

[68]. There are many other drugs and chemicals applied topically that may have increased systemic toxicity as skin barrier properties change.

Inadvertent systemic toxicity from cosmeceuticals and other products have occurred. For example, phenol can be cardiotoxic: a phenol and croton oil solution used in deep chemical peels caused cardiac arrhythmias, including atrial and ventricular tachycardia, premature ventricular beats, and bigeminy; people with diabetes mellitus, hypertension, and depression may be at higher risk [68]. There is also concern about mercury-containing skin care products (such as skin-lightening creams and soaps, local antiseptics, etc.), and their potential to cause neurotoxicity or nephrotoxicity with enough systemic absorption [68]. Arsenic is another toxic metal that is used (or is a contaminant) in cosmetics, medications, pigments, and natural health products that when applied onto skin over time or in sufficient amounts can result in systemic toxicity effects, including psychoses, seizures, multiorgan failure and death [68]. Be cognizant that *any* drug or chemical that touches the skin has the potential for percutaneous absorption that may result in systemic distribution and possible systemic toxicity.

21.2.11 DOES EXFOLIATION AFFECT TOPICAL ABSORPTION?

Exfoliation is part of a natural skin cell renewal process: keratinocytes begin as boxlike basal cells at the base of the epidermis, then migrate up towards the skin surface, flattening out to become a layer of overlapping corneocytes which have no nuclei—thus termed dead skin cells—which are then “sloughed off” i.e. exfoliated. Drugs or chemicals bound to skin cells could either be lost by the exfoliation process or be absorbed deeper into the dermis; thus, exfoliation can affect drug bioavailability after topical administration. Urea, which is minimally absorbed topically, can be used as an exfoliation marker [73].

21.2.12 DOES WASHING AFFECT TOPICAL ABSORPTION?

There are two opposing wash effects that can affect topical absorption of drugs and chemicals. Loss by exfoliation can be enhanced by washing [3] even hours after application [73] if there is drug remaining in the SC, and this would be a “washing-off” effect. Note that for highly lipid-soluble drugs or chemicals (e.g. pesticides), washing with soap and water may not be sufficiently effective in removing them [74].

In fact, the opposite may happen: washing the site of application in between doses may actually enhance topical absorption/penetration, and this would be a “wash-in” effect [75–77]. (See also Section 2.13.) Be aware that washing may promote drug or chemical penetrance through the skin, leading to toxicity, e.g. with insect repellents [75–77]. Care should be taken when insect repellents are used, especially in children. The U.S. Environmental Protection Agency (EPA) recommends that instructions on the label be followed [6] for insect repellent products, and they should be used according to the time of day when mosquitoes are most active, which may vary for the species and type of diseases transmitted [6]. Care should also be taken in the work environment if there is occupational exposure to chemicals: workers should be counseled to wear protective clothing and use protective equipment and be warned about the “wash-in” phenomenon [6]. They should be aware that the mechanical friction from handwashing may increase percutaneous absorption, in particular of inorganic compounds [75].

21.2.13 DOES RUBBING OR MASSAGING AFFECT TOPICAL ABSORPTION?

There are two important concepts regarding whether rubbing or massaging affect topical absorption: *rub enhancement* and *rub resistance*, both of which occur with rubbing/massaging. One example of rub enhancement relates to sunscreen application and washing: the mechanical stress of skin washing can massage the sunscreen deeper into the hair follicle [78], and