
28 The Fate of Material Remaining in Skin in *In Vitro* Absorption Studies

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28.1 INTRODUCTION

When conducting *in vitro* studies to determine the percutaneous absorption of chemicals, it has been recognized that lipophilic compounds and compounds that bind in the skin can present a problem in the *in vitro* measurement of percutaneous absorption. The skin reservoir is defined as the amount of applied chemical that remains in the skin (i.e., in the stratum corneum, epidermis, and dermis) at the end of an *in vitro* absorption study. The skin reservoir may be considered part of the material available for systemic absorption. However, when the skin reservoir is significant compared to levels measured in the receptor fluid, the contribution of the skin reservoir to systemic absorption should be examined. Compounds that are insoluble in water may not partition freely from excised skin into an aqueous receptor fluid. The problem was alluded to by Franz (1), who in selecting compounds for the study, omitted highly water-insoluble compounds to avoid results that were limited due to insolubility. The methodological problem that a skin reservoir creates may not be limited to lipophilic compounds. Studies with alpha hydroxy acids (AHAs), such as glycolic acid and lactic acid, have shown that very polar compounds can still be substantially retained in skin at the end of a 24-hour absorption study (2).

28.2 MODIFICATION OF RECEPTOR FLUID

The receptor fluid used in *in vitro* dermal absorption studies is important and should not act as a rate-limiting step in the permeation process due to the limited solubility of the test compound in the receptor medium (3). A buffered salt solution, such as HEPES-buffered Hanks' balanced salt solution (HHBSS), or saline solution may be an appropriate receptor fluid for determining skin absorption for hydrophilic compounds, but it is not likely to be applicable for lipophilic compounds. Attempts have been made to overcome the solubility problem by modifying the receptor fluid composition. Bovine serum albumin (BSA) is sometimes added to the receptor fluid to increase the solubility of lipophilic compounds. Brown and Ulsamer (4) found that the skin permeation of the hydrophobic compound hexachlorophene increased twofold when normal saline was replaced with 3% BSA in a physiological