12.3.5.11 Selegiline

Although no data were found, the Summary Basis of Approval document for selegiline stated that locations at the upper torso or upper thigh provided similar absorption; however, application to the upper buttocks was not bioequivalent and resulted in greater absorption (42).

12.3.5.12 Testosterone

Yu and colleagues (35) determined differences in absorption of testosterone via a transdermal system in hypogonadal men. There were no significant differences in testosterone absorption between application sites of the upper buttocks, back, and upper arms (Table 12.8) (38).

12.4 DISCUSSION

There are many chemical and cutaneous properties to appreciate when suggesting mechanisms for regional variation in percutaneous absorption. As summarized by Law et al. (1), skin is a complex organ with many factors varying by region. There are differences in anatomy from one individual to another, adding yet another layer of complexity (33). Prior studies suggest regional variation in percutaneous absorption by physiological mechanisms such as skin irritation, erythema, and blanching (44). It is beyond the scope of this overview—but of clinical and biological relevance—to relate regional variation in flux to endpoints such as irritant and allergic contact dermatitis (45).

This overview specifically focused on quantifiable data pertaining to percutaneous absorption, such as urinary excretion data, cutaneous disappearance of chemical, and pharmacokinetics of blood plasma. In general, the head, neck, and genital regions appear more absorptive than other body regions. The abdomen, chest, back, and thighs proved less absorptive. Differences at anatomical sites in appendage density, skin anatomy, stratum corneum thickness, sebum production, and proximity of vascular blood supply to the cutaneous surface are factors suggested to affect cutaneous absorption.

There are several ways to calculate percutaneous absorption. It is important to recognize where inaccuracies may arise based on each method used. For example, measuring the amount of chemical that disappears from a solution or a gel without protection on the skin surface over a period of hours or days allows for error (17). Disappearance of the chemicals could be achieved by multiple mechanisms in addition to percutaneous absorption. The studies may have assumed that if the chemical disappeared, its entirety had been percutaneously absorbed. However, the chemical could be rubbed off due to limited or no protective barrier. In addition, the top layers of the stratum corneum slough off over time by physiological mechanisms, so it is possible some of the chemical may have been removed along with the sloughed-off cells in lengthier studies.

The urinary excretion method also allows for error, as chemicals may be excreted via other mechanisms such as exhaled air or feces. In addition, the chemical may build up in other locations in the body and therefore is not excreted in the urine.

Studies quantifying absorption utilizing blood plasma levels are also complex based on where the drug deposits in the body and the effects of renal and fecal excretion, among a myriad of other bodily processes. Although no study method is fully accurate in quantifying percutaneous absorption, the data collected are helpful, as we can create comparisons of the absorption among varying body regions. Guy and Maibach (5) suggested a formula to calculate percutaneous absorption dependent on body region. This can be used as a tool as new transdermal medication patches, gels, and solutions continue to be developed. For example, Wester et al (46) determined percutaneous absorption of piperonyl butoxide and pyrethrin at the forearm and subsequently calculated the percutaneous absorption of those chemicals from the forehead. Such data can be used as an approximate model for future work in the pharmaceutical industry or when determining how to best design protective clothing for the occupation worker.

Interestingly, when using the forearm as a reference, the review data showed similar ratios of absorption for a certain body site for several chemicals regardless of molecular weight or partition