

COMPARISON OF *IN VITRO* MODELS OF PERCUTANEOUS ABSORPTION.

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As part of a Colgate-Palmolive sponsored program to validate an *in vitro* percutaneous absorption model, three reference materials with extensive *in vivo* human and *in vitro* (animal and human) data were evaluated in three *in vitro* models. The objective of this study was to determine if the results are consistent with data published in the literature. The test methods used in this study were based upon guidance by the US Food and Drug Administration, and are consistent with the Office of Economic Cooperation and Development Draft Test Guidelines (2000). The *in vitro* models evaluated were human donor skin, engineered human tissue (MatTek Corporation, Model EPI-606X) and slaughterhouse-derived pig skin. The reference materials in each model were testosterone (petrolatum vehicle), benzoic acid (petrolatum and acetone), and caffeine (ethanol). The octanol/water partition coefficients ($\log P_{ow}$) for these materials are 3.32, 1.87, and -0.07, respectively. Each reference material was evaluated at least twice in each model. The tissues were mounted in flow-through diffusion cells (PermeGear, Inc., 0.64 cm² surface area), qualified for barrier function by ³H₂O passage, followed by the application of a finite dose of ¹⁴C-labeled test material (~4 μg/cm²). The study duration was 24 hours. The recovery of caffeine and testosterone was similar (typically > 90%) in all models (a slightly lower recovery was observed in one trial with testosterone in pig tissue [mean = 81%]). Recovery of benzoic acid was notably lower, probably due to sublimation, with the highest recovery in the petrolatum preparation, as compared to the acetone preparation. In human and pig skin, the rank order for skin penetration was benzoic acid (petrolatum) > testosterone > benzoic acid (acetone) > caffeine. In Model EPI-606X, the rank order of penetration was benzoic acid (petrolatum) > testosterone > caffeine > benzoic acid (acetone). The results of these studies were reproducible and consistent with data published in the literature.