ELECTROMAGNETOPHORESIS: POTENTIAL FOR ENHANCED SKIN PENETRATION OF PEPTIDES

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Introduction

Dermaportation (DP; OBJ Ltd) is a platform technology that applies electromagnetic pulses to enhance skin permeation by electromagnetophoresis. Transdermal flux increases during field exposure have been observed for a number of small molecules such as caffeine, diclofenac diethylammonium 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 peptidelike 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) or α-aminolevulinic acid in PBS (2% w/v) was applied to the skin surface in the donor compartment. DP coils were placed around the diffusion cells and activated from 0-4 h in the case of α -aminolevulinic acid 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 and HPLC 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 Vials containing 3 mL of 1 mg/mL dipeptide solution were stored under these conditions. 100 µL samples were withdrawn at 0, 20, 45, 60 min, 2h, 3h, 4h, 5h and 6h.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.

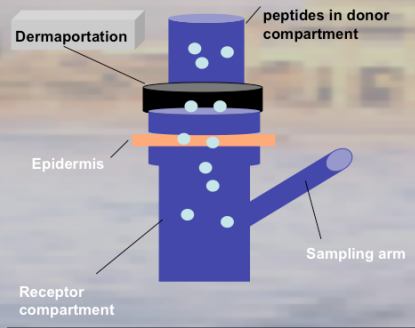

Fig.1: Franz-type diffusion cell with Dermaportation

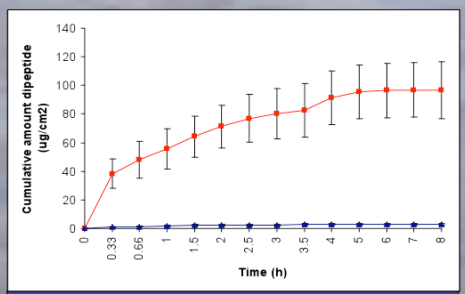

Fig. 2: Cumulative penetration across human epidermis for passive (■) or Dermaportation (▲) applied from 0-4h (mean ± sem: n=9)

Reference

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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.

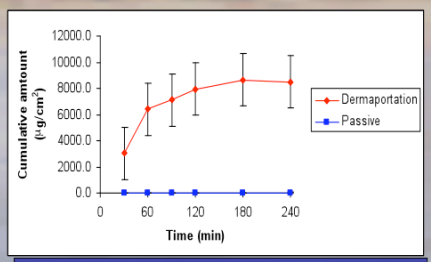

Fig.3: Cumulative penetration (µg in receptor: mean ± SEM; n=4) of ALA by passive diffusion and with Dermaportation

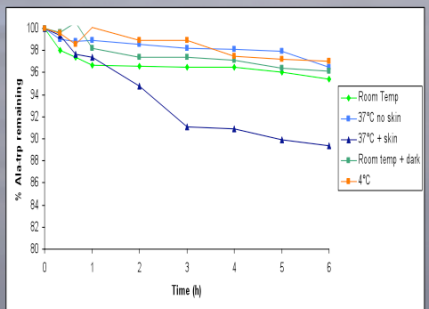

Fig.4: Ala-Trp degradation in solution at varying conditions

Table 1: Skin permeation of Ala-Trp and 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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