Comparative Permeability of Lipid Nanocarriers for Hydrophilic and Hydrophobic Drugs in Healthy and Inflamed Skin Models

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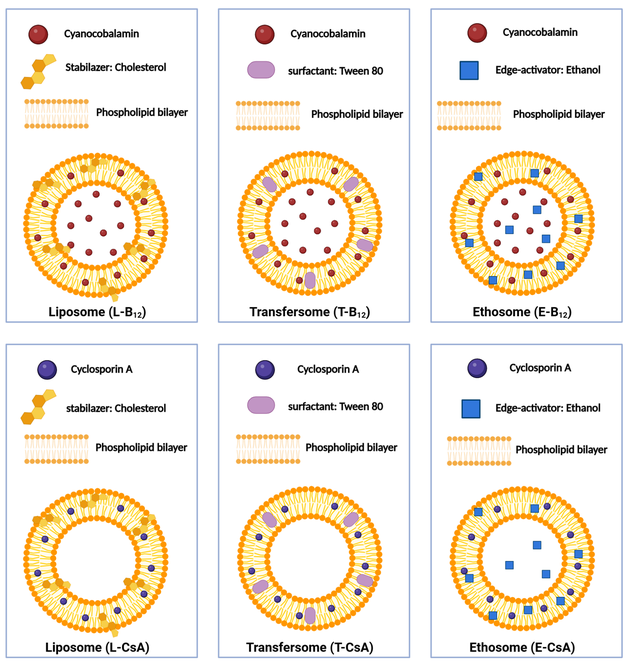
INTRODUCTION & GOAL

- ✓ **Lipid nanocarriers constitute a promising strategy for enhancing the transdermal delivery of drugs.**
- ✓ **Comprehensive comparisons of their behaviour across different skin types and conditions are limited**.
- ✓ **Goal:** This study evaluates the transdermal permeability of hydrophilic (cyanocobalamin) and hydrophobic (cyclosporin A) model drugs formulated in liposomes, transfersomes, and ethosomes through human, porcine, and murine skin, including inflamed conditions (mice).

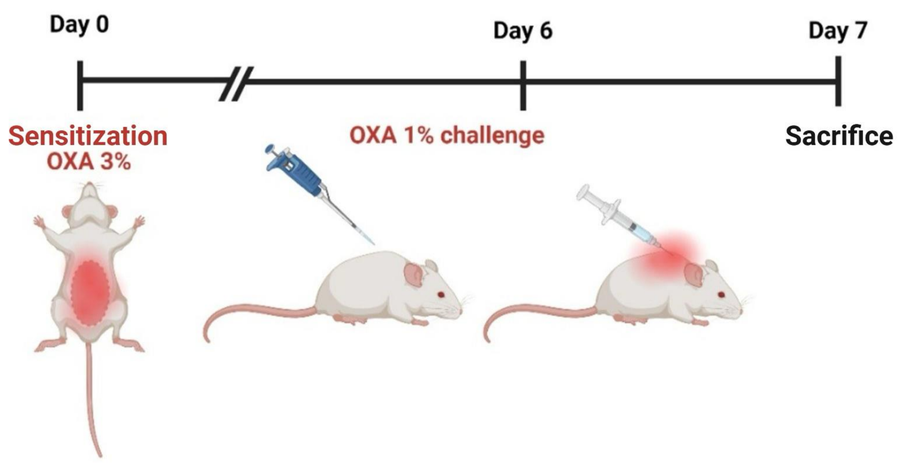
METHODOLOGY

Lipid nanocarriers preparation

- Liposomes ➔ Bangham's method
- Transfersomes ➔ ➔ Bangham's method
- Ethosomes ➔ Touitou's method



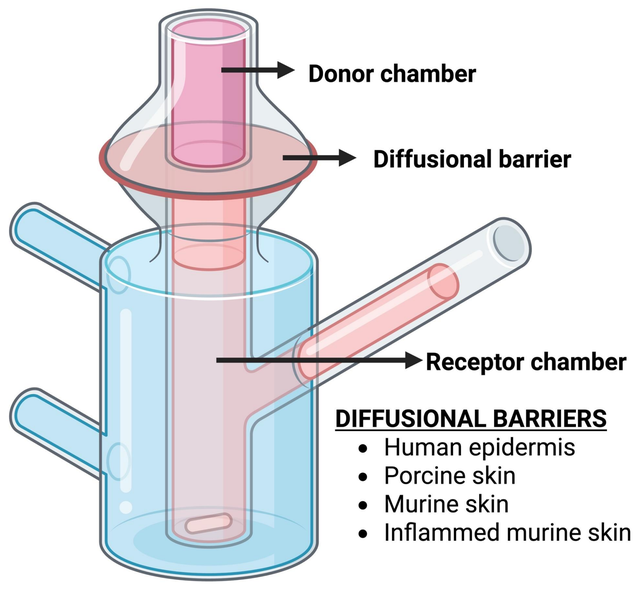
Induction of *in vivo* skin inflammation



- **Mice skin was obtained from Swiss CD-1 adults .**
- **Inflammation was triggered by topical Oxazolone (OXA) topical administration.**

Ex vivo permeability study

Ex vivo skin permeability studies were conducted using Franz-diffusion cells using four diffusional barriers.



RESULTS

Table 1: Permeability parameters: maximum flux (Jmax); permeability constant (Kp); and latency time (lag time); for B12-loaded lipid nanocarriers and free drug calculated for the different skin types.

	L-B12	T-B12	E-B12	Free B12
Human Skin				
Jmax (µg/cm²/h)	1.2 ± 0.2	1.9 ± 0.3	2.7 ± 1.1	-
Kp * 10-7 (cm/s)	1.7 ± 0.3	2.7 ± 0.4	5.6 ± 2.2	-
Lag Time (h)	5.6 ± 3.4	1.1 ± 0.8	5.7 ± 1.0	-
Porcine Skin				
Jmax (µg/cm²/h)	1.0 ± 0.6	1.7 ± 0.8	1.5 ± 0.4	-
Kp (cm/s)	1.3 ± 0.7	2.4 ± 1.1	2.8 ± 0.5	-
Lag Time (h)	23.8 ± 0.4	14.5 ± 1.6	17.1 ± 2.1	-
Healthy Mice Skin				
Jmax (µg/cm²/h)	0.9 ± 0.3	1.8 ± 1.2	5.8 ± 3.0	-
Kp (cm/s)	11.1 ± 3.3	8.02 ± 5.2	18.8 ± 9.8	-
Lag Time (h)	4.9 ± 4	3.7 ± 6.4	0*	-
Inflamed Mice Skin				
Jmax (µg/cm²/h)	0.8 ± 0.4	2.6 ± 1.5	9.6 ± 6.3	-
Kp (cm/s)	9.0 ± 4.1	12.0 ± 6.7	31.1 ± 20.6	-
Lag Time (h)	17.5 ± 11.4	7.5 ± 9.0	16.7 ± 7.8	-

Table 2: Permeability parameters: maximum flux (Jmax); permeability constant (Kp); and latency time (lag time); for CsA-loaded lipid nanocarriers and free drug calculated for the different skin types.

	L-CsA	T-CsA	E-CsA	Free CsA
Human Skin				
Jmax (µg/cm²/h)	-	1.2 ± 0.2	3.78 ± 1.7	-
Kp * 10-7 (cm/s)	-	3.8 ± 0.4	5.6 ± 0.23	-
Lag Time (h)	-	7.8 ± 3.2	3.5 ± 1.3	-
Porcine Skin				
Jmax (µg/cm²/h)	-	-	-	-
Kp (cm/s)	-	-	-	-
Lag Time (h)	-	-	-	-
Healthy Mice Skin				
Jmax (µg/cm²/h)	3.5 ± 0.3	7.1 ± 0.7	6.0 ± 1.2	-
Kp (cm/s)	5.6 ± 0.6	14.6 ± 1.4	15.1 ± 3.0	-
Lag Time (h)	12.3 ± 3.6	7.8 ± 3.2	3.5 ± 1.3	-
Inflamed Mice Skin				
Jmax (µg/cm²/h)	6.0 ± 1.4	5.7 ± 1.4	9.0 ± 5,4	-
Kp (cm/s)	9.4 ± 2.1	10.8 ± 2.6	24,4 ± 14.6	-
Lag Time (h)	6.5 ± 3.1	15 ± 9.5	16.7 ± 7.8	-

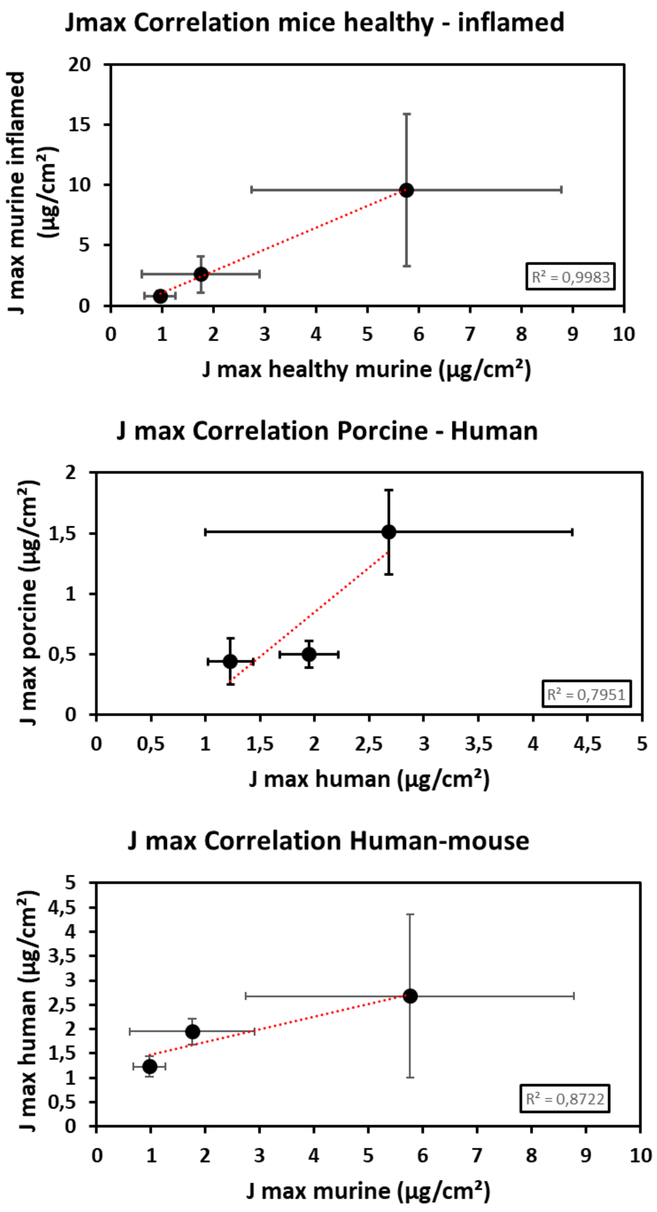


Figure 1: Jmax correlation between three skin pairs for B12-loaded liposome, transfersome and ethosomes.

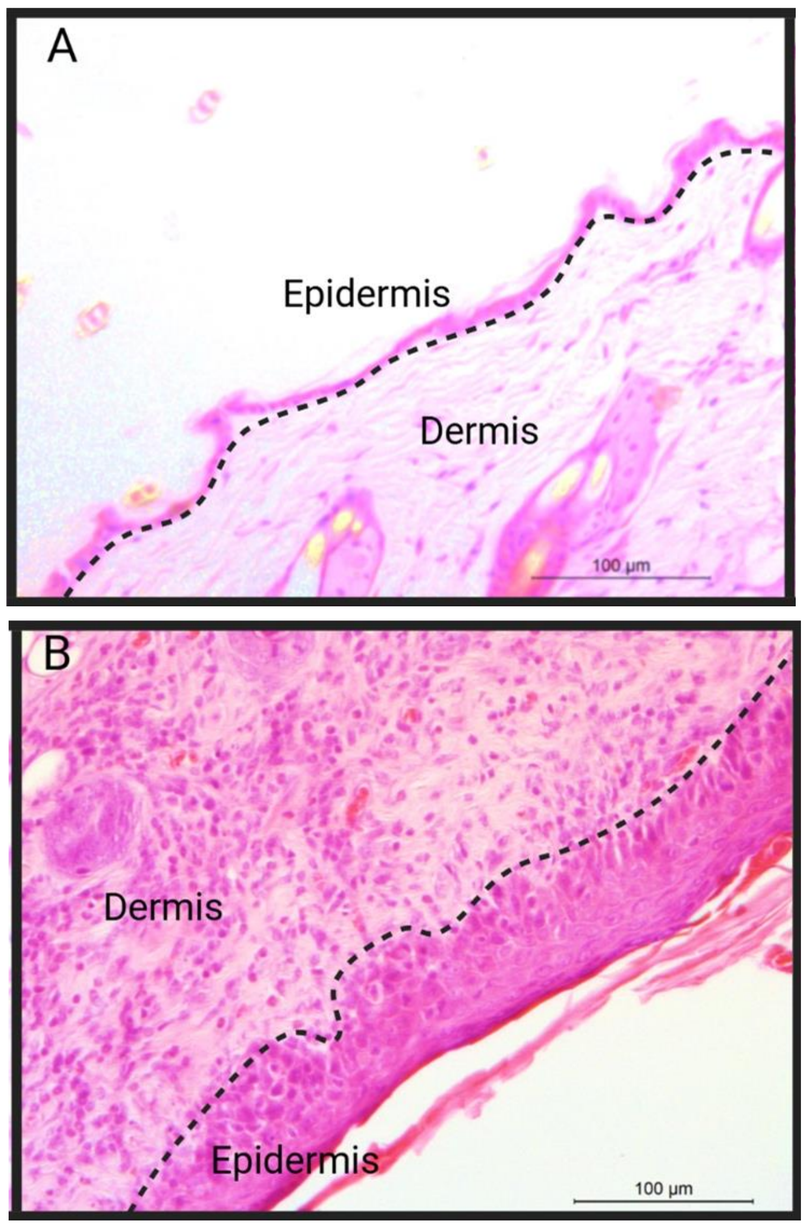


Figure 2: Histopathological differences between healthy murine skin (A) and inflamed murine skin after OXA challenge (B). Samples stained with Eosin & Hematoxylin stain.

CONCLUSIONS

- Transfersomes and ethosomes improve transdermal delivery of hydrophilic and hydrophobic drugs.
- Permeability is enhanced in inflamed skin. Rodent skin is often more suitable for permeability studies.
- These findings highlight the importance of considering the nanocarrier type and skin type/state in transdermal drug delivery systems development and preclinical modelling.

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