
19 Understanding Skin Metabolism—Effect on Altering *In Vitro* Skin Absorption and Bioavailability of Topically Applied Chemicals

Jeffrey J. Yourick and Margaret E.K. Kraeling
Office of Applied Research and Safety Assessment,
Food and Drug Administration, Laurel, Maryland

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19.1 INTRODUCTION

The skin is the largest organ of the body. The skin can also be considered a barrier from environmental factors, as well as a route of exposure for local and systemic absorption of chemicals. Skin possess the capacity to metabolize chemicals that diffuse through the protective stratum corneum barrier. Ideally, metabolism can be viewed as a protective measure for chemicals that are absorbed to guard against toxins having an adverse systemic effect. However, we must also be cognizant that skin metabolism can transform dermally applied nontoxic chemicals to toxic metabolites that would subsequently be available for systemic absorption (1).

Early studies found that benzo[a]pyrene could be metabolized by mouse skin floating in tissue culture media, which indicated the potential importance of the metabolism of compounds during skin absorption (2). In 1984, a skin permeability chamber was developed to be easy to use, maintain metabolic integrity, and measure penetration (3). This study found that *in vitro* skin absorption can be affected by metabolism. Therefore, characterization of chemical skin absorption is a function of both skin metabolism and diffusional properties.

Skin has long been known to have a reduced level of metabolic capacity when compared with the liver. Human skin expresses basal levels of messenger RNA (mRNA) for many of the cytochrome