PCCA Lipoderm® Breakthrough Study

Lipoderm® Proven to Deliver Four Drugs Simultaneously Through Human Skin *In Vitro* – FIRST STUDY OF ITS KIND!

Study

Evaluation of the Percutaneous Absorption of Ketamine HCl, Gabapentin, Clonidine HCl and Baclofen in Lipoderm® Into Human Trunk Skin, *In Vitro*, Using the Franz Skin Finite Dose Model

NEW LIPODERM STUDY!

These four drugs were selected due to their frequent use in topical pain formulations. Until now, no study had been performed to evaluate the ability of a vehicle to deliver these actives simultaneously through human skin. Additionally, it is common for compounders to put multiple actives in a transdermal vehicle, and it is important to know that their vehicle is actually capable of delivering more than one active. The study was designed to evaluate the percutaneous absorption pharmacokinetics of ketamine HCl, gabapentin, clonidine HCl and baclofen. Absorption was measured in human cadaver skin, *in vitro*, using the finite dose technique and Franz Diffusion Cells, a specific study design that is the gold standard in the pharmaceutical industry. **This study resoundingly demonstrates that Lipoderm® has the power and reliability compounders are looking for.**

The products were tested on replicate sections from three different cadaver skin donors, for the percutaneous absorption of ketamine HCl, gabapentin, clonidine HCl and baclofen over a 48-hour dose period. At pre-selected times after dose application, the dermal receptor solution was removed in its entirety, replaced with fresh receptor solution, and an aliquot saved for subsequent analysis. In addition, the epidermis and dermis were recovered and evaluated for drug content. The samples were analyzed for ketamine HCl, gabapentin, clonidine HCl and baclofen content by High Performance Liquid Chromatography (HPLC)/MS.

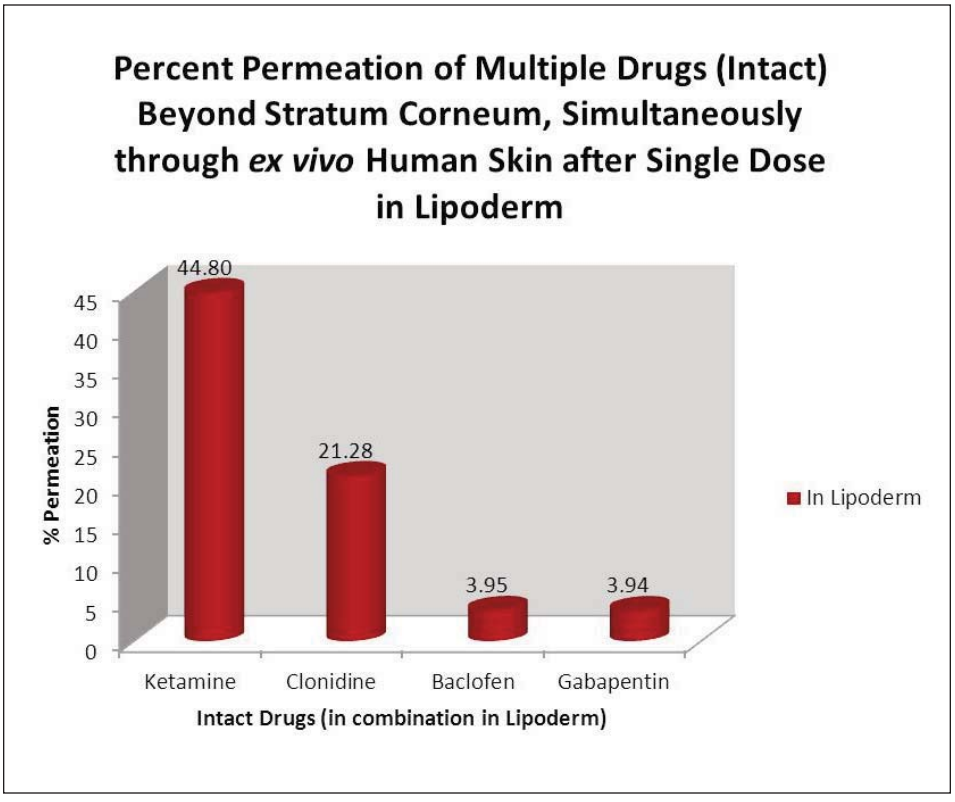

Figure 1: Total % Permeation of Applied Dose Beyond Stratum Corneum After a Single Dose

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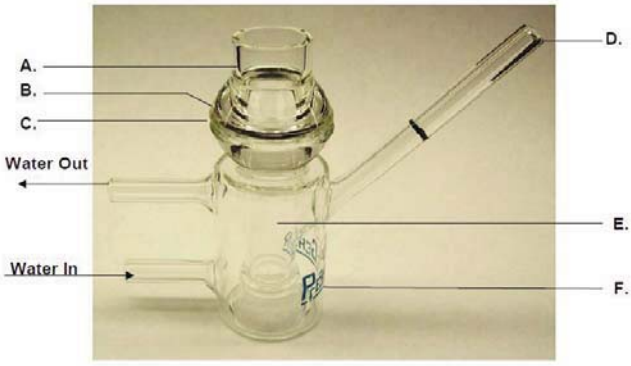
Methods and Procedures

Percutaneous absorption was measured using the *in vitro* cadaver skin finite dose technique. Human cadaver trunk skin without obvious signs of skin disease, obtained within ~24-48 hours of death, was used in this study. Skin from three donors was cut into multiple smaller sections large enough to fit on static 1.0 cm^2 Franz diffusion cells. To assure the integrity of each skin section, its permeability to tritiated water was determined before application of the test products. All formulations were then applied to the skin sections using a positive displacement pipette set to deliver 5 µL formulation/cm^2. The dose was spread across the surface with the Teflon® tip of the pipette. At preselected times after dosing (2, 4, 8, 12, 24, 32, and 48 hours), the reservoir solution was removed in its entirety, replaced with fresh reservoir solution, and an aliquot saved for subsequent analysis.

FRANZ DIFFUSION CELL



A. Chamber Chimney (open to environment)
B. Skin (nominal 1.0 or 2.0 cm^2)
C. O-ring Seal
D. Sampling Port
E. Receptor Solution Compartment
F. Water Jacket

Results

The data indicate that PCCA's Lipoderm® delivered ketamine HCl, gabapentin, clonidine HCl and baclofen, simultaneously (and intact), into and through human cadaver skin, *in vitro*. The absorption profiles indicate a rapid penetration to a peak flux for gabapentin and baclofen occurring approximately one (1) hour after dose application, and approximately four (4) hours for ketamine HCl. Clonidine HCl exhibited a rapid penetration to an initial peak flux occurring one (1) hour after dose application, but also a secondary peak at approximately 40 hours, possibly due to a depot of some of the applied dose in the epidermis. (See Figures 1 through 5.) This one-of-a-kind study validates the ability of Lipoderm® to deliver four drugs simultaneously through human skin. This information is of great value for pharmacists and physicians utilizing topical preparations for various pain syndromes.

Formulation Tested

Lipoderm® Formula (PCCA Formula #7919)
To Make 100 gm

Ketamine HCl USP CIII		5 gm
Gabapentin USP		10 gm
Clonidine HCl USP		0.2 gm
Baclofen USP		2 gm
Propylene Glycol USP		10 gm
Base, PCCA Lipoderm®	q.s.	100 gm

Base, PCCA Lipoderm®
PCCA #30-3338

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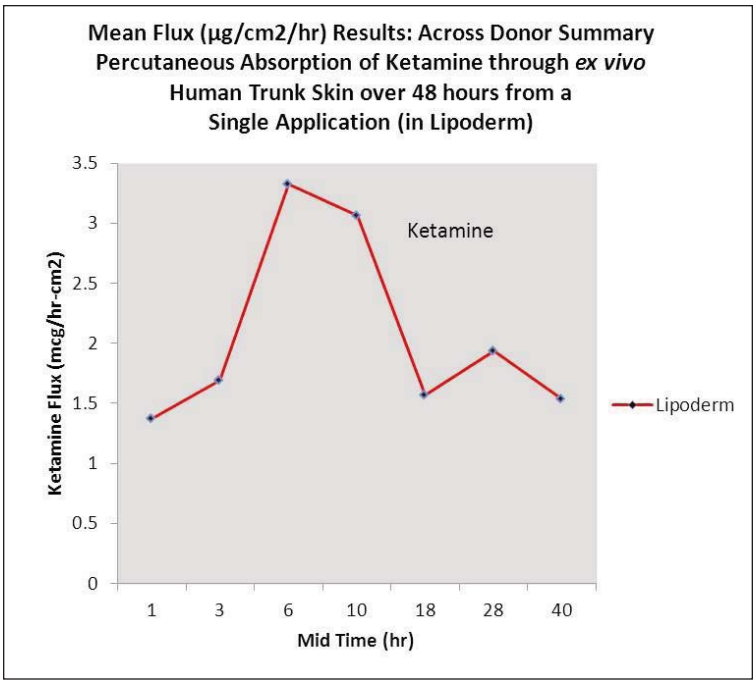

Figure 2: Ketamine Flux versus Time

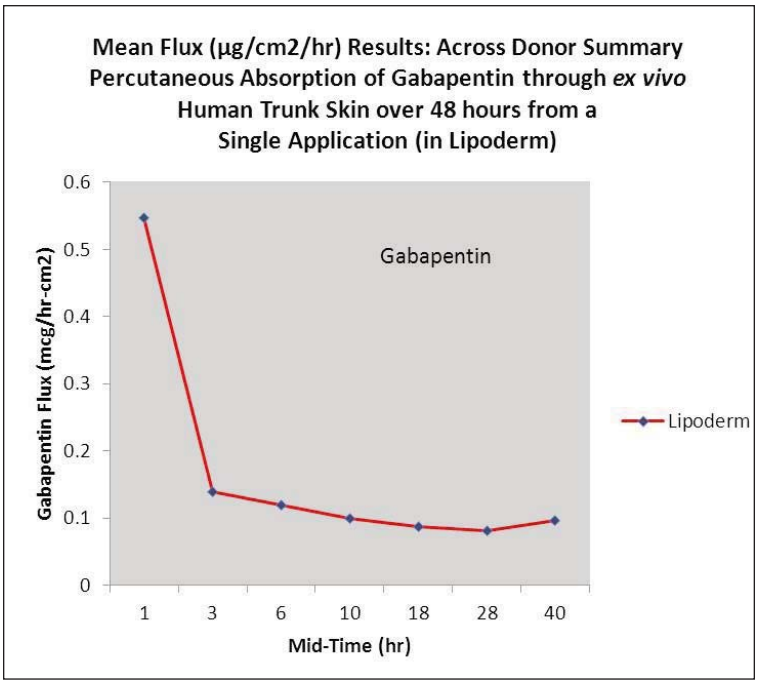

Figure 3: Gabapentin Flux versus Time

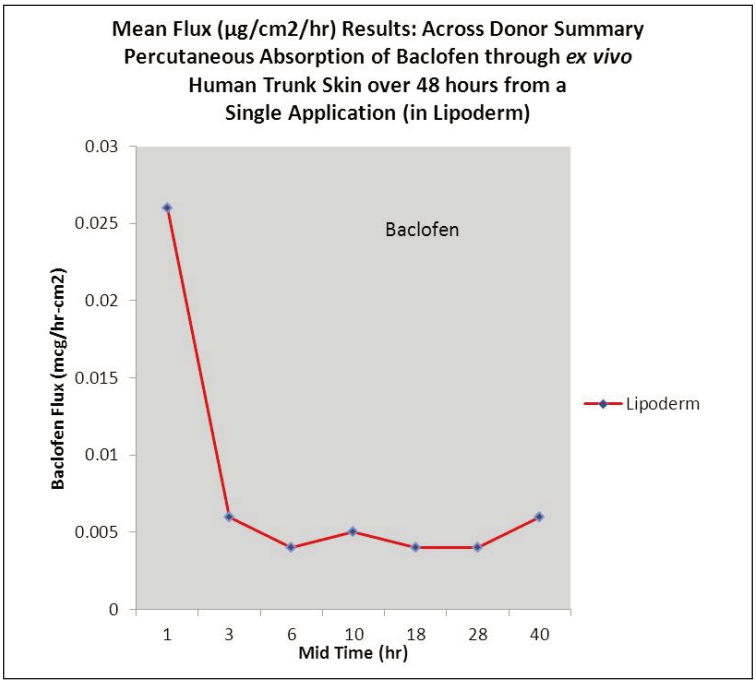

Figure 4: Baclofen Flux versus Time

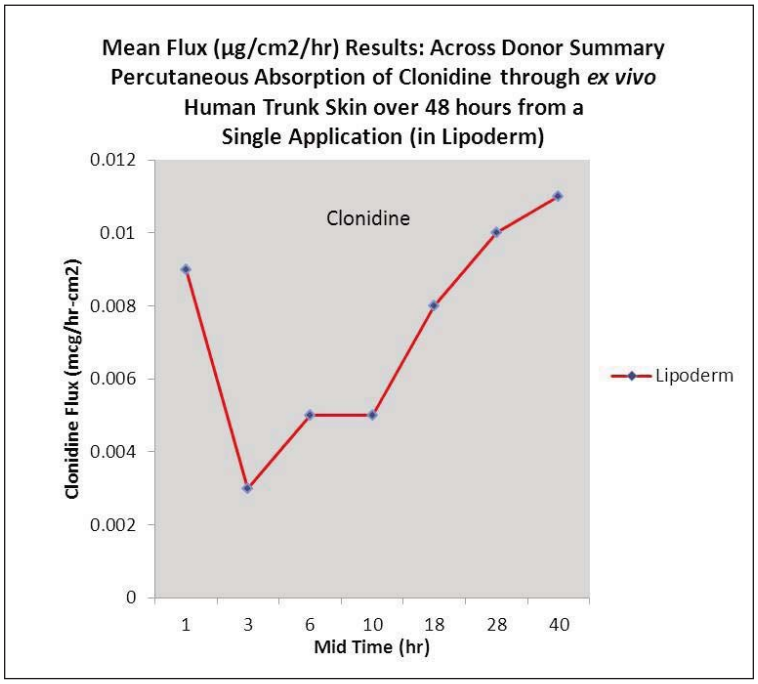

Figure 5: Clonidine Flux versus Time

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compound with confidence®