient is an important parameter for drug delivery.

In the late 1800s, Ernest Overton discovered that substances that dissolve in lipids pass more easily into the cell than those that dissolve in water. This was some of the first evidence that cells were surrounded by a lipid membrane. The phospholipid membrane can greatly modify the permeation of molecules into the cell. The membrane acts as a barrier to passive diffusion of water-soluble molecules. The correlation between permeability and solubility is named Overton's Rule.

Tortuosity is an indication of how the structure of a porous medium restricts the flow of gases or liquids through the material. In this sense, tortuosity is to fluid flow what the structure of a wire (cross-section, length, etc.) is to the flow of electricity. It is a property discussed at the SCC Annual Scientific Seminar[3] and found on the Website of the Graduate School of Southampton Oceanography Centre[4].

Figure 2 shows two ways a material can penetrate a brick-and-mortar structure such as the stratum corneum, with the corneocytes as the bricks. The materials can go straight through all the components, or have to bend around the impenetrable materials. Most delivery of cosmetic actives follows the intercellular route. A third possibility, the appenda-geal route, utilizes sweat glands and hair follicles. Yet another equation is needed to show the influence of the corneocytes.

When $\kappa D_L/D_P > 1000$, the corneocyte arrangement has a large impact on skin permeation, where κ is the lipid/protein partition coefficient; D_L is the diffusivity in the lipid phase; and D_P is the diffusivity in the protein phase.

This mad dash through some of the names, concepts, and equations describing diffusion and permeation is intended to show how cosmetic concepts of the delivery of actives, so obviously related to drug delivery, is also related to larger scientific concepts developed by some of the greatest technical minds over the last century and a half. For those with less interest in diffusion equations, Table 1 lists the major factors influencing percutaneous absorption. The technological approach is a portal to virtually every fundamental concept of physics, chemistry, and biology. GCI

The same principles governing percutaneous absorption or transepidermal water loss apply to the flow of liquids and pollutants in and out of layers of sediment.

References:
1. Presentation Speech by Professor S. Arrhenius, chairman, Nobel Committee.
2. Fick, Adolf, Ann. Physik, Leipzig, 170, p. 59,1855, for Physics of the Royal Swedish Academy of Sciences.
3. Kasting, Gerald B., et al., "Dye Localization and Estimation of Lipid Pathlength in Human Stratum Corneum," SCC Annual Scientific Seminar, May 10, 2001.
4. www.soc.soton.ac.uk/SOES/GRAD-SCHOOL/projects2001/boudreau_tort.htm.

Steve Herman is director of R&D of AFF International. He has more than 30 years of experience in the industry, primarily in fragrance application. He serves as an adjunct professor in the FDU Masters in Cosmetic Science program, and has been active in numerous capacities with the SCC. He may be reached at (973) 244-5880, or by e-mail: GCISteve@aol.com.