Transdermal drug delivery technology

OBJ LIMITED

PRESS RELEASE

Tuesday, 17 March 2009

OBJ DATA PRESENTED AT MAJOR INTERNATIONAL CONFERENCE

OBJ Limited (ASX: OBJ) is pleased to advise that peer-reviewed data was presented by Dr Heather Benson of Curtin University at the 3rd Symposium of Skin and Formulation and 10th Skin Forum, held in Versailles, France.

Dr Benson presented OBJ data from its Naltrexone permeation work and its work with Peptides.

The poster presentations are attached and further information on the presentations and the Symposium can be located at http://www.apgi.org/skin.htm.

- Ends -

For more information:

Mr Jeff Edwards Director

P +618 9443 3011
E info@obj.com.au
W www.obj.com.au

About OBJ:

OBJ is an early-stage drug delivery Company focused on the development of transdermal drug delivery technology for use in the pharmaceutical and cosmetic industries. The Company is developing two drug delivery technologies for the transdermal delivery of pharmaceutical and cosmetic compounds through or into the skin without the need for injections. The foundation technology, Dermaportation (DP), is a powered drug delivery technology that uses battery power to generate time-varying electromagnetic fields. The Company's second technology, Enhanced Transdermal Polymer (ETP) is an unpowered drug delivery technology that uses a magnetic gradient technique to enhance transdermal delivery. The DP platform is designed to be integrated into a battery-operated transdermal patch for pharmaceutical applications, whereas the ETP platform is intended as a powerless patch targeted at the competitive over-the-counter pharmaceutical and cosmetic markets.

ELECTROMAGNETOPHORESIS: POTENTIAL FOR ENHANCED SKIN PENETRATION OF DRUGS AND COSMETICS

Heather A E Benson[1], Jeffery Edwards[2],Gayathri Krishnan[1], Sarika Namjoshi[1]

[1] School of Pharmacy, Curtin University ofTechnology,Perth, WA, Australia and

[2]OBJ Ltd, Perth, WA, Australia

Introduction

Dermaportation (DP) is a proprietary electromagnetophoresis technology (OBJ Ltd) that applies low energy pulsed electromagnetic fields to enhance the movement of substances through the skin. Skin permeation enhancement has been observed for therapeutic molecules including aminolevulinic acid[1], NSAIDs, caffeine, naltrexone hydrochloride, local anaesthetics and a dipeptide, Ala-Trp. DP has also been found to enhanced transdermal penetration in both animal and human pilot studies.

Objectives

The purpose of the present work was to investigate electromagnetophoresis on the skin permeation of caffeine, lidocaineHCl (LH), prilocaineHCl (PH) and naltrexoneHCl (NTX).

Methods

Skin Permeation Study

Human epidermis and silicone membrane were mounted in vertical Franz type diffusion cells (Fig 1). The epidermal membrane was hydrated with PBS for 1h while the silicone membrane for 16h before commencing the permeation experiment. The donor compartment was filled with either caffeine in PBS (1mg/mL), LH in PBS (25 mg/mL), PH in PBS (25 mg/mL) or NTX in PBS (5mg/mL) and the receptor compartment was filled with PBS (pH 7.4). DP coils were placed around the donor compartment, 8 mm above the epidermis and activated for either 0-4h (NTX), 0-0.5h (LH & PH) or 0-2h (caffeine). Control cells containing drug solution received no DP.

Methods

Sampleswere collected and analysed by HPLC with UV detection. The duration of the experiment varied from 0-8h for NTX and 0-4h for LH and PH.

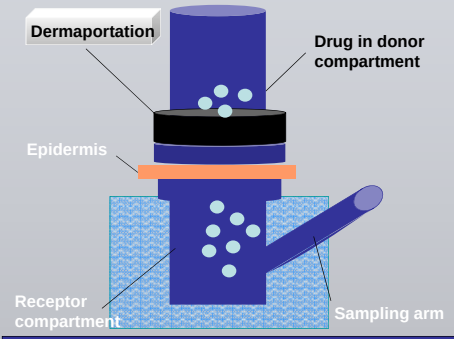

Fig.1: Franz-type diffusion cell with Dermaportation

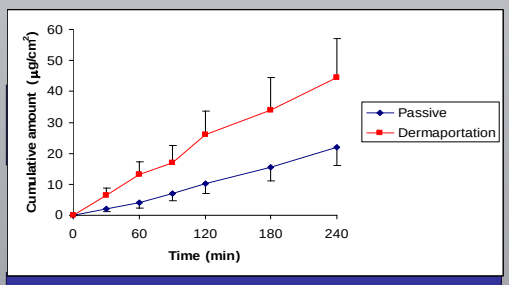

Fig. 2: Cumulative amount of PH permeated by passive diffusion or Dermaportation (mean ± SEM; n=5)

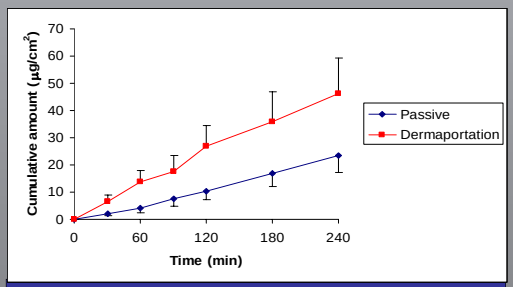

Fig. 3: Cumulative amount of LH permeated by passive diffusion or Dermaportation (mean ± SEM; n=5)

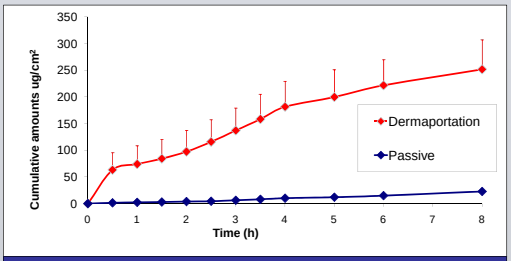

Fig.4:Cumulative amount of NTX permeated epidermis by passivediffusion or Dermaportation (mean ± SEM; n=8)

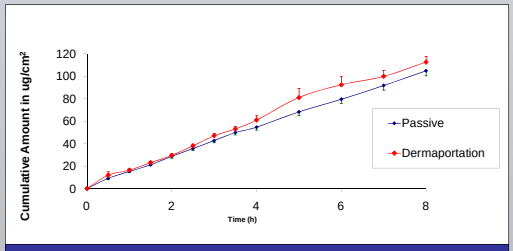

Fig.5:Cumulative amount of NTX permeated silicone by passive diffusion or Dermaportation (mean ± SEM; n=5)

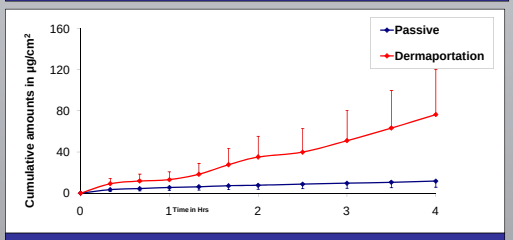

Fig.6: Cumulative amount of caffeine permeated by passive diffusion or Dermaportation (mean ± SEM; n=5)

Results

Low-energy pulsed electromagnetic fields enhanced the skin penetration of all the four compounds investigated in this study. An early surge phase of greater penetration enhancement was seen during the application of magnetic energy with this reducing when the energy was terminated. This suggests that the enhancement effect on the skin is transient and reversible. Magnetic energy did not enhance silicone membrane permeation, suggesting that there is an interaction with the epidermal membrane.

Table 1:Skin permeation data of compounds with Dermaportation and passive treatment

	Caffeine		NaltrexoneHydrchloride		LidocaineHydrochloride		Prilocaine Hydrochloride	
Treatment	**DP**	**Passive**	**DP**	**Passive**	**DP**	**Passive**	**DP**	**Passive**
Area Under Curve of Mean cumulative permeation (mAu)	137.51	29.51	1786.76	119.62	5892.44	2593.81	5267.16	2444.53
Permeability coefficient Kp (cm/h)	2.4×10^{-2}	2.0×10^{-4}	6.3×10^{-2}	6×10^{-3}	7.72×10^{-3}	3.94×10^{-3}	7.35×10^{-3}	3.7×10^{-3}
Enhancement Ratio ER	11.70		10		2		1.98	

Conclusions

Dermaportation significantly enhanced the trans-epidermal delivery of caffeine, NTX, LH & PH in vitro when compared to passive diffusion. Magnetic energy enhanced permeation across human epidermis but not a synthetic membrane suggesting that the enhancement effect is related to the skin structure. The effect was transient and reversible. Investigation and optimisation of the mechanism of enhancement is continuing.

Reference

1. Namjoshi et al. J Chrom B, 852: 49-55, 2007

ELECTROMAGNETOPHORESIS: POTENTIAL FOR ENHANCED SKIN PENETRATION OF PEPTIDES

SarikaNamjoshi[1], Yan Chen[1], Jeffery Edwards[2],Heather A E Benson[1]

[1] School of Pharmacy, Curtin University ofTechnology,Perth, WA, Australia and
[2]OBJ Ltd, Perth, WA, Australia

Introduction

Dermaportation(DP; OBJ Ltd) is a platform technology that applies electromagnetic pulses to enhance skin permeation by electromagnetophoresis. Transdermal flux increases during field application have been observed for a number of small molecules such as caffeine, diclofenacdiethylammonium salt and naltrexone hydrochloride. In the present work, the effect of DP application on skin permeability of a dipeptide was evaluated.

Objectives

To assess the effect of low-energy pulsed electromagnetic fields on the movement of a small peptide like drug and a dipeptide (α-aminolevulinic acid and Ala-Trp) through human skin in vitro.

Methods

Skin permeation study

Human epidermis was mounted in vertical Franz type diffusion cells (Fig 1). The epidermis was equilibrated with phosphate buffered saline (PBS, pH 7.4) for 1h. Ala-Trp in PBS (1 mg/mL) oraminolevulinicacidin PBS (2% w/v) was applied to the skin surface in the donor compartment. DP coils were placed around the upper diffusion chamber 8 mm above the epidermal surface and activated from 0-4 h in the case of α-aminolevulinicacid and for 0-8h in case of Ala-Trp. Control cells received no DP. Samples of the receptor solution (PBS pH 7.4) were taken over an 8h period and analysed by HPLC with UV detection for the dipeptide andHPLC with fluorescent detection for ALA, using validated assay procedures.

Methods

Stability study

The stability of Ala-Trp was determined at different temperatures (37°C, room temp, room temp (dark) and at 4°C) and in contact with skin, to estimate the stability during skin diffusion experiments. Vials containing 3 mL of 1 mg/mLdipeptide solution were stored under these conditions. 100 µL samples were withdrawn at 0, 20, 45, 60 min, 2h, 3h, 4h, 5h and 6h. The samples were then diluted to give a final theoretical concentration of 20 µg/mL and analysed by HPLC.

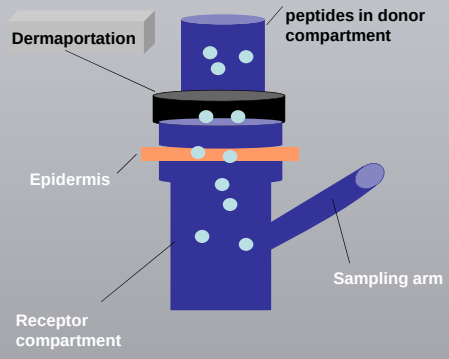

Fig.1: Franz-type diffusion cell with Dermaportation

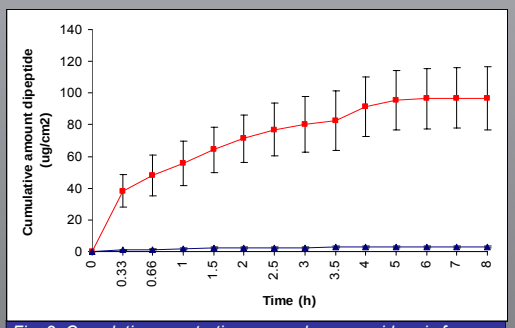

Fig. 2: Cumulative penetration across human epidermis for passive (■) or Dermaportation (▲) applied from 0-4h (mean ± sem: n=9)

Reference

Namjoshi et al. J Chrom B, 852: 49-55, 2007

Results

The results indicate an increase in the flux of ALA after 4 hours in cells where DP was applied as compared to cells where the solution was applied without DP (Fig. 3). At 4h, 8mg(i.e. ≈40% applied dose) of the applied dose of the drug had permeated to the receptor. The flux values were assessed during the period of DP application (Table 1). Flux increased for both ALA and Ala-Trp during DP application compared with control (no DP).

Ala-Trp degraded in the presence of skin at 37°C, with significant degradation from 1 h onwards (Fig. 3). Degradation was also seen in the skin diffusion study but was lower than that observed under the same conditions in the stability study.

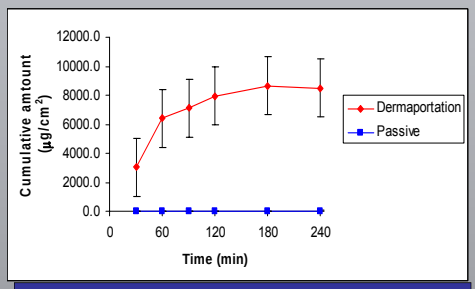

Fig.3: Cumulative penetration (µg in receptor: mean ± SEM; n=4) of ALAby passive diffusion and with Dermaportation

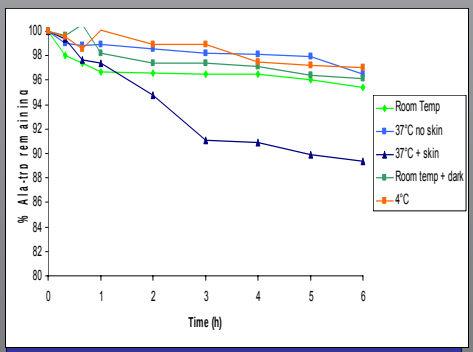

Fig.4: Ala-Trp degradation in solution at varying conditions

Table 1:Skin permeation of Ala-Trpand 5-ALA HCL with Dermaportation and passive diffusion

	5-Aminolevulinic acid		Ala-Trp	
Treatment	**DP**	**Passive**	**DP**	**Passive**
Transdermal flux (µg/cm² h)	76.57	0.12	19.427	0.7782
Permeability coefficient (cm/h)	3.82	6×10^{-3}	1.942×10^{-3}	7.7×10^{-4}
Enhancement ratio (during DP application)	288		34.67	

Conclusions

Dermaportation significantly enhanced the trans-epidermal delivery of Ala-Trp and 5-AL in vitro when compared to passive diffusion. Dermaportation may provide an effective means of delivering molecules which are highly susceptible to degradation, such as peptides, in higher amounts and in a relatively short duration of time, for a range of dermatological and cosmetic applications.

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Curtin University of Technology