OBJ LIMITED
Active transdermal drug delivery

# Trial Summary| Naltrexone

## Dermaportation increases Naltrexone penetration of human epidermis ex-vivo

### Objective

The opioid antagonist naltrexone is used for the treatment of alcohol dependence and other addictions. However, the use of naltrexone is restricted due to low oral bioavailability (5% to 40%), gastro-intestinal side-effects, and patient non-compliance. An effective transdermal naltrexone would provide a convenient alternative to oral naltrexone administration. Here, the effect of the standard Dermaportation waveforms on the transdermal diffusion of naltrexone was evaluated.

### Method

Human skin was obtained following abdominoplasty surgery under existing approval from the Human Research Ethics Committee of Curtin University.

The epidermis was heat separated from the dermis using standard procedures (Kligman and Christophers 1963). The epidermis was mounted in Franz-type diffusion cells with the stratum corneum facing the donor compartment. Skin integrity was determined by conductance measurement. The receptor compartment was filled with phosphate buffered saline pH 7.4, stirred continuously and maintained at 37°C throughout the experiment. Naltrexone (0.5% w/v) in phosphate buffered saline (pH 7.4) was applied to the donor side of the epidermis.

Dermaportation was applied from time 0 to 4 h. Samples were removed from the receptor fluid at time points up to 8h. At each time point the receptor fluid volume was replaced with fresh receptor solution preheated to 37°C. Four Dermaportation cells and 4 passive cells (no Dermaportation) were conducted using skin from the abdominal region of a female donor. The content of naltrexone in receptor fluid samples was analysed by HPLC with ultraviolet detection using a validated assay procedure.

The cumulative amount of naltrexone in receptor versus time was plotted and flux values calculated from the slopes per group.

### Result

Dermaportation enhanced the skin penetration of naltrexone ($flux_{0\text{-}2h}$ 152.6µg/cm$^2$/h), when compared with that of passive administration ($flux_{0\text{-}2h}$ 1.6µg/cm$^2$/h). In the course of the experiment, Naltrexone diffused faster and in more quantity when treated with Dermaportation for 240 min, compared with passive administration (Time by Treat interaction: $F_{12,72}$=4.57; p<0.05). The largest increase in Dermaportation-related diffusion was achieved in the first 150min (150min: $F_{1,6}$=6.10; p<0.05; see Figure 1).

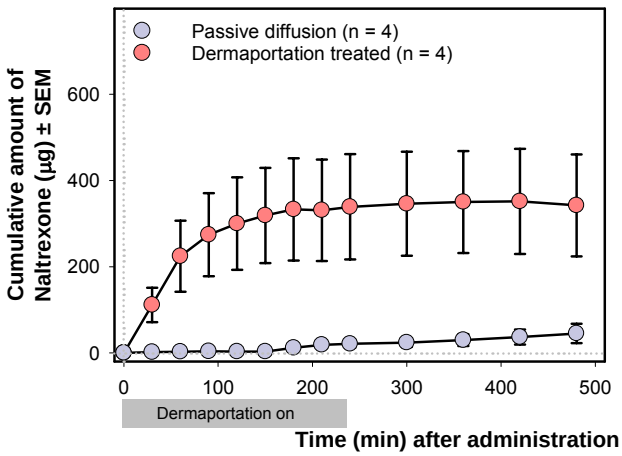


***Figure 1:*** *The average cumulative amount of naltrexone in the receptor chamber of a standard Franz-type diffusion set-up is depicted for passive and Dermaportation induced penetration through excised human epidermis. Dermaportation was switched on from 0-240min (grey bar).*

### Summary

Dermaportation was successful at delivering naltrexone through excised human epidermis, with a flux rate in the first 2 hours of 95 times that of passive diffusion. Dermaportation has the potential to provide a more effective and convenient delivery system for naltrexone, than the current oral delivery method.

REFERENCES:
*Kligman A, Christophers E.* Preparation of isolated sheets of human stratum corneum. Arch Dermatol 88: 70-73 (1963).