Ketoprofen Transdermal Study

Ketoprofen in PCCA Lipoderm® Outperforms PLO in Transdermal Testing!

PCCA Lipoderm® now PROVEN to Deliver the NSAID Ketoprofen Through Human Skin *In Vitro*

As part of an ongoing effort to create the highest quality products, PCCA has aggressively studied the ability of Lipoderm® and PLO to deliver ketoprofen across human skin. PCCA teamed up with the highly regarded dermatologic laboratory **PRACS Institute – Cetero Research** to conduct this study. Using PCCA's Special Micronized Ketoprofen USP, PCCA Lipoderm performed better than PLO.

Study

Evaluation of the Percutaneous Absorption of Ketoprofen, *In Vitro*, Using the Human Cadaver *(Ex Vivo)* Skin Model

The study was designed to evaluate the percutaneous absorption pharmacokinetics of PCCA's Special Micronized Ketoprofen. Absorption was measured in human cadaver skin, *in vitro*, using the finite dose technique and Franz Diffusion Cells.

The products were tested on replicate sections from three different cadaver skin donors, for the percutaneous absorption of PCCA's Special Micronized Ketoprofen 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 ketoprofen content by High Performance Liquid Chromatography (HPLC).

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 a single donor 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 pre-selected times after dosing (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.

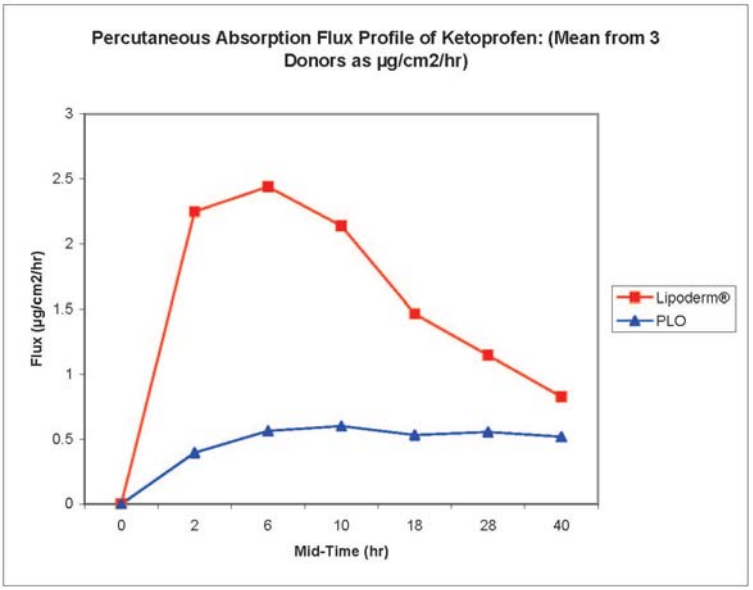

Figure 1: PCCA Lipoderm® demonstrates a superior ability to deliver ketoprofen transdermally versus PLO.

Results

The data indicate that PCCA's Special Micronized Ketoprofen did penetrate into and through human cadaver skin, *in vitro*, from the test formulations provided. The absorption profiles indicate a rapid penetration to a peak flux occurring at approximately 7-8 hours after dose application followed by a steady decline thereafter. PCCA Lipoderm performed significantly better than PLO at delivering PCCA's Special Micronized Ketoprofen through human skin (*see **Figure 1***). This formulation also delivered PCCA's Special Micronized Ketoprofen more rapidly than all other formulations. Lipoderm with pentylene glycol as the wetting agent showed an

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continued

even better total permeation result versus PLO, with the difference being statistically significant ($p<0.01$, *see* ***Figure 2***). While this formulation delivered the most ketoprofen across the skin (total absorption), it was not as quick as the other Lipoderm formula.

Formulas Tested

Lipoderm® Formula

Ketoprofen USP, PCCA Special Micronized		10% W/W
Diethylene Glycol Mono Ethyl Ether, NF		2% W/W
Propylene Glycol		8% W/W
PCCA Lipoderm®	q.s.	to 100%

PLO Formula

Ketoprofen USP, PCCA Special Micronized		10% W/W
Diethylene Glycol Mono Ethyl Ether, NF		2% W/W
Propylene Glycol		8% W/W
Lecithin Isopropyl Palmitate Solution		22% W/W
Poloxamer 407 20% Solution	q.s.	to 100%

A third formula, using Pentylene Glycol as a wetting agent, also was evaluated:

Lipoderm® Formula with Pentylene Glycol

Ketoprofen USP, PCCA Special Micronized		10% W/W
Pentylene Glycol		10% W/W
PCCA Lipoderm®	q.s.	to 100%

PCCA PRODUCT INFORMATION

PCCA Lipoderm® . . . . . PCCA #30-3338
500 g
2500 g
12500 g 0
25000 g

Ketoprofen USP,
PCCA Special Micronized . . . . PCCA #50-3849
25 g
100 g
1000 g

Pentylene Glycol . . . . . PCCA #30-3811
500 g

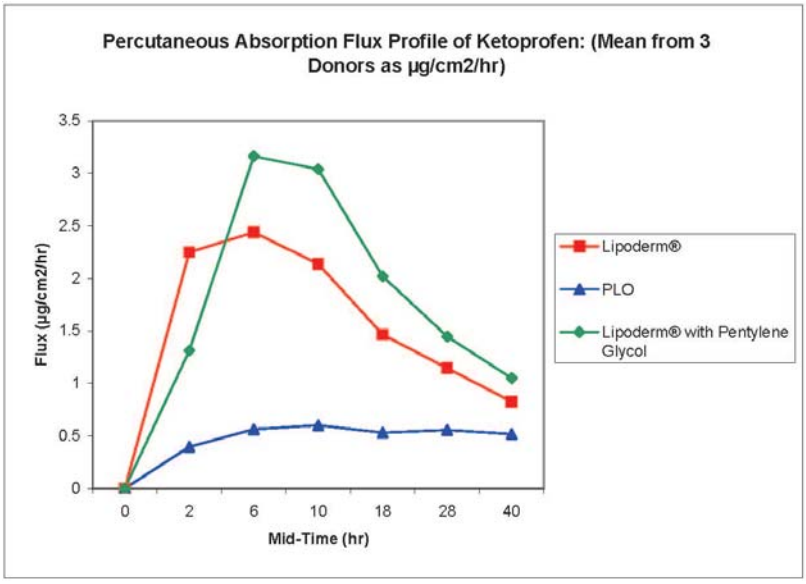

Figure 2: The use of pentylene glycol 10% in PCCA Lipoderm® as wetting agent increases extent of percutaneous absorption, but is a little slower.

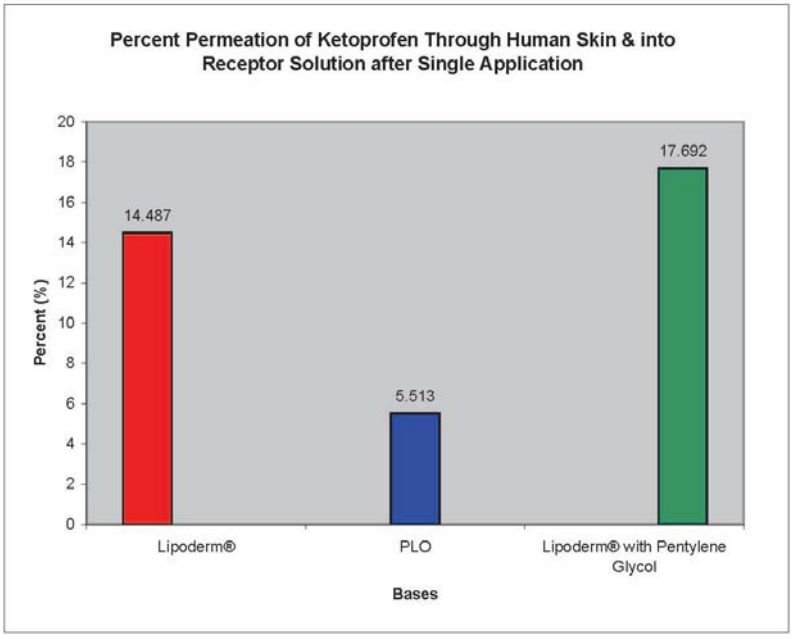

Figure 3: Percent of applied ketoprofen dose that was delivered completely through human skin *in vitro* was significantly better with PCCA Lipoderm® versus PLO.

PCCA