Salt-Stable LO Transdermal Studies

Study

Evaluation of the Percutaneous Absorption of Benzocaine + Lidocaine HCl + Tetracaine HCl and Ketoprofen + Ibuprofen + Cyclobenzaprine HCl + Piroxicam, In Vitro, Using the Epiderm Skin Model

The study was designed to evaluate the percutaneous absorption pharmacokinetics of Humco's Salt-Stable LO. Absorption was measured in human epidermal cultures, in vitro, using the finite dose technique and Franz Diffusion Cells.

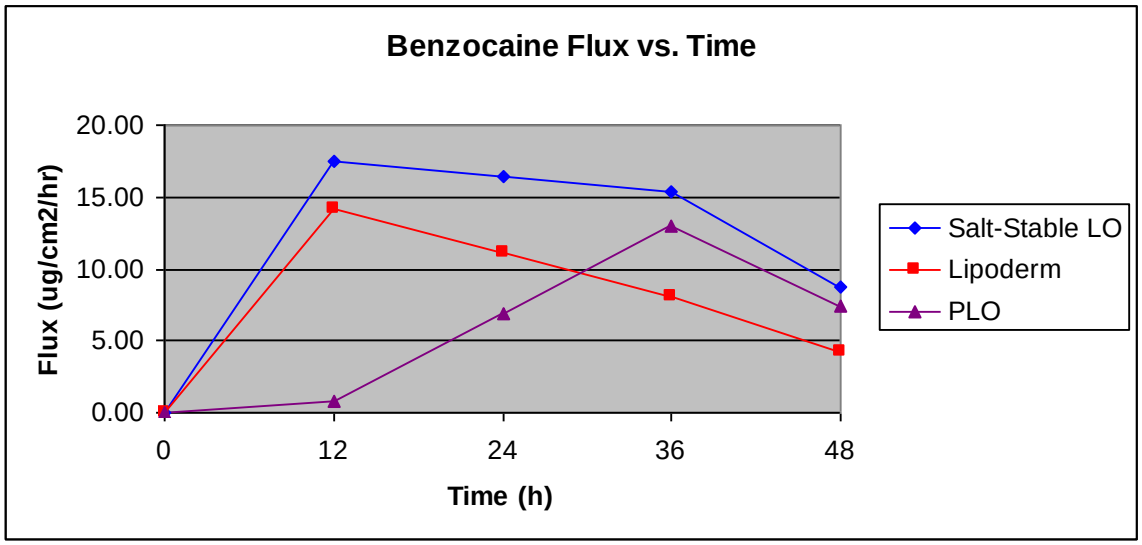
The two formulas were tested on standardized sections with three different transdermal compounding bases, for the percutaneous absorption of Benzocaine + Lidocaine HCl + Tetracaine HCl and Ketoprofen + Ibuprofen + Cyclobenzaprine HCl + Piroxicam over a 48-hour dose period. At pre-selected times after dose application, the dermal receptor solution was removed in its entirety, replaced with fresh receptor solution, and an aliquot saved for subsequent analysis. The samples were analyzed for Benzocaine, Lidocaine HCl, Tetracaine HCl, Ketoprofen, Ibuprofen, Cyclobenzaprine HCl and Piroxicam content by High Performance Liquid Chromatography (HPLC).

The in vitro human Epiderm skin model has proven to be a valuable tool for the study of percutaneous absorption and the determination of the pharmacokinetics of topically applied drugs. The model uses human epidermal skin mounted in specially designed diffusion cells that allow the skin to be maintained at a temperature and humidity that match typical in vitro conditions. A finite dose of formulation is applied to the outer surface of the skin and drug absorption is measured by monitoring the rate of appearance in the receptor solution bathing the inner surface of the skin. Data defining total absorption, as well as rate of absorption can be accurately determined in this model.

Results

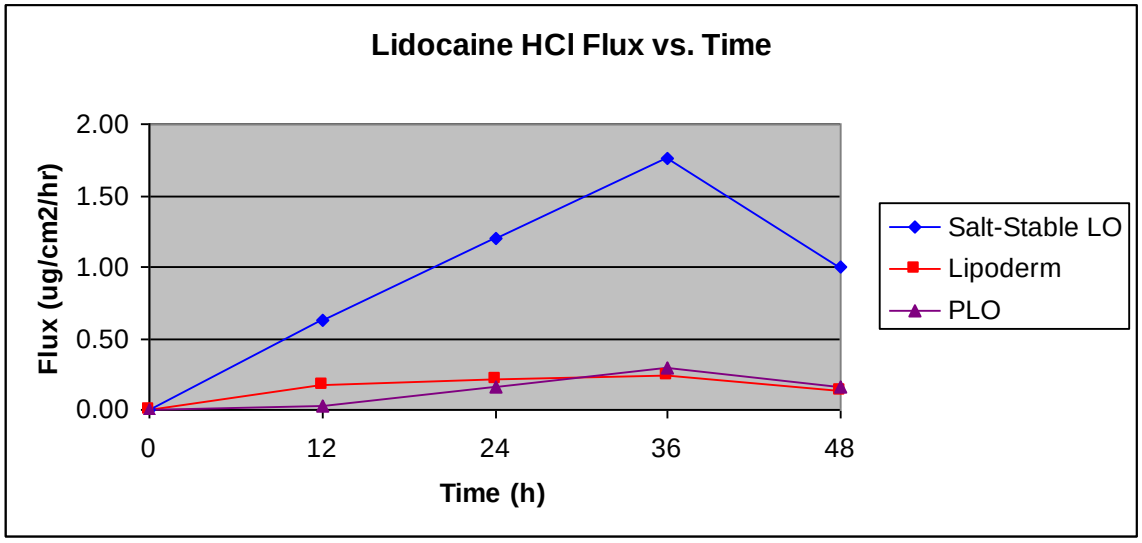
Benzocaine

The data indicate that Benzocaine did penetrate into and through human epidermal cultures, in vitro, from the test formulations provided. The absorption profiles indicate a rapid penetration to a peak flux occurring at approximately 12 hours after dose application followed by a steady decline thereafter. Humco Salt-Stable LO performed comparable to PCCA Lipoderm and significantly better than PLO at delivering Benzocaine through human skin.



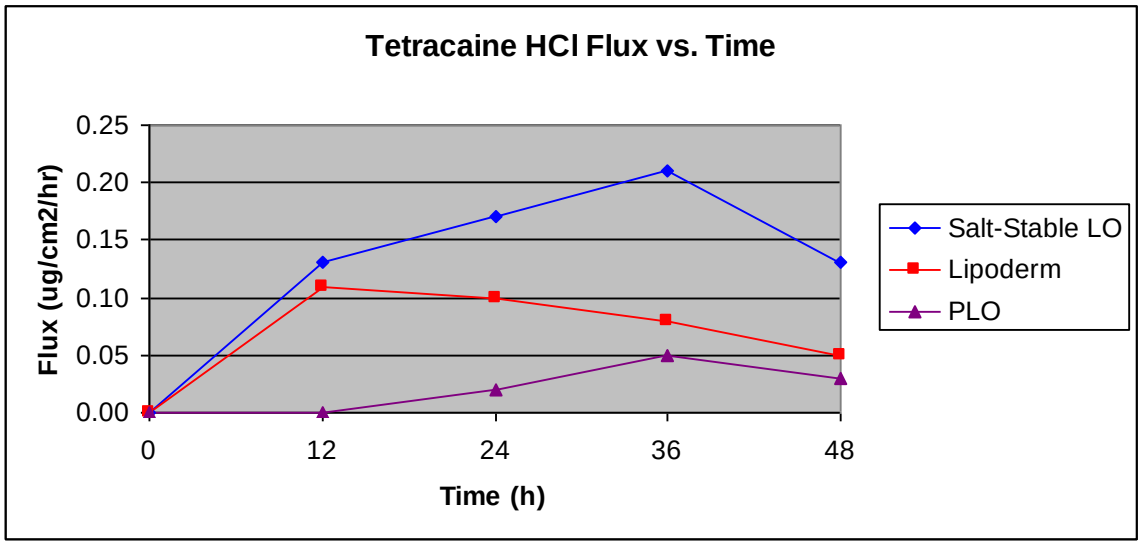
Lidocaine HCl

The data indicate that Lidocaine HCl did penetrate into and through human epidermal cultures, in vitro, from the test formulations provided. The absorption profiles indicate a steady penetration to a peak flux occurring at approximately 36 hours after dose application. Humco Salt-Stable LO performed significantly better than both PCCA Lipoderm and PLO at delivering Lidocaine HCl through human skin.



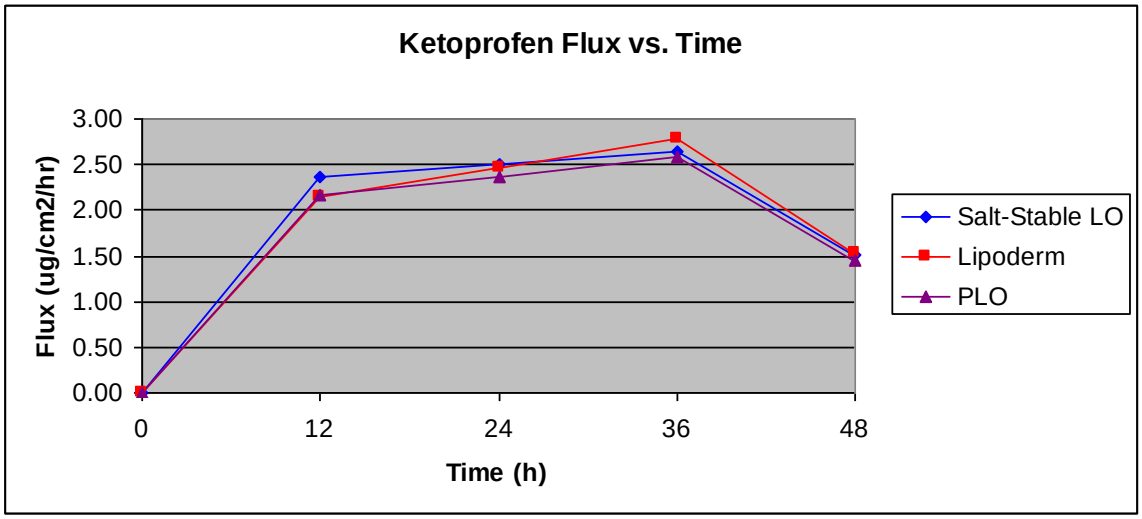
Tetracaine HCl

The data indicate that Tetracaine HCl did penetrate into and through human epidermal cultures, in vitro, from the test formulations provided. The absorption profiles indicate a steady penetration to a peak flux occurring at approximately 36 hours after dose application. Humco Salt-Stable LO performed significantly better than both PCCA Lipoderm and PLO at delivering Tetracaine HCl through human skin.



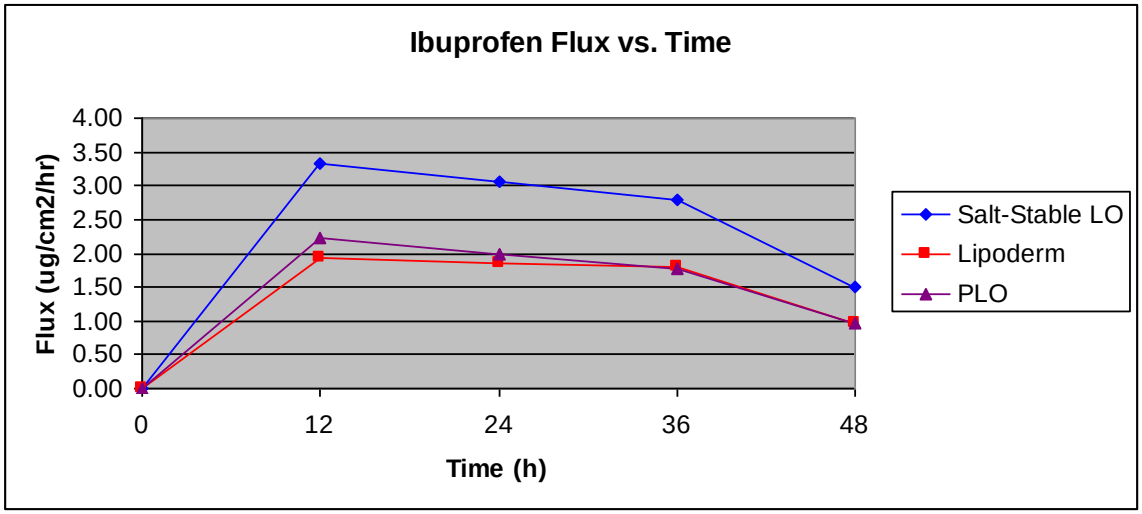
Ketoprofen

The data indicate that Ketoprofen did penetrate into and through human epidermal cultures, in vitro, from the test formulations provided. The absorption profiles indicate a steady penetration to a peak flux occurring at approximately 36 hours after dose application. Humco Salt-Stable LO performed comparable to both PCCA Lipoderm and PLO at delivering Ketoprofen through human skin.



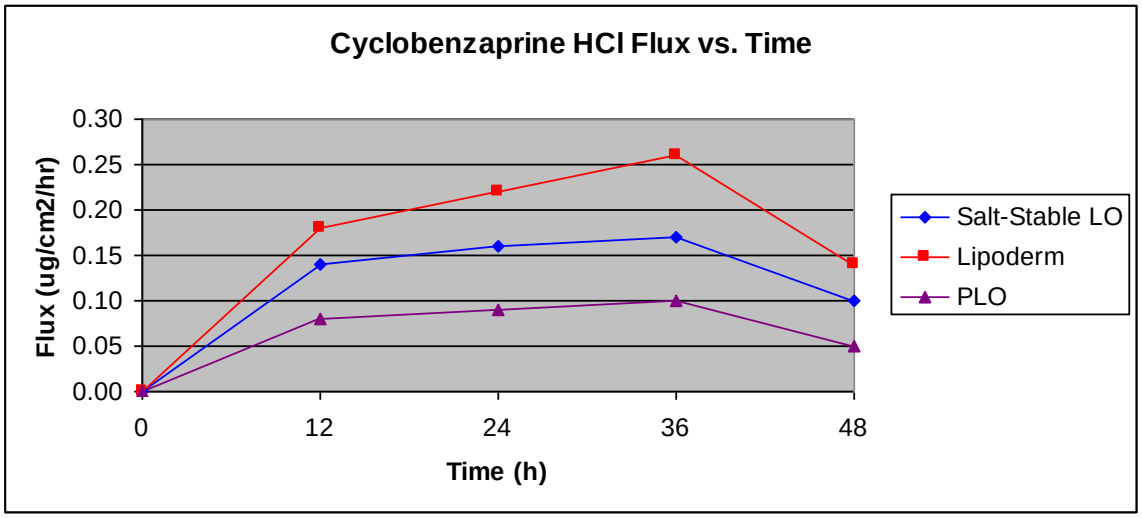
Ibuprofen

The data indicate that Ibuprofen did penetrate into and through human epidermal cultures, in vitro, from the test formulations provided. The absorption profiles indicate a rapid penetration to a peak flux occurring at approximately 12 hours after dose application followed by a steady decline thereafter. Humco Salt-Stable LO performed significantly better than both PCCA Lipoderm and PLO at delivering Ibuprofen through human skin.



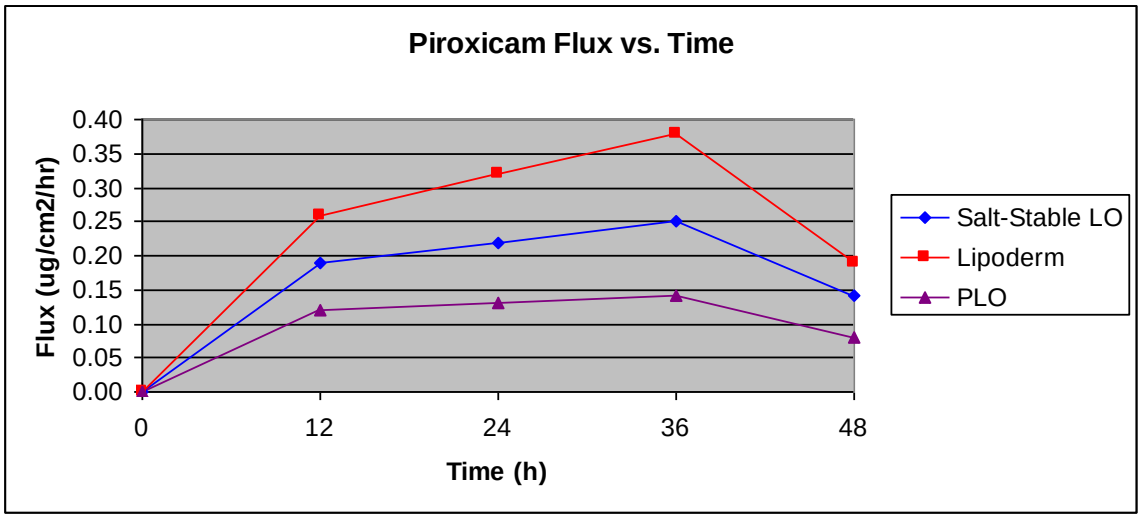
Cyclobenzaprine HCl

The data indicate that Cyclobenzaprine HCl did penetrate into and through human epidermal cultures, in vitro, from the test formulations provided. The absorption profiles indicate a steady penetration to a peak flux occurring at approximately 36 hours. Humco Salt-Stable LO performed comparable to both PCCA Lipoderm and PLO at delivering Cyclobenzaprine HCl through human skin.



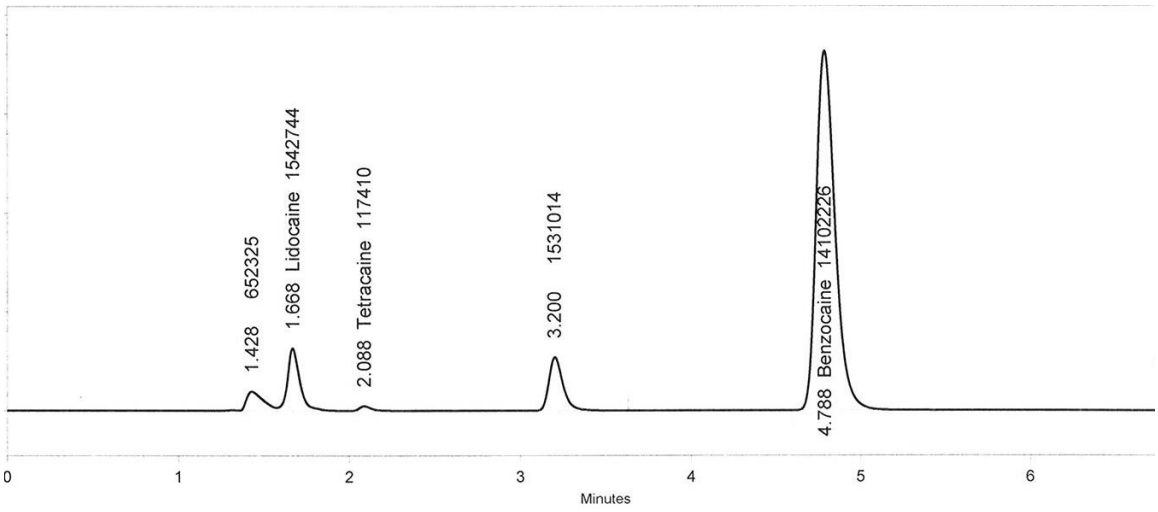
Piroxicam

The data indicate that Piroxicam did penetrate into and through human epidermal cultures, in vitro, from the test formulations provided. The absorption profiles indicate a steady penetration to a peak flux occurring at approximately 36 hours. Humco Salt-Stable LO performed comparable to both PCCA Lipoderm and PLO at delivering Piroxicam through human skin.

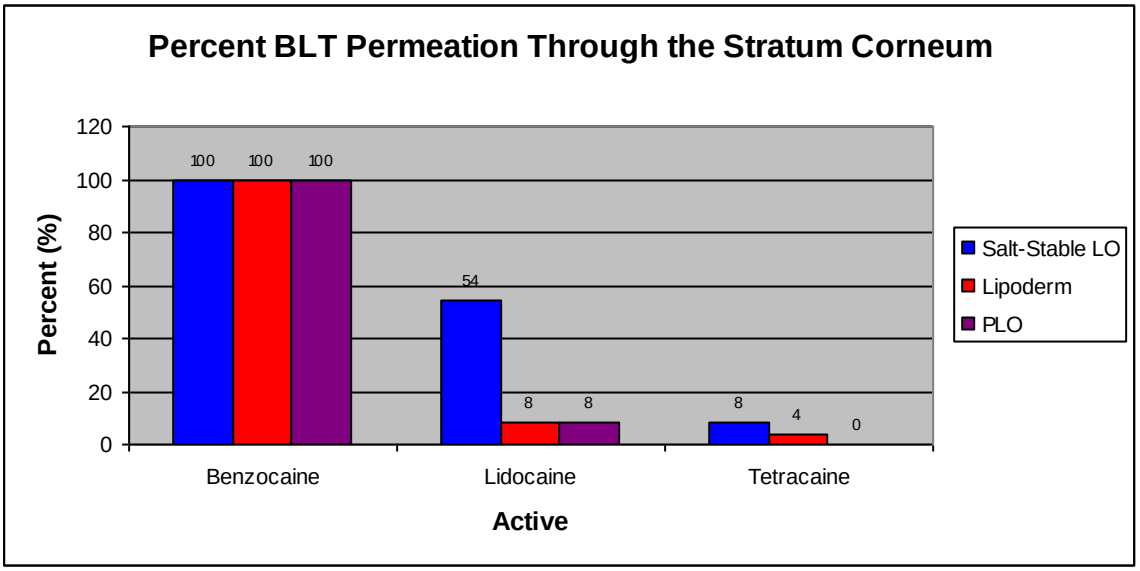


20% Benzocaine / 6% Lidocaine HCl / 4% Tetracaine HCl

The data indicate that the actives do penetrate into and through human epidermal cultures. Based on total penetration (through the skin into the reservoir solution), the data rank orders the test formulations as Humco Salt-Stable LO > PCCA Lipoderm > PLO.



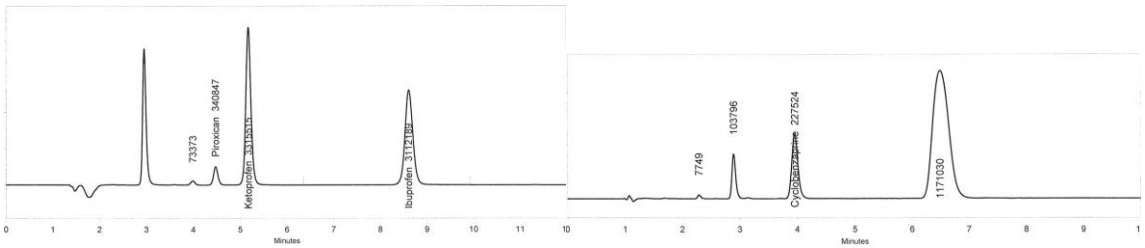
Sample Chromatogram of 20% Benzocaine / 6% Lidocaine HCl / 4% Tetracaine HCl



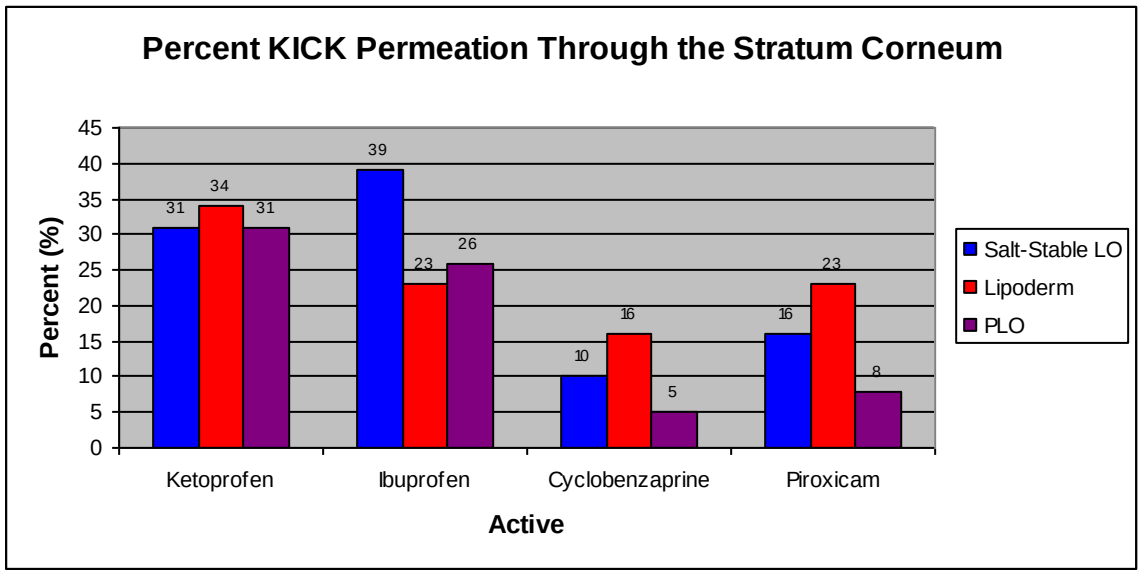
The total percent of applied dose that penetrated past the Stratum Corneum with Humco Salt-Stable LO was 45% more than PCCA Lipoderm and 50% more than PLO.

10% Ketoprofen / 10% Ibuprofen / 2% Cyclobenzaprine HCl / 2% Piroxicam

The data indicate that the actives do penetrate into and through human epidermal cultures. Based on total penetration (through the skin into the reservoir solution), the data rank orders the test formulations as Humco Salt-Stable LO = PCCA Lipoderm > PLO.



Sample Chromatograms of 10% Ketoprofen / 10% Ibuprofen / 2% Cyclobenzaprine HCl / 2% Piroxicam



The total percent of applied dose that penetrated past the Stratum Corneum with Humco Salt-Stable LO was comparable to PCCA Lipoderm and 37% more than PLO.