

Humco's SaltStable LS Advanced™ Transdermal Penetration Study

**2% Baclofen + 1% Bupivacaine + 2% Cyclobenzaprine + 5% Diclofenac +
6% Gabapentin + 3% Ibuprofen + 10% Ketamine + 3% Pentoxifylline**

Study

Evaluation of the Percutaneous Absorption of Pentoxifylline + Ketamine HCl + Ibuprofen + Cyclobenzaprine HCl + Diclofenac Na + Baclofen + Bupivacaine HCl + Gabapentin, In SaltStable LS Advanced™, Into Human Skin, In Vitro, Using the Franz Skin Finite Dose Model

The study was designed to evaluate the percutaneous absorption pharmacokinetics of pentoxifylline, ketamine HCl, ibuprofen, cyclobenzaprine HCl, diclofenac Na, baclofen, bupivacaine HCl and gabapentin in a single formulation using Humco's SaltStable LS Advanced™ base. Absorption was measured in human epidermal cultures, in vitro, using the finite dose technique and Franz Diffusion Cells. The eight drugs were selected due to their frequent use in compounding topical pain formulations along with compounding multiple actives in one formulation.

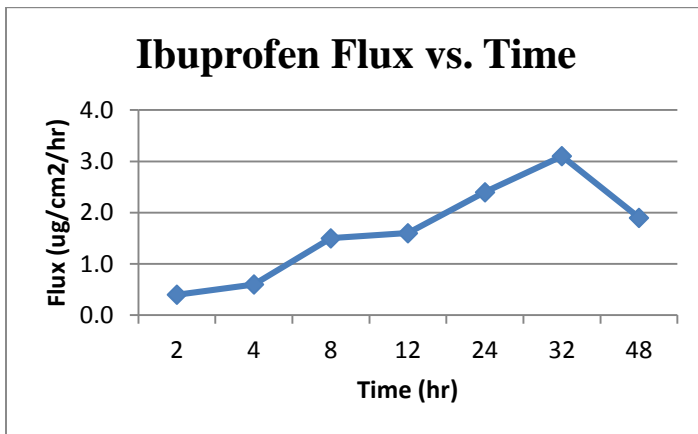
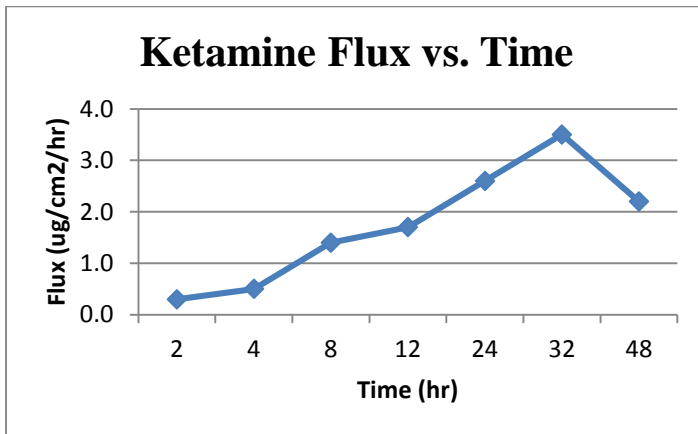
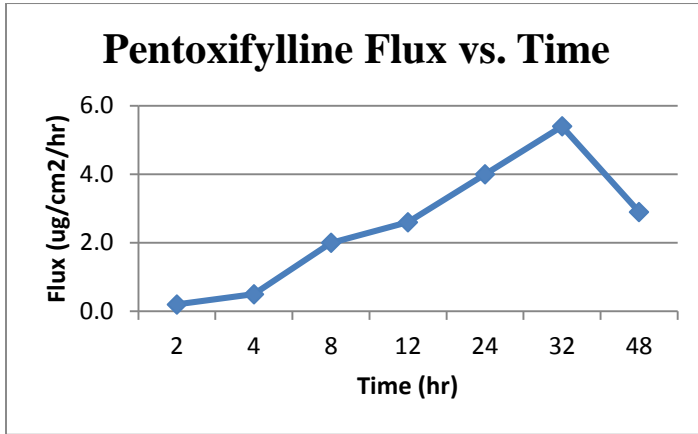
The formula was tested on standardized sections with Humco's SaltStable LS Advanced™ transdermal compounding base, for the percutaneous absorption of pentoxifylline + ketamine HCl + ibuprofen + cyclobenzaprine HCl + diclofenac Na + baclofen + bupivacaine HCl + gabapentin over a 48-hour dose period. At 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. High Performance Liquid Chromatography (HPLC) analyzed the samples for pentoxifylline, ketamine HCl, ibuprofen, cyclobenzaprine HCl, diclofenac Na, baclofen, bupivacaine HCl and gabapentin content.

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.

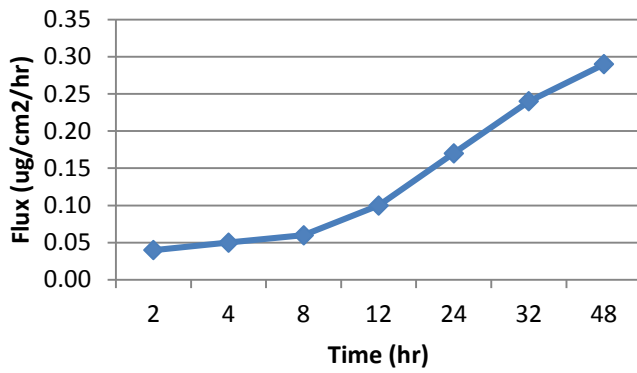
Results

Humco's SaltStable LS Advanced™ compounding base is a proven transdermal delivery vehicle able to deliver multiple drugs beyond the stratum corneum, simultaneously into and through the human skin after a single dose.

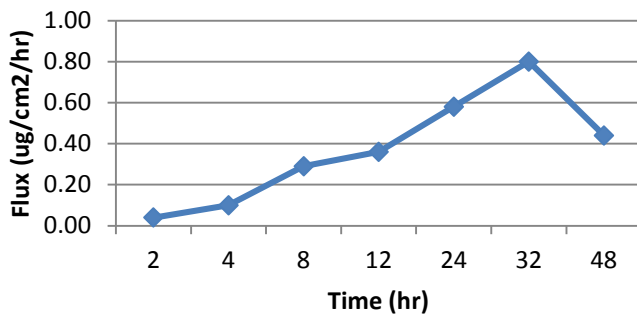
The data indicates that Humco's SaltStable LS Advanced™ delivered pentoxifylline, ketamine HCl, ibuprofen, cyclobenzaprine HCl, diclofenac Na, baclofen, bupivacaine HCl and gabapentin simultaneously (and intact) into and through human epidermal cultures, in vitro, from the test formulation provided. The absorption profiles indicate pentoxifylline, ketamine HCl, ibuprofen, diclofenac Na, and bupivacaine HCl had a steady penetration occurring for 32 hours after dose application. And cyclobenzaprine HCl, baclofen and gabapentin had a steady penetration occurring for 48 hours after dose application.



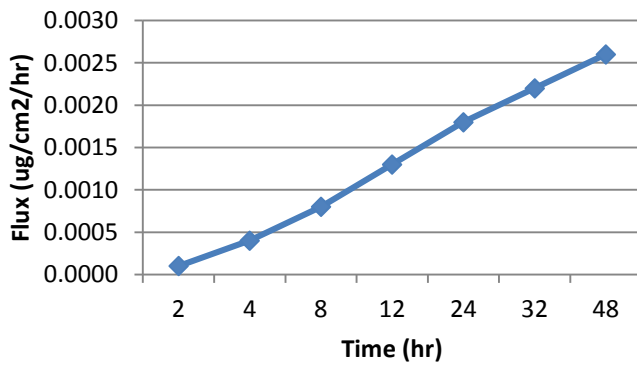
Cyclobenzaprine Flux vs. Time

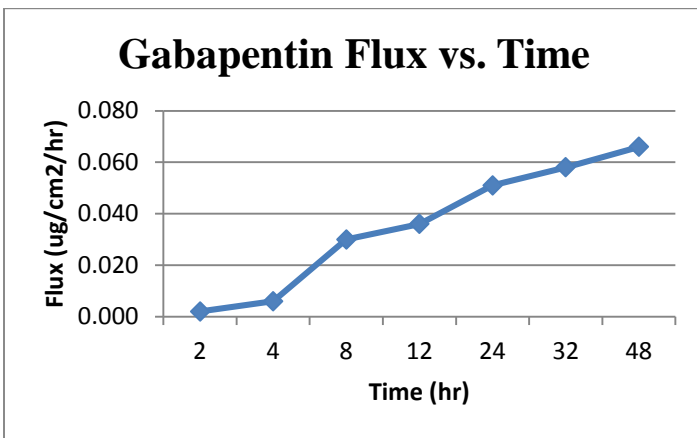
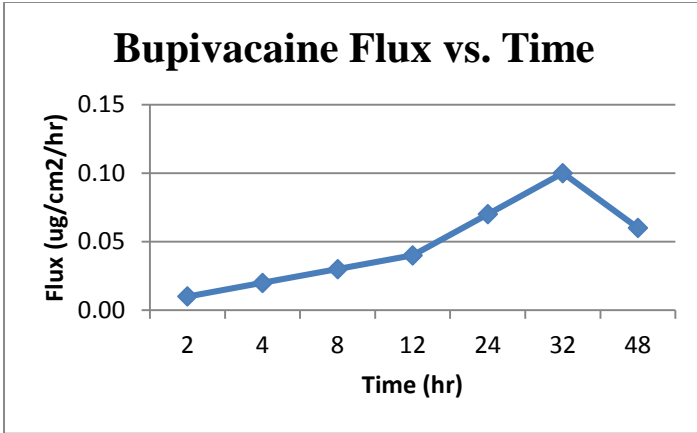


Diclofenac Flux vs. Time



Baclofen Flux vs. Time





Sample Chromatogram of Pentoxifylline, Ketamine HCl, Ibuprofen, Cyclobenzaprine HCl, Diclofenac Na, Baclofen, Bupivacaine HCl and Gabapentin

