The two formulations were the same except for slight variation in pH. Statistically, there was no difference in absorption between the two formulations. However, a careful examination of the individual values in Table 9.5 shows consistency within individuals. Analysis of variance (ANOVA) for individual variation showed statistical significance for receptor fluid ($p = 0.02$) and skin content ($p = 0.000$); therefore, when comparing treatments for *in vitro* percutaneous absorption, it is recommended that each treatment be a part of each skin source.

9.2 TRANSEPIDERMAL WATER LOSS

Water comprises about 60% of adult human body weight. The body obtains water from the intake of foods and fluids and leaves the body visibly via urine, sweat, and feces. Additionally, the body loses water continuously by evaporation from the respiratory passages and skin surface—termed insensible water loss, since we do not feel that we are actually losing water all the time. The amount of water that is leaving the body at rest is about 700 mL/day at an ambient temperature of 20°C (10, 11). The average water loss by diffusion through the skin is 300 to 400 mL/day, even in a person who is born without sweat glands (11) or whose sweat glands are inactivated (12). In other words, the water molecules themselves actually diffuse across the skin (11). This invisible natural process of water diffusion is called TEWL (10).

The TEWL has been related to the skin barrier function by a series of investigations. For instance, studies in the past have established that washing the skin surface with fat solvents did not increase the rate of water loss, but light sandpapering of the skin surface (13) or tape stripping of the whole SC (14, 15) resulted in increased TEWL. As the permeation rate of water across full-thickness skin, epidermis, or SC turned out to be approximately the same, it was realized that SC acts as the principal barrier to TEWL (16). Furthermore, a high rate of TEWL has been detected by patients with SC disorders, like psoriasis or ichthyosis (17). The TEWL is therefore taken as a measure of the skin barrier integrity, which mainly resides in the SC.

Anatomical skin site is an important variable with respect to baseline TEWL, which can be ranked from the highest to the lowest values: palm > sole > forehead = postauricular skin = dorsum of hand > forearm = upper arm = thigh = chest = abdomen = back (18). It can actually be related to the SC thickness of the particular body regions (19). Studies of different areas of the forearms showed the differences between three sites: (1) the site close to the wrist showed the highest values in all cases; (2) the nearest elbow region showed a slightly higher value than the median site; and (3) the median site (20, 21). Statistically, only the wrist region differed significantly from the other sites. The fact that the sweat gland density and activity varied on the forearm increasing towards the wrist could be one, but not the only, explanation for the higher value of the wrist region (22). Another hypothesis is that the wrist region is more exposed to mechanical and atmospheric influences than the others and the SC there could be more easily and regularly irritated, leading to increased TEWL values (22). An emotional influence on the wrist region was also suggested to play a role.

9.2.1 Correlation of Percutaneous Absorption and TEWL

Percutaneous absorption can be performed *in vivo* with human volunteers and animals. It can also be done *in vitro* with cadaver skin, human and animal, in a diffusion system. Percutaneous absorption is by passive diffusion only, from a higher concentration progressively to a lower concentration. The TEWL has a passive diffusion component where water from the body (high concentration) passes out through the skin to a lower concentration, the environment. This would be baseline TEWL. The TEWL also has an active component: the release of water through sweat glands for heat dissipation or nervous response. In *vivo* TEWL studies would contain both passive and active water transport; however, cadaver skin in *in vitro* studies would only have the passive transport.