



FIGURE 29.7 Extended DB1 absorption study in fuzzy rat skin. Absorption values are the $X \pm SE$ from two separate rat studies. Each individual absorption value within a study was determined by averaging three to four replicate diffusion cell measurements for each time interval point. (From Reference 17.)

contained in the viable epidermis/dermis layer (data not shown). To examine the fate of DB1 from the skin reservoir, an absorption study in rat skin was extended to 72 hours (Figure 29.7). The extended absorption study (skin washed after 24 hours) revealed that little (0.16% of the applied dose) of the DB1 that penetrated skin within 24 hours (2.6% of the applied dose; Table 29.3) moves through the skin to be absorbed into the receptor fluid over 72 hours. No rat skin metabolism of DB1 was found by HPLC analysis of skin or receptor fluid.

29.3.3 DB1 DISCUSSION

In summary, the skin reservoir can often contribute to the amount of material considered absorbed in diffusion cell studies. When the skin reservoir is significant compared to levels in receptor fluid, the contribution of the skin reservoir to systemic absorption should be examined. Therefore, it is important to determine the fate of chemicals remaining in the skin at the end of a typical 24-hour *in vitro* absorption study. An extended (72 hours) absorption study demonstrated that the DB1 remaining in the skin did not appreciably move into the receptor fluid beyond the extent measured after 24 hours. The barrier property of skin in diffusion cell studies has been shown to remain intact for 72 hours (18). Therefore, it seems reasonable to disregard the skin content as absorbed material. For exposure assessment purposes, the amount of DB1 considered systemically bioavailable would simply be the DB1 absorbed in the receptor fluid at 24 hours. With further investigation of the skin reservoir, it was determined not appropriate to add the skin levels of DB1 to the receptor fluid levels to characterize the total of absorbed material. This essentially reduced the percentage of applied dose absorbed being considered for exposure estimates from 3.3% to 0.2% for DB1.

29.4 HAIR DYE ABSORPTION: CORRELATION WITH PARTITION COEFFICIENTS

Percutaneous absorption through human skin of a homologous series of hair dyes was investigated (9). The hair dyes studied were p-phenylenediamine, o-phenylenediamine, 2-nitro-p-phenylenediamine, 2-amino-4-nitrophenol, 4-chloro-m-phenylenediamine, and 4-amino-2-nitrophenol. A compound's oil and water solubility properties affect its ability to diffuse across the epidermal membrane. The permeability constants for these dyes were compared to the octanol/water and