**OBJ**

LIMITED

Active transdermal drug delivery

Trial Summary | ETP and DP data summary

Summary of data per drug (August 2007)

Objective

Dermaportation and ETP are electromagnetic transdermal drug delivery technologies. It is hypothesized that a drug push and a skin effect underlie the transdermal drug delivery efficacy of these two technologies. It is also hypothesized that drugs respond differently to the ETP and Dermaportation settings. The current summary of trials has been assembled for investigating drug-technology interactions.

Method

All studies have either been performed on human or on piglet ear epidermis. The epidermis was mounted in vertical Franz type diffusion cells (stratum corneum facing up), according to the method of Kligman and Christophers (1963). Drug in its vehicle (1ml) was applied to the donor compartment of diffusion cells, with vehicle in the receptor compartment (3.0 mL; 37°C). Receptor solutions were either stirred via a magnetic stirrer or manually. Dermaportation coils were placed around the exterior cells, and ETP material was suspended precisely above the donor solution. In some studies a combination of Dermaportation and ETP was investigated. As a control, passive diffusion cells were chosen. Samples of the receptor solution were removed and replaced with fresh buffer during the experiments. All samples were analysed for drug content by HPLC with UV detection by a validated method, or by spectrophotometer. The cumulative amount of drug in receptor versus time was plotted.

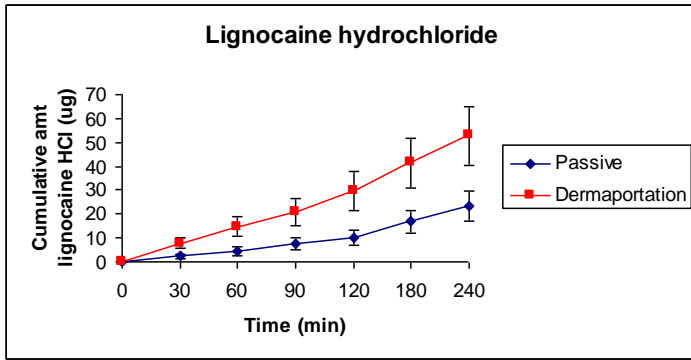
Drugs in this summary

The following drugs appear in this summary:

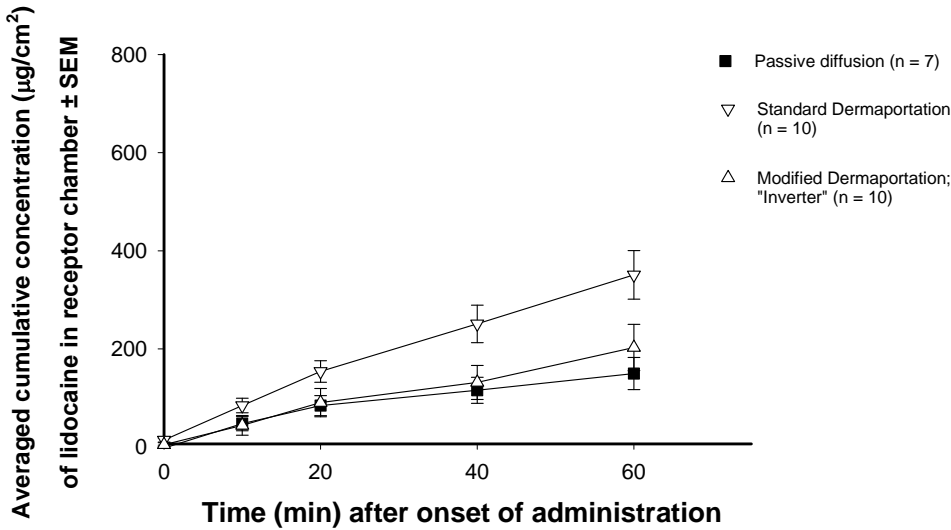
1. Lidocaine hydrochloride
2. Prilocaine hydrochloride
3. Caffeine
4. Hydrocortisone
5. 5-Aminolevulinic acid
6. Diclofenac sodium
7. Diclofenac diethylammonium salt
8. Ibuprofen
9. Tetracaine hydrochloride
10. Tetracaine gel
11. Testosterone
12. Estradiol
13. Dipeptide
14. Naltrexone
15. Sumatriptan Succinate

1. Lidocaine hydrochloride

1.A. Dermapotiation (Standard)



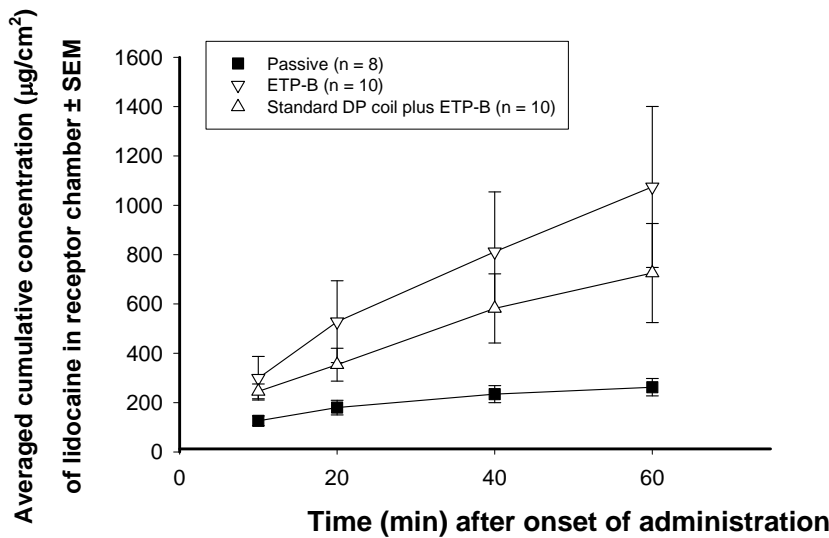
Human data. Detailed data is found in Curtin Lidocaine report.



Piglet data, Studynumber OBJ-DAT-SNA-027. Detailed data is found in appendix 1.A.1

1.B. ETP plus/minus DP

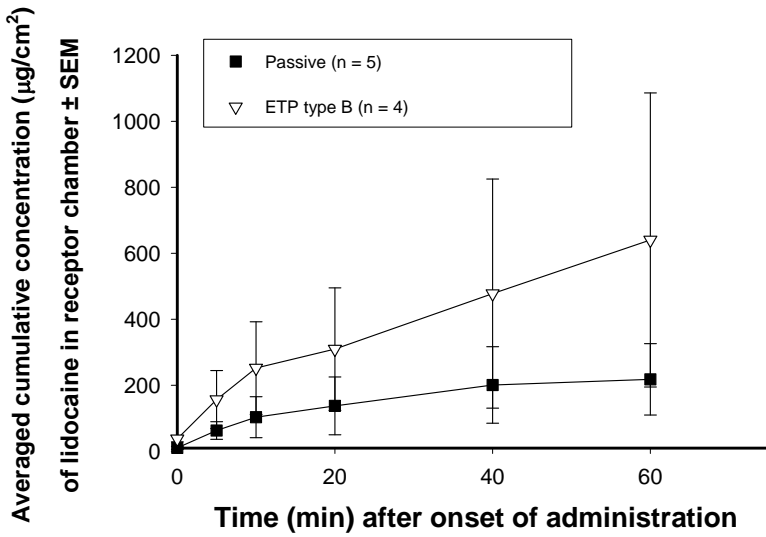
Only piglet data is available.



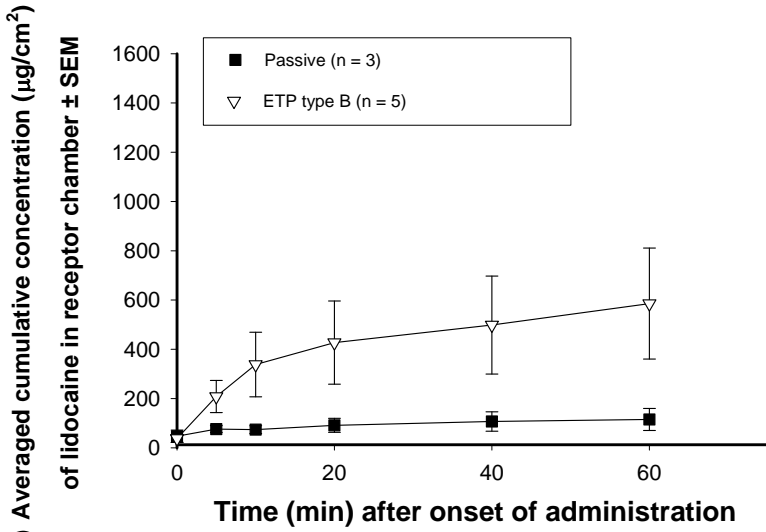
Study OBJ-DAT-SNA-007
Detailed data is found in appendix 1.B.1



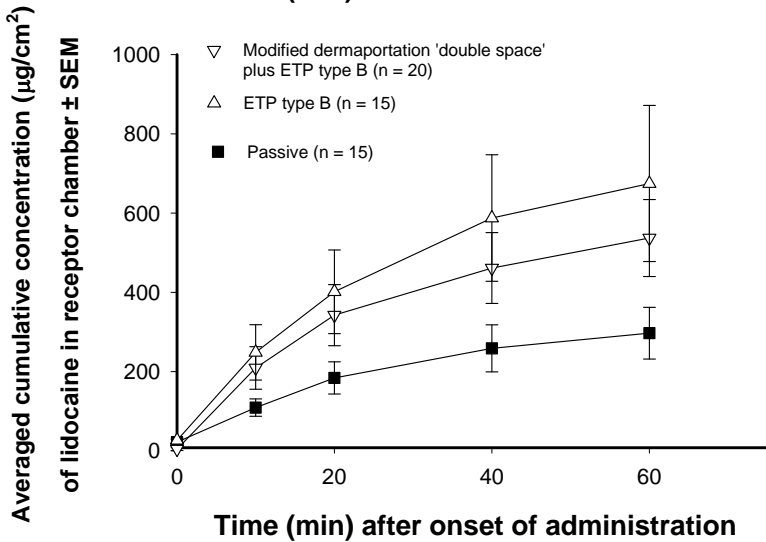
Study OBJ-DAT-SNA-015
Detailed data is found in appendix 1.B.2



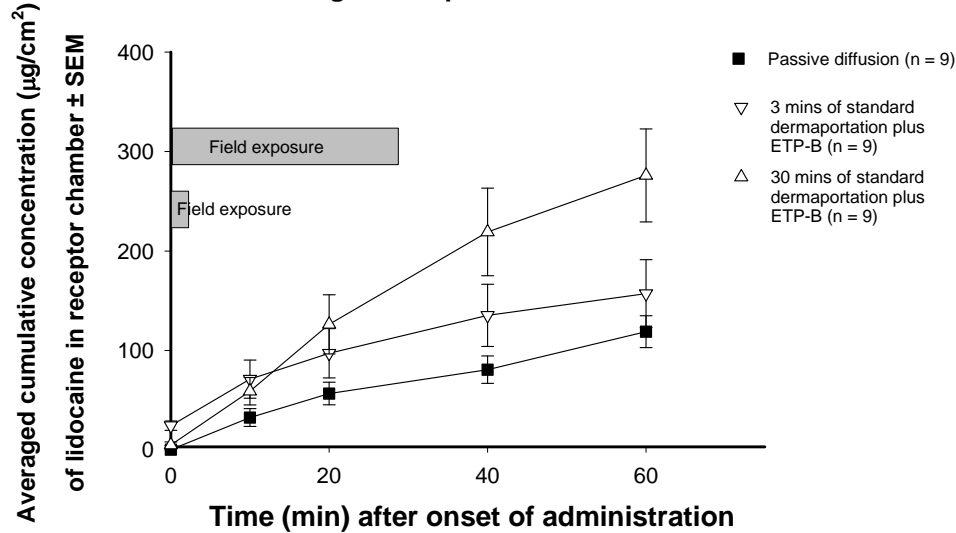
Study OBJ-DAT-HHI-043
Detailed data is found in appendix 1.B.3



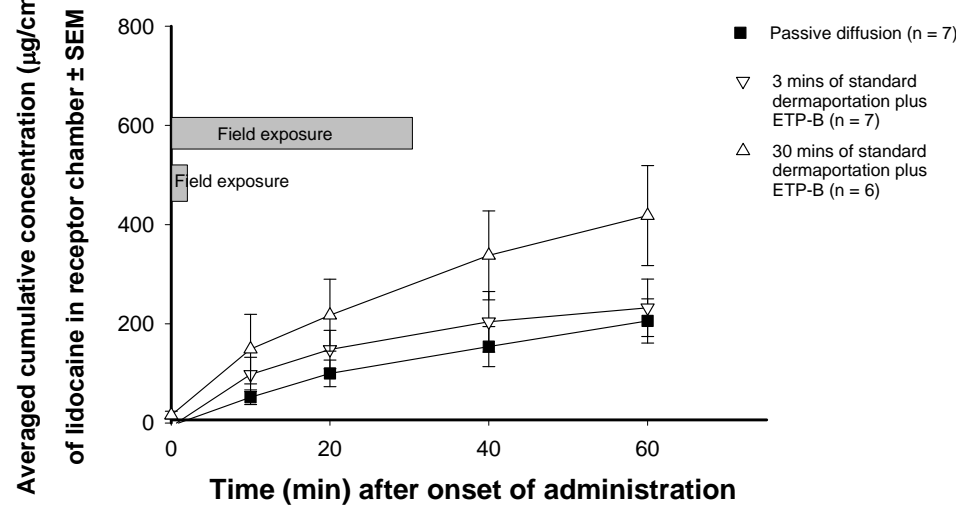
Study OBJ-DAT-SNA-019
Detailed data is found in appendix 1.B.4



1.C. ETP short versus long field exposure



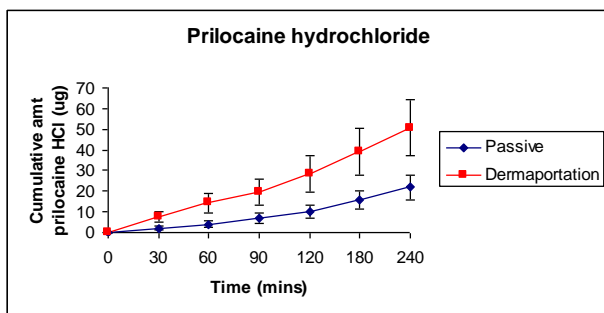
Study *OBJ-DAT-HHI-054*: Appendix 1.C.1 contains detailed data.



Study *OBJ-DAT-SNA-024*: Appendix 1.3 contains detailed data.

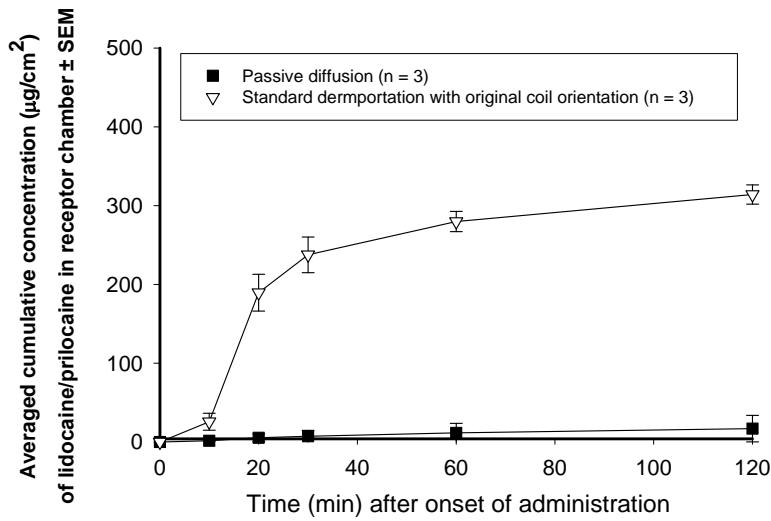
2. Prilocaine hydrochloride

Dermaportation (Standard)



Human data. Detailed data is found in Curtin Lidocaine/prilocaine report.



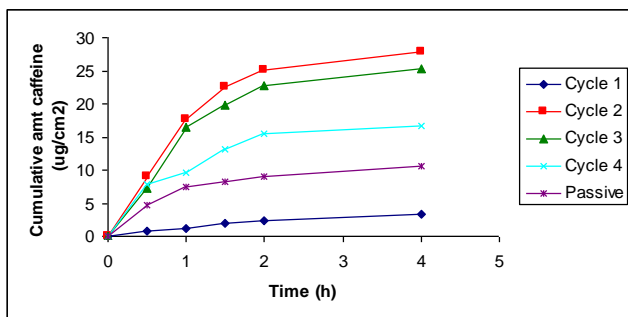


Piglet data, *Study number OBJ-DAT-HHI-015*. Detailed data is found in appendix 2.1

The ETP technology has not been investigated with prilocaine.

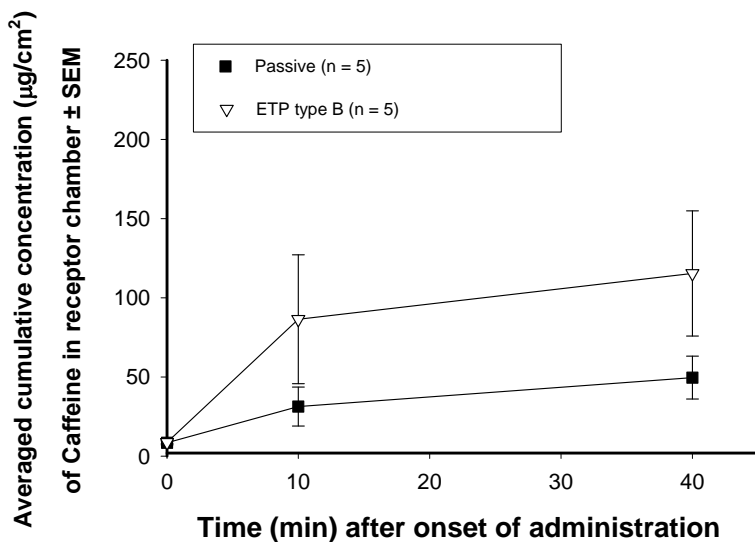
3. Caffeine

3.A Dermportation (Standard)



Human data. Detailed data is found in Curtin caffeine report.

3.B ETP

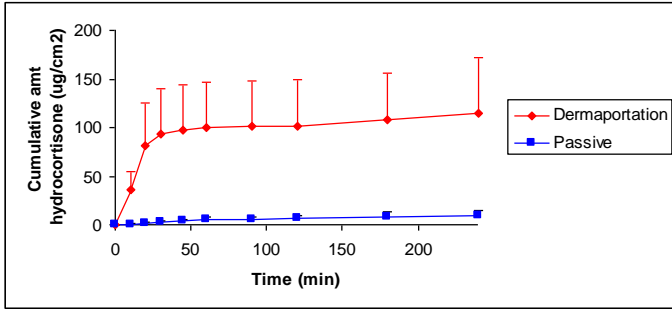


Study *OBJ-DAT-SNA-012*: Appendix 3.B.1 contains detailed data.



4. Hydrocortisone

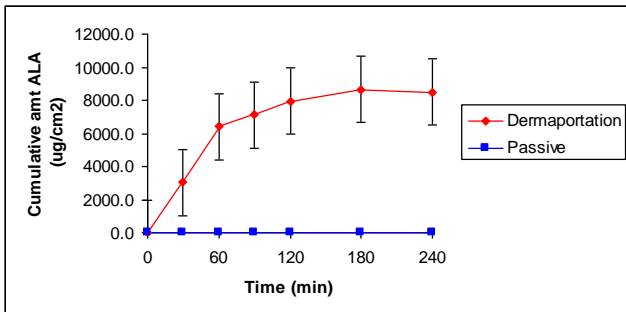
Dermaportation (Standard)



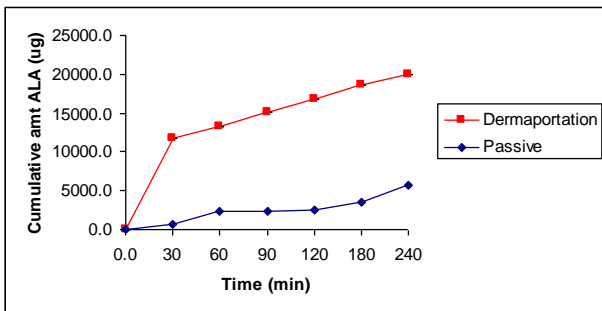
Human data. Detailed data is found in Curtin hydrocortisone report.

5. 5-ALA

Dermaportation (Standard)



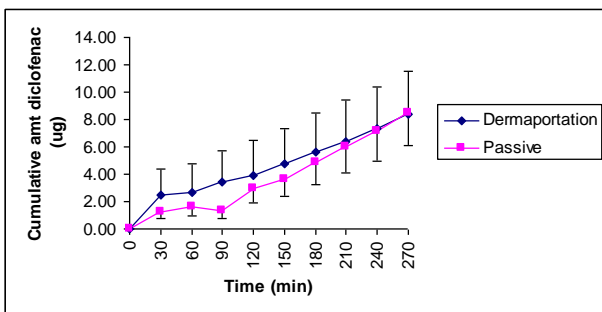
Human data, 2% ALA solution. Detailed data is found in Curtin 5-ALA report.



Human data, 20% ALA solution. Detailed data is found in Curtin 5-ALA report.

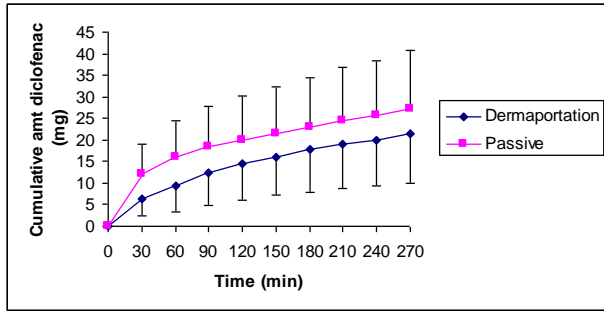
6. Diclofenac sodium

Dermaportation (Standard)



Human data. Detailed data is found in Curtin diclofenac report.

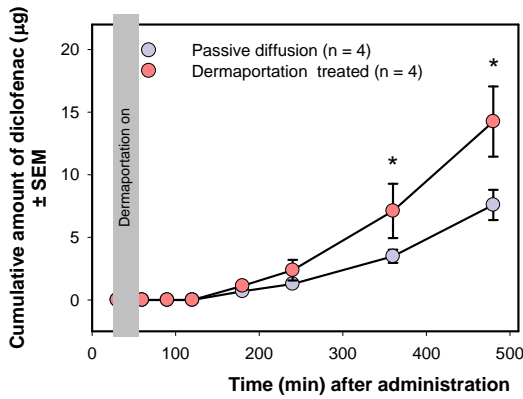




Human data (replication). Detailed data is found in Curtin diclofenac report.

7. Diclofenac diethylammonium salt

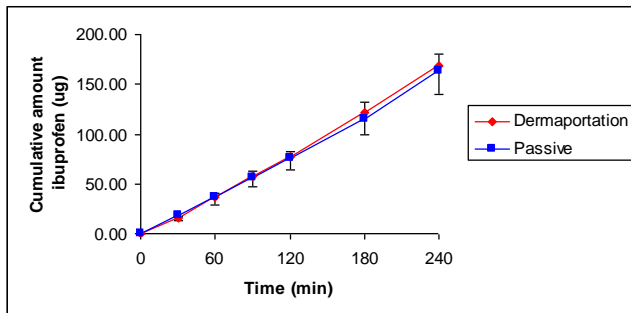
Dermaportation (Standard)



Human data, Voltaren. Detailed data is found in Curtin Voltaren report, and the poster presented in Copenhagen. **Note, that Dermaportation was only on for a short period, therefore, this study will only show a skin effect, and not a drug push effect (poster Copenhagen).**

8. Ibuprofen

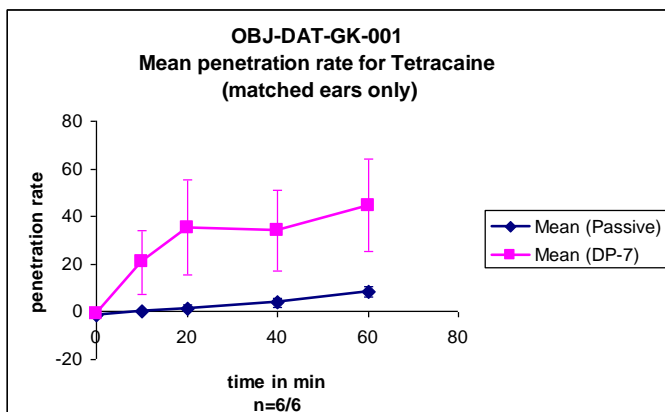
Dermaportation (Standard)



Human data. Detailed data is found in Curtin ibuprofen report.

9. Tetracaine HCL

Dermaportation (Standard)

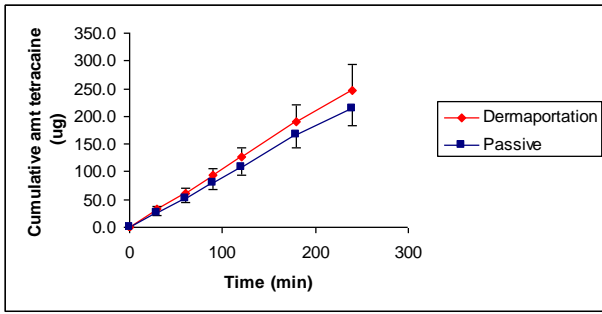


Piglet data, wave form 7, Studynumber OBJ-DAT-GKR-001.



10. Tetracaine gel/Ametop

Dermaportation (Standard)



Human data. Detailed data is found in Curtin Ametop report.

Ametop has not been tested in vitro at the OBJ facilities. However, in vivo we saw an enhancement of DP-Ametop diffusion with a faster onset of a low Ametop dose (compared with passive).

11. Testosterone

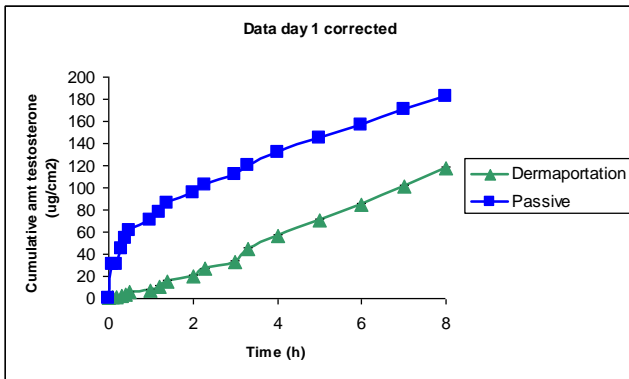
Dermaportation of Testosterone through Human epidermis (protocol 1 incl caffeine in donor).

49 yr old female abdominal skin sample Day 1 (22/08/06)

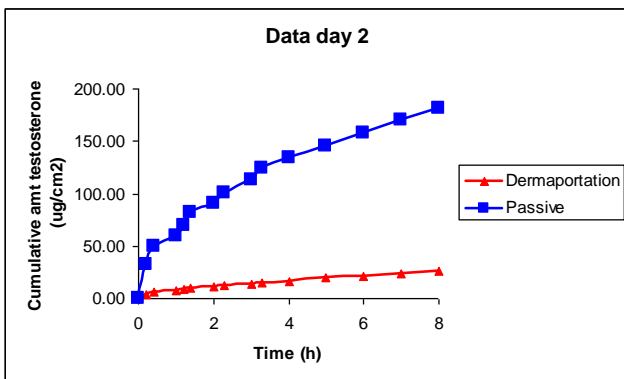
Donor: 4mg/ml testosterone in 1:1 ethanol:water (incl 100 mg/ml caffeine in donor)

Receptor: 4% BSA in PBS at pH 7.4

DP card 2 applied for 4h



Human data (Curtin). Report not received yet.

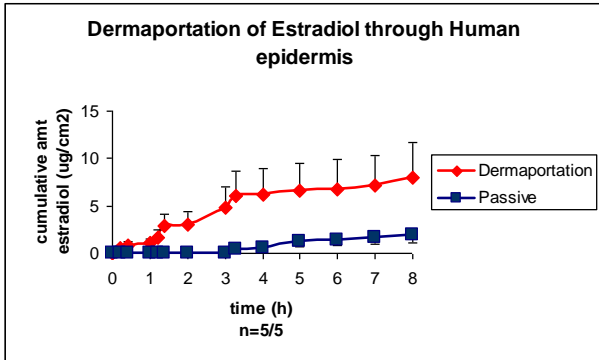


Human data (Curtin). Report not received yet.



12. Estradiol

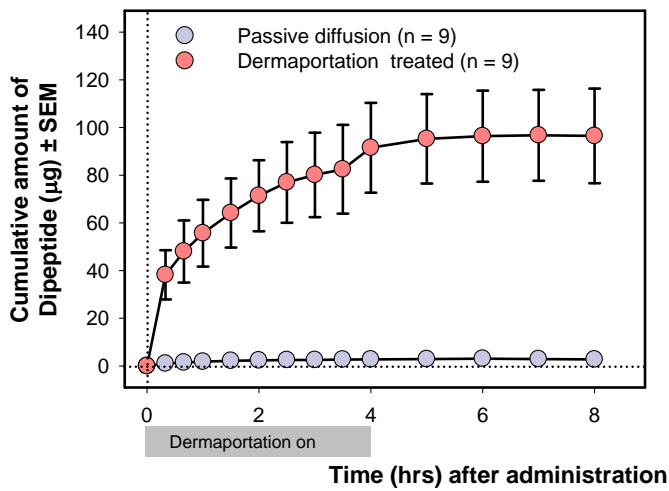
Dermaportation (Standard)



Human data. Detailed data is found in Curtin Estradiol report.

13. Dipeptide: Ala-trp

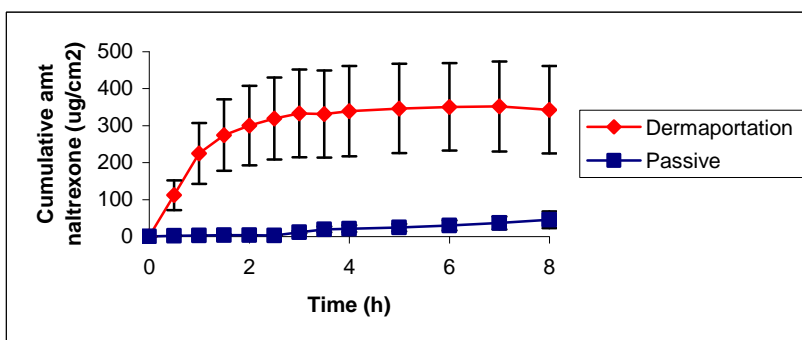
Dermaportation (Standard)



Human data. Detailed report has not been received yet from Curtin.

14. Naltrexone HCL

Dermaportation (Standard)

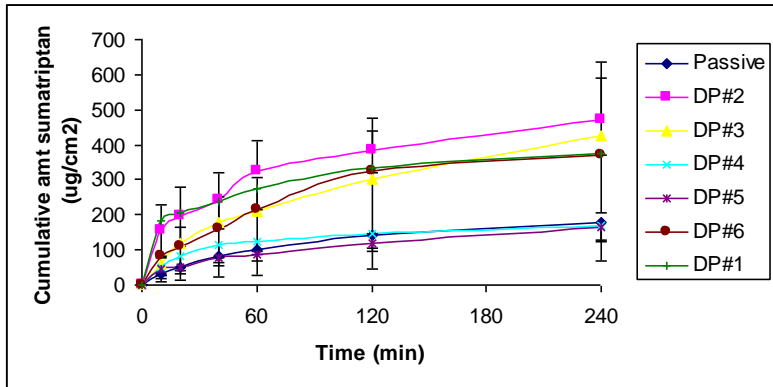


Human data. Detailed data is found in Curtin Naltrexone report, or in the Naltrexone Trial Summary..

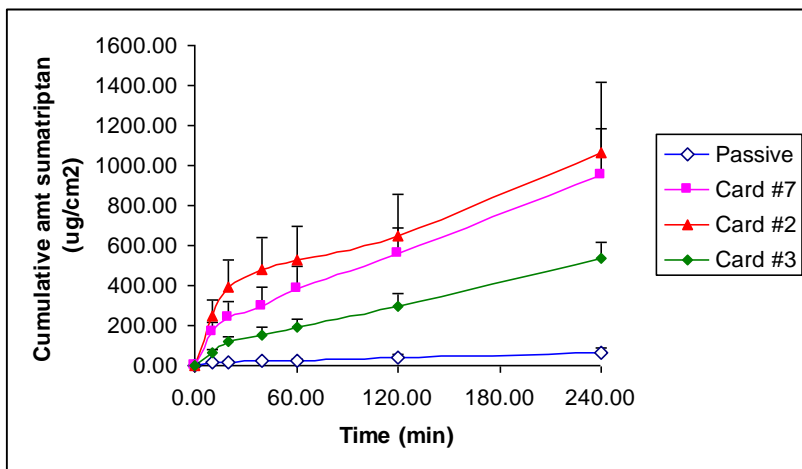


15. Sumatriptan Succinate

15.A Dermaportation (Standard, 4hrs)

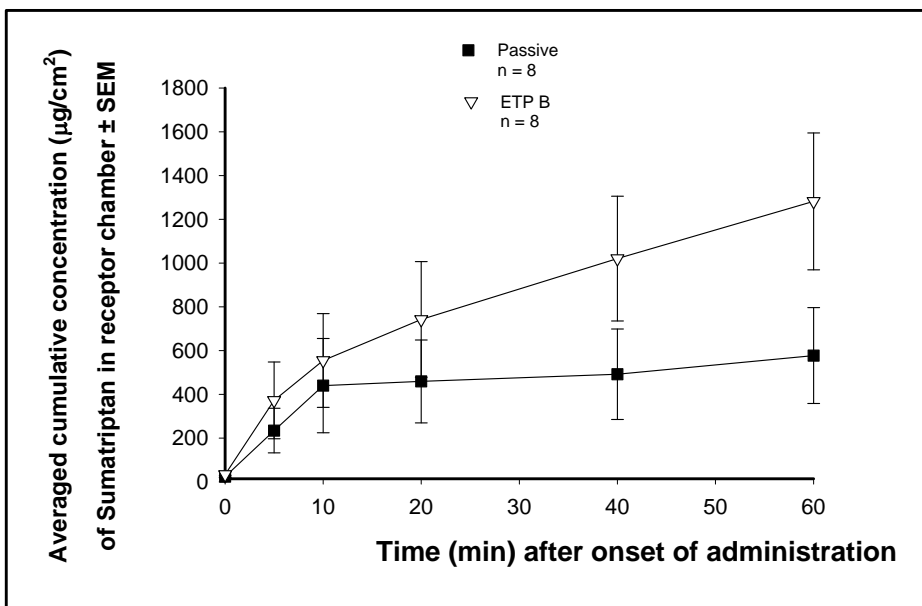


Human data. DP1 is the standard, and DP2 is waveform7 field.



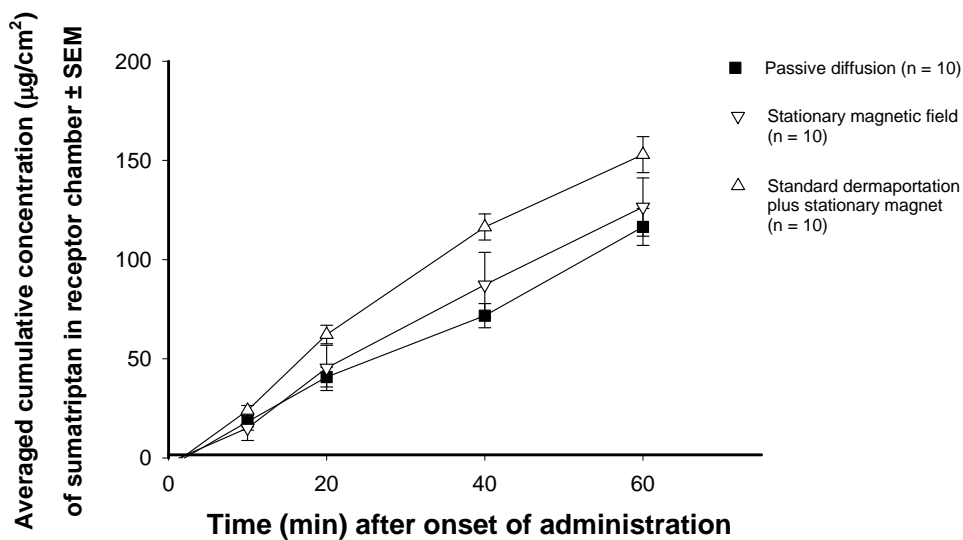
Human data. DP2 is the Wave form7.

15.B ETP (Continuous)



Study OBJ-DAT-SNA-008: Piglet data; Sumatriptan succinate 10mg/ml in PBS.





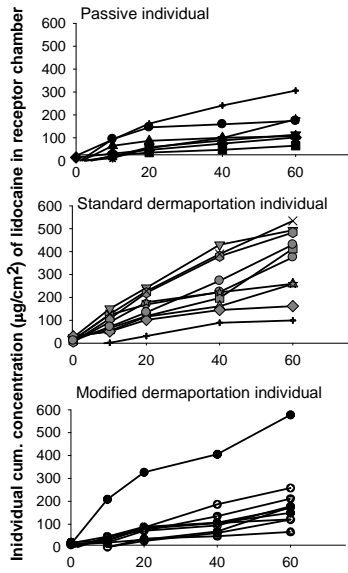
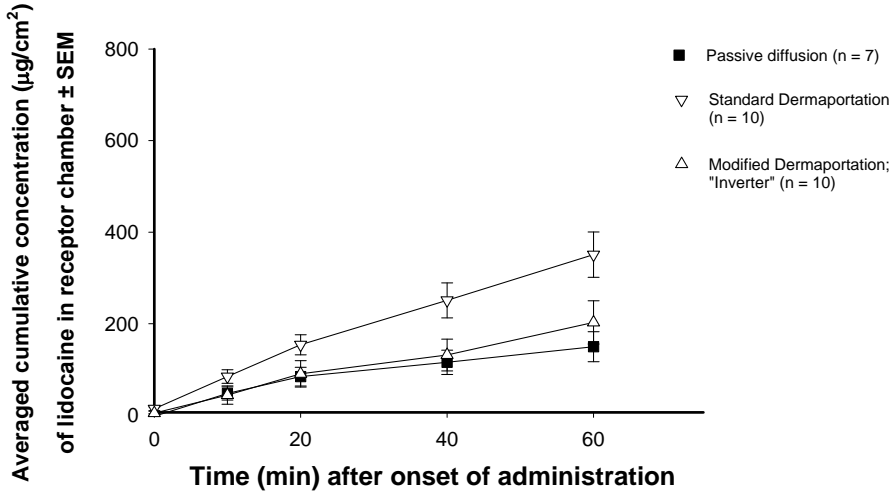
Study OBJ-DAT-HHI-061: Appendix 15.B contains detailed data.

Note, this study was performed with an artificial membrane.



Appendix 1.A.1

OBJ-DAT-SNA-027: Effects of standard and modified dermaportation on the delivery of lidocaine hydrochloride through excised land race piglet ear epidermis



Membrane: piglet ear epidermis, land race
Drug: lidocaine hydrochloride
Donor conc.: 5mg/ml
Vehicle: PBS
delivery system: Standard dermaportation - parallel at 3 volts per coil.
 Modified dermaportation - "Inverter"; parallel at 3 volts per coil
Stirring: Manual stirring, pipette
Date: 13/03/2007

Cells 28, 30 and 31 were excluded from analysis.

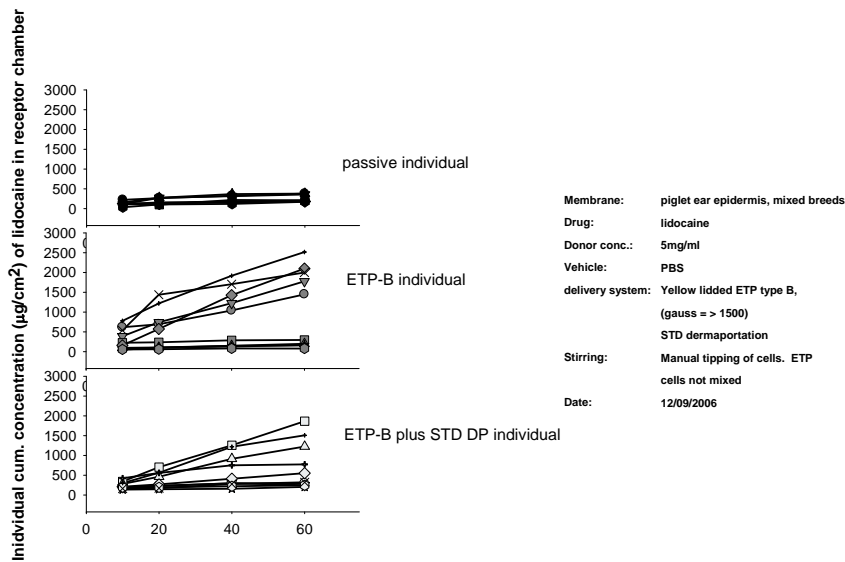
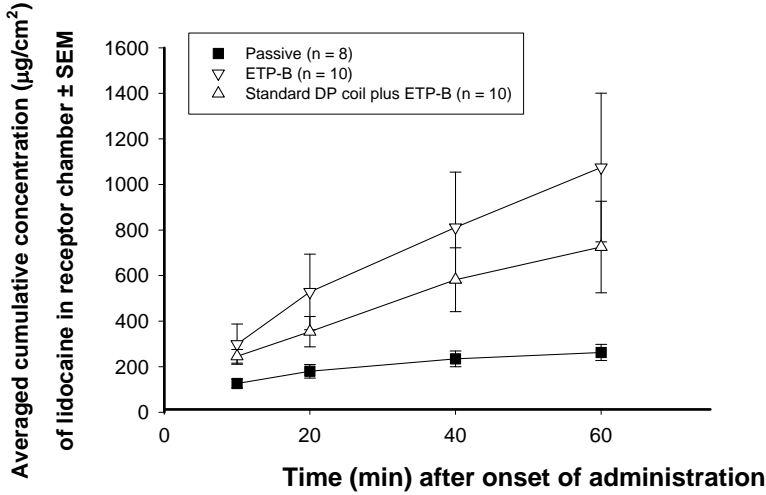
Cell 28 – Passive cell no. 3 Cell 30 – Passive cell no. 5
 Cell 31 – Passive cell no. 6

Cell 28 – The level of fluid in the receptor compartment was high. Upon staining, it was seen that the cell was on the edge of the skin.
 Cell 30 – The level of fluid in the receptor compartment was high. Upon staining, it was seen that the cell was on the edge of the skin.
 Cell 31 – The level of fluid in the receptor compartment was high. Upon examination under the microscope, it was seen that there were holes at the boundary of the cell.



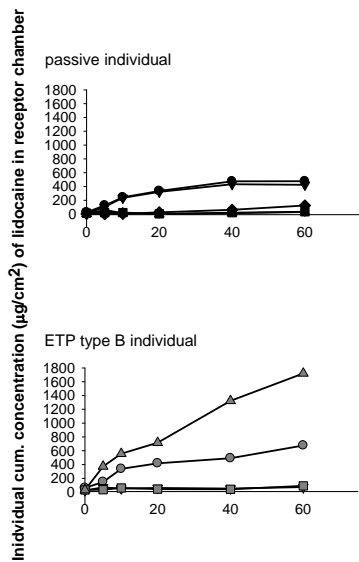
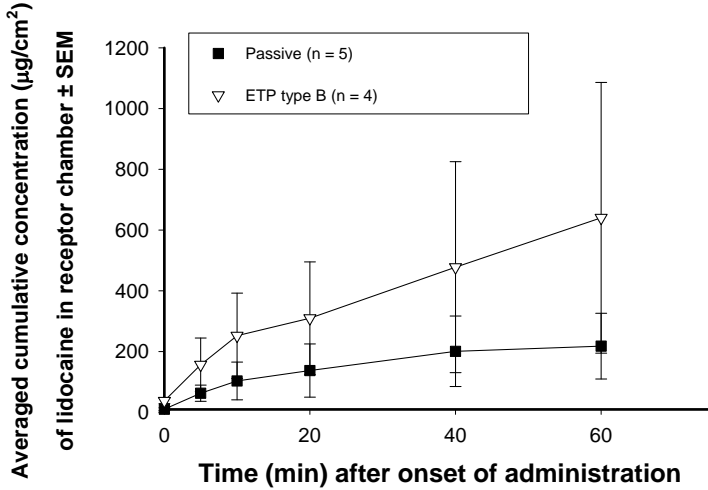
Appendix 1.B.1

OBJ-DAT-SNA-007: Effects of ETP-B field plus/minus STD DP coils on the delivery of lidocaine through excised piglet ear epidermis



Appendix 1.B.2

OBJ-DAT-SNA-015: Effects of ETP type B field on the delivery of lidocaine hydrochloride through cross breed excised piglet ear epidermis



Membrane: piglet ear epidermis, cross breed
Drug: lidocaine hydrochloride
Donor conc.: 5mg/ml
Vehicle: PBS
delivery system: Adjustable yellow capped ETP type B

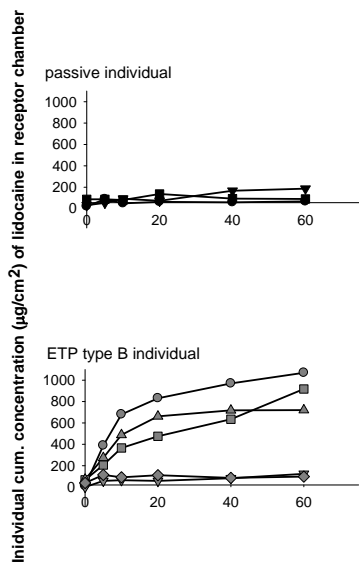
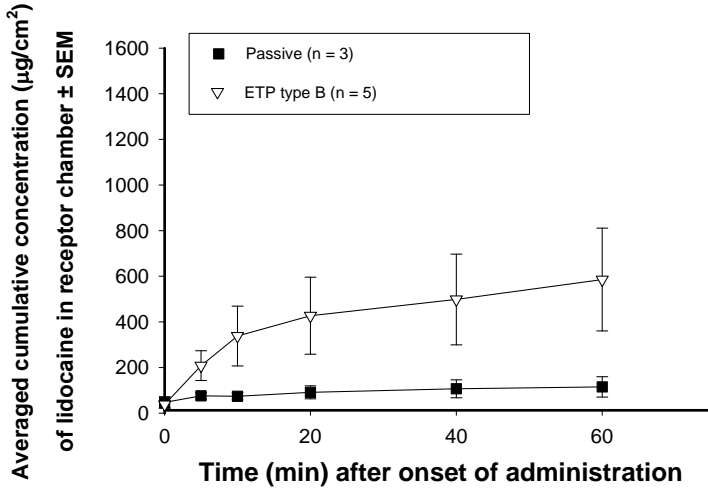
Date: 08/11/2006

N.B. Cells were mixed every 5 min via pipetting technique.



Appendix 1.B.3

OBJ-DAT-HHI-043: Effects of ETP type B field on the delivery of lidocaine hydrochloride through excised land race piglet ear epidermis



Membrane: piglet ear epidermis, land race
Drug: lidocaine hydrochloride
Donor conc.: 5mg/ml
Vehicle: PBS
delivery system: Adjustable yellow capped ETP type B

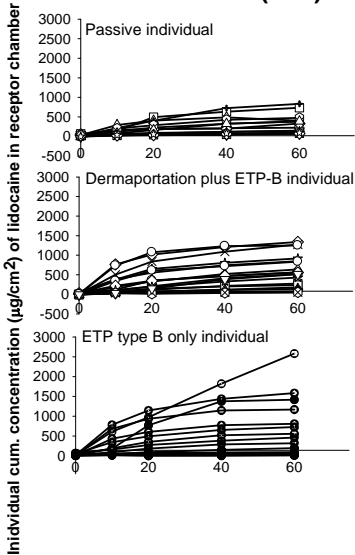
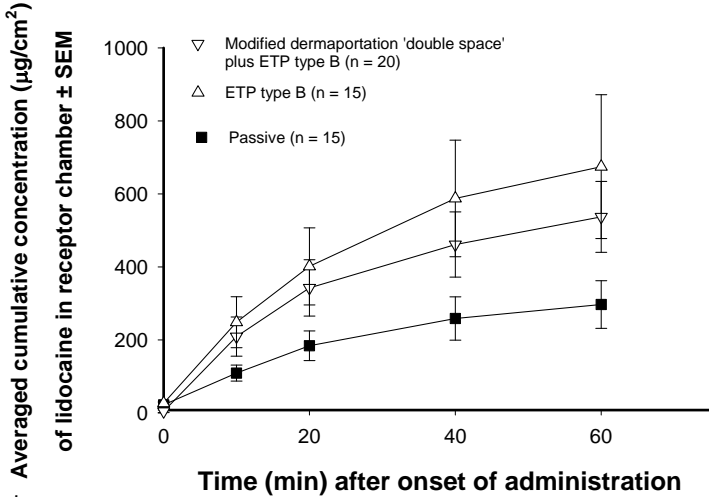
Stirring: Manual, pipette

Date: 08/11/2006



Appendix 1.B.4

OBJ-DAT-SNA-019: Effects of dermaportation and ETP fields on the delivery of lidocaine hydrochloride through excised land race piglet ear epidermis. Pooled data from OBJ-DAT-HHI-048 and OBJ-DAT-SNA-018

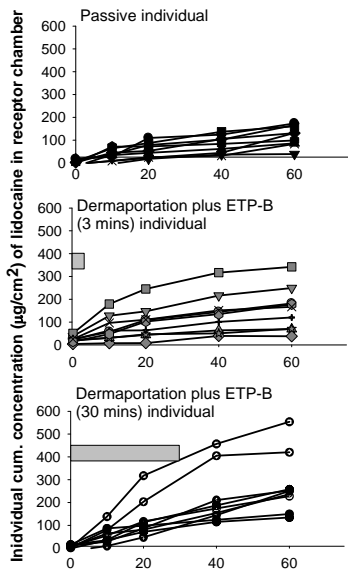
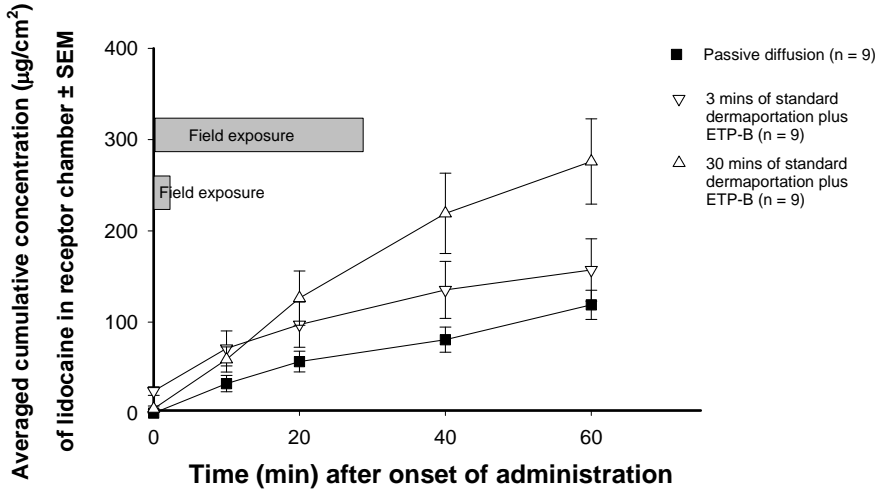


Membrane: piglet ear epidermis, land race
Drug: lidocaine hydrochloride
Donor conc.: 5mg/ml
Vehicle: PBS
delivery system: Adjustable yellow capped ETP type B Modified dermaportation 'double space' - parallel at 3 volts per coil.
Stirring: Manual stirring, pipette
Date: 01/12/2006



Appendix 1.C.1

OBJ-DAT-HHI-054: Effects of standard dermaportation and ETP type B field delivery times on the delivery of lidocaine hydrochloride through excised land race piglet ear epidermis



Membrane: piglet ear epidermis, land race
Drug: lidocaine hydrochloride
Donor conc.: 5mg/ml
Vehicle: PBS
delivery system: Adjustable yellow capped ETP-B
 Standard dermaportation - parallel at 3 volts per coil.
Stirring: Manual stirring, pipette
Date: 18/01/2007

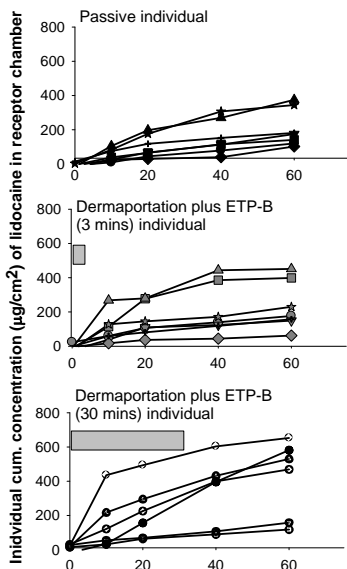
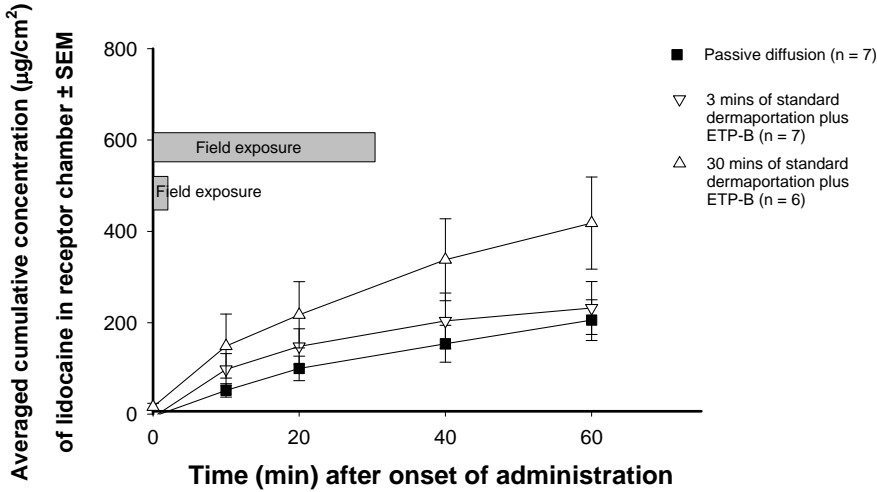
N.B. Cells 2, 30 and 43 were excluded.
 Cell 2 – Passive diffusion cell no. 2
 Cell 30 – 3 mins DP plus ETP-B cell no. 10
 Cell 43 – 30 mins DP plus ETP-B cell no. 8

Cell 2: The donor solution was depleted at 60 mins. Upon staining, a small hole was found in the skin, within the boundary of the cell.
 Cell 30: Upon staining, a small tear was found in the skin, in the centre of the cell boundary.
 Cell 43: Upon staining, a tear was found in the skin, within the boundary of the cell.



Appendix 1.C.2

OBJ-DAT-SNA-024: Effects of standard dermaportation and ETP type B fields on the delivery of lidocaine hydrochloride through excised land race piglet ear epidermis



Membrane: piglet ear epidermis, land race
Drug: lidocaine hydrochloride
Donor conc.: 5mg/ml
Vehicle: PBS
delivery system: Adjustable yellow capped ETP-B
Standard dermaportation - parallel at 3 volts per coil.
Stirring: Manual stirring, pipette
Date: 16/01/2007

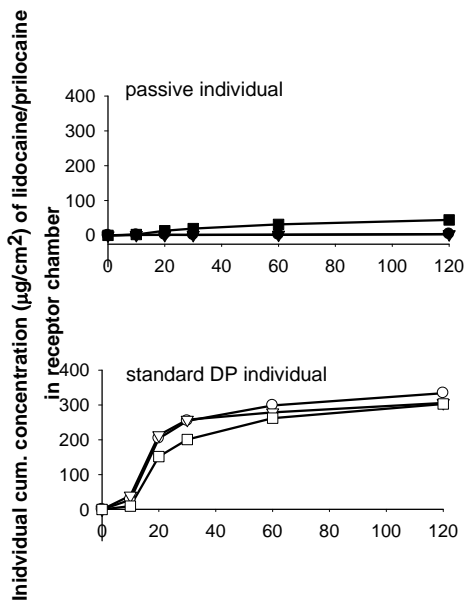
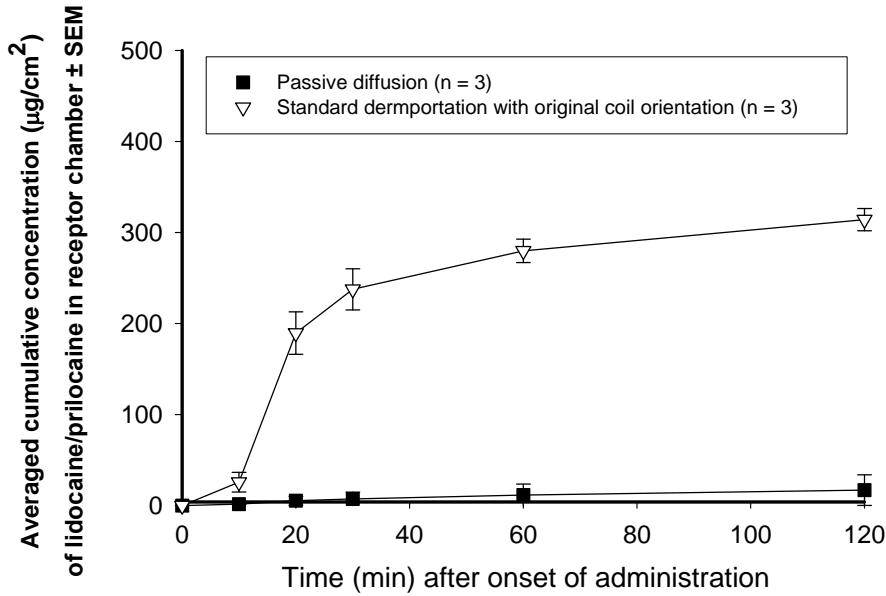
N.B. Cells 5, 12, 15, 17, 19, 26, 31, 34 and 45 were excluded.
 Cell 5 - 3 mins DP plus ETP cell no. 5 Cell 26 - Passive diffusion cell no. 6
 Cell 12 - 3 mins DP plus ETP cell no. 7 Cell 31 - 30 mins DP plus ETP cell no. 1
 Cell 15 - 3 mins DP plus ETP cell no. 10 Cell 34 - 30 mins DP plus ETP cell no. 4
 Cell 17 - Passive diffusion cell no. 2 Cell 35 - 30 mins DP plus ETP cell no. 5
 Cell 19 - Passive diffusion cell no. 4 Cell 45 - 30 mins DP plus ETP cell no. 10

Cell 5: The level of the receptor fluid was level with the tip of the side arm and the donor solution was depleted. Upon examination under the microscope, a hole was found in the skin, within the boundaries of the cell.
 Cell 12: Upon staining, small tears were found in the skin, within the boundaries of the cell.
 Cell 15: The level of the receptor fluid was level with the tip of the side arm and the donor solution was depleted. Upon staining, two holes were found in the skin, within the boundaries of the cell.
 Cell 17: The level of the receptor fluid was high and the donor solution was depleted. Upon examination under the microscope, holes were found in the skin, within the boundaries of the cell.
 Cell 19: The cell was already leaking at equilibration and was removed before the 0 min sample. Upon staining, a large hole was found in the skin, within the boundaries of the cell.
 Cell 26: The level of the receptor fluid was high and the donor solution was depleted. Upon examination under the microscope, holes were found in the skin, within the boundaries of the cell.
 Cell 31: The level of the receptor fluid was level with the tip of the side arm and the donor solution was 0.6ml at 60 min. Upon staining, small tears were found in the skin, within the boundaries of the cell.
 Cell 34: The donor solution volume was 0.6ml at 60 mins. Two tears were found in the skin, within the boundaries of the cell.
 Cell 35: The receptor fluid was high and the donor solution volume was 0.6ml at 60 mins. Upon staining, it was found that the boundaries of the cell were on the edges of the skin.
 Cell 45: The cell was already leaking at equilibration and was removed before the 0 min sample. Upon staining, a large hole was found in the skin, within the boundaries of the cell.



Appendix 2.1

OBJ-DAT-HHI-015: Effects of coil orientation of standard dermaportation on the delivery of prilocaine hydrochloride through excised adult pig stomach epidermis



Membrane: adult pig stomach epidermis, unknown breed.

Drug: lidocaine and prilocaine hydrochloride

Donor conc.: 5mg/ml

Vehicle: PBS

delivery system: Standard dermaportation; serial at 12 volts.

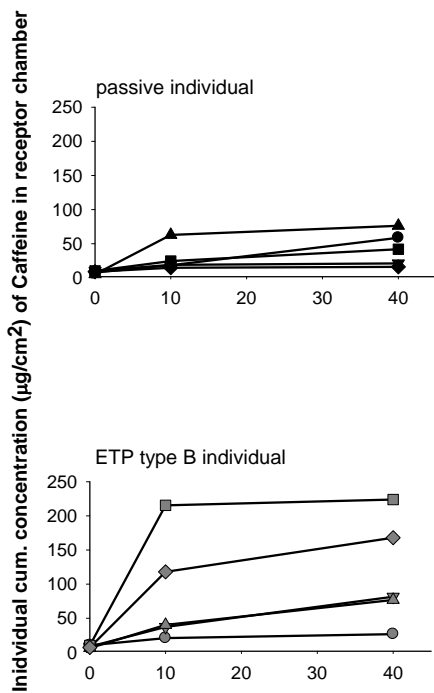
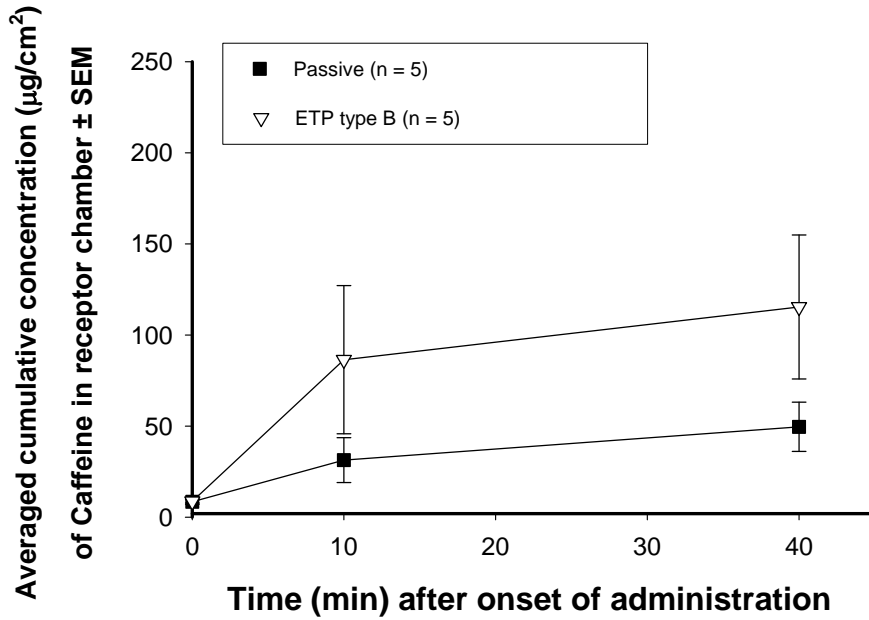
Stirring: Magnetic stirrer

Date: 13/04/2006



Appendix 3.B.1

OBJ-DAT-SNA-012: Effects of ETP type B on the delivery of Caffeine through excised piglet ear epidermis.

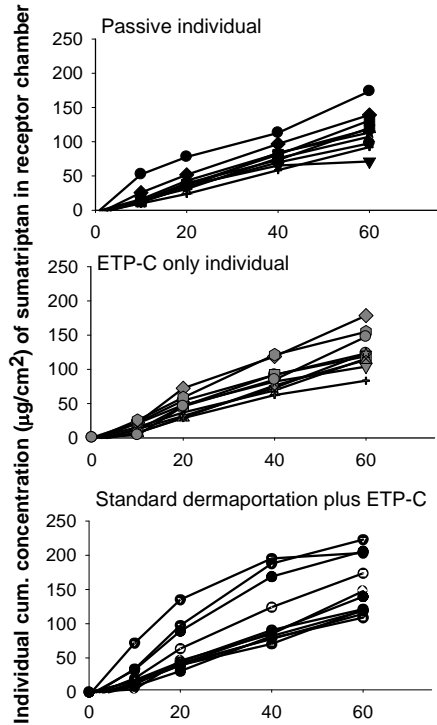
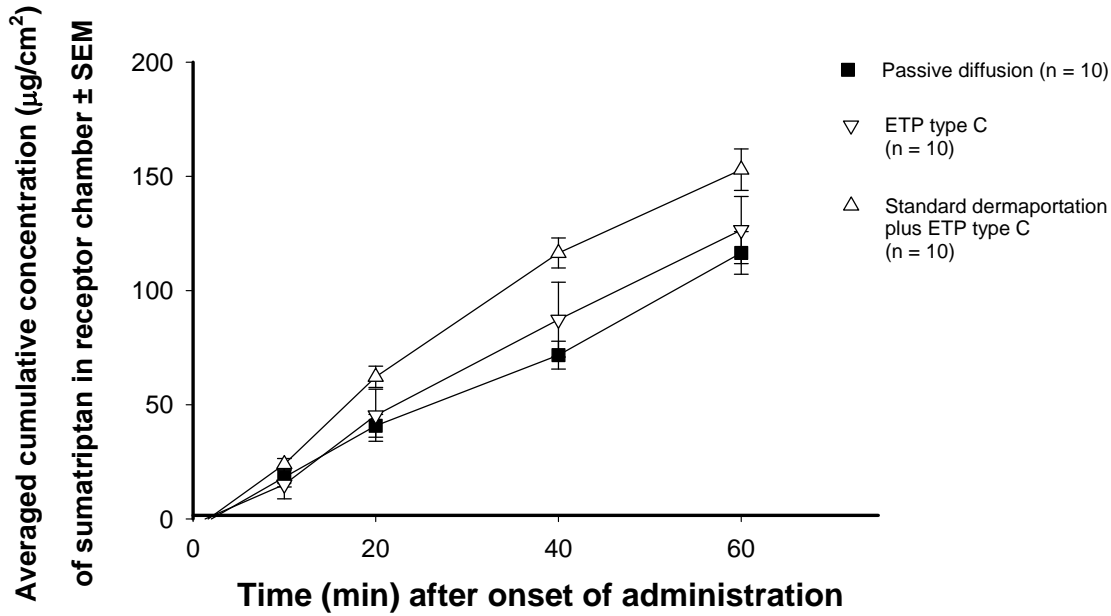


| | |
|-------------------------|--|
| Membrane: | Piglet ear epidermis, Land race |
| Drug: | Caffeine |
| Donor conc.: | 2mg/ml |
| Vehicle: | PBS |
| delivery system: | Yellow lidded ETP-B, (gauss = > 1500) |
| Date: | 13/10/2006 |



Appendix 15.B

OBJ-DAT-HHI-061: Effects of standard dermaportation and ETP-C fields on the delivery of sumatriptan succinate through artificial dialysis membrane



| | |
|-------------------------|---|
| Membrane: | Artificial membrane; dialysis tubing |
| Drug: | Sumatriptan succinate |
| Donor conc.: | 1mg/ml |
| Vehicle: | PBS |
| delivery system: | Standard dermaportation - parallel at 3 volts per coil. ETP-C |
| Stirring: | Manual stirring, pipette |
| Date: | 20/03/2007 |

