

# Dermal Exposure and Absorption of Chemicals and Nanomaterials

JE Riviere and NA Monteiro-Riviere, Kansas State University, Manhattan, KS, USA

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## Abbreviations

AUC	Area under the concentration-time profile	MF	Mixture factor
ICP-OES	Inductively coupled plasma-optical emission spectroscopy	PEG	Polyethylene glycol
IPPSF	Isolated perfused porcine skin flap	TEM	Transmission electron microscopy
LFER	Linear free energy relationships	TEWL	Transepidermal water loss

## Introduction

The skin is a primary interface between the body and the environment, making it particularly relevant to assess dermal toxicity after occupational or environmental exposure to chemicals. The skin is also the primary exposure route for cosmetics and is the preferred route of administration for topically applied drugs targeted either locally for dermatological applications or transdermally for systemic therapy. Recent advances in nanotechnology result in potential exposure of skin to nanoparticles after occupational or consumer product use (e.g., sunscreens).

Absorption and toxicity are intertwined when evaluating the potential for a chemical or drug to cause dermal toxicity. A barrier is defined as something that obstructs or retards movement. In dermatotoxicology, this obstruction refers to the impediment of chemical or particle movement across or into the skin. This barrier is most often viewed as restricting diffusion, but also could be considered as retarding absorption of intact drug via metabolism in the skin. Topically applied chemicals may either penetrate the skin to have a local effect and/or be absorbed across the skin and result in systemic absorption and distribution throughout the body. In order for realistic toxicological risk assessments to be made, the rate and extent of material absorption must be quantitated. The focus of this chapter will be to review approaches used to assess this phenomenon.

## Structure and Function of Skin

The skin is the largest organ of the body accounting for some 20% of body weight in most species. Its function is to protect the internal organs from extremes in temperature fluctuations, as well as to prevent systemic exposure to allergens, pollutants, toxic chemicals, and organisms including bacteria, fungi, parasites, and viruses universally found in the environment. It is also the primary organ involved in interpersonal communications between individual animals, a function supported by pelage and glandular secretions. The skin of humans and most animals is morphologically quite similar across species. The skin has several types of appendages (depending on the species) including hair follicles, sebaceous and sweat glands, spines, quills, scales, spurs, horns, claws, nails, and hooves. The specific and comparative anatomy of skin and hair has been reviewed extensively elsewhere (Montagna, 1967; Monteiro-Riviere, 2006).

On the histological level, the skin can be divided into two very distinct regions: the epidermis and the dermis (Figure 1). The epidermis consists of stratified squamous keratinized epithelium that undergoes a programmed proliferation and differentiation that will eventually result in the formation of the major barrier to chemical penetration: the stratum corneum. Two primary cell types exist in the epidermis: keratinocytes and non-keratinocytes including melanocytes, Merkel cells (tactile epithelioid cells), and

<sup>1</sup>Change History: August 2014, JE Riviere and NA Monteiro-Riviere updated sections on QSPMR mixture models and nanomaterial absorption, and added new references.

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