T1030-03-14

INVESTIGATION OF PHENOXYETHANOL PERMEATION USING THE SKIN PARALLEL ARTIFICIAL MEMBRANE PERMEABILITY ASSAY (PAMPA) MEMBRANE AND MAMMALIAN SKIN: CORRELATION AND RANK ORDER

Annisa Rahma[a], Majella E. Lane[a], Bálint Sinkó[b]

a School of Pharmacy, University College London, London WC1N 1AX, United Kingdom

b Pion Inc., Billerica, Massachusetts 01821, United States

CONTACT INFORMATION: annisarahma@fa.itb.ac.id

PURPOSE

•Phenoxyethanol (PE) is the most commonly used preservative ingredient in baby wipe formulations (0.5-1% v/v in the cleansing liquid).

•Some baby wipe formulations also contain cetylpyridinium chloride (CPC), a quaternary surfactant with antimicrobial activity.

•To date there is no information in the published scientific literature regarding skin permeation of PE in the presence of surfactant(s).

•The skin Parallel Artificial Membrane Permeability Assay (PAMPA) model has been proposed as a high throughput tool for *in vitro* skin permeation.

OBJECTIVE(S)

- The main aim of the present study was to assess the suitability of the skin PAMPA model for prediction of skin permeation of PE in the presence and absence of CPC in model formulations.
- A secondary aim was to investigate the rank order for permeation of PE from these formulations in the skin PAMPA membrane, porcine skin and human skin.

METHOD(S)

Permeation of PE from various formulations (Table 1) was determined *in vitro* using the skin PAMPA model and Franz diffusion cells (Fig. 1) with excised porcine skin or human skin. Permeation studies were conducted for 1 h in the PAMPA model with applied doses ranging from 3-10 µL/cm^2. For Franz diffusion studies, the assay was conducted for 24 h with an applied dose of 10 µL/cm^2.

Table 1. PE Formulations used in permeation studies

Formulation	PE (%)	CPC (%)	Vehicle
PG1	1	-	PG[1]
PG2	1	0.2	PG[1]
PG3	1	1	PG[1]
WP1	1	-	WP[2]
WP2	1	0.2	WP[2]
WP3	1	1	WP[2]

[1] propylene glycol; [2] water-propylene glycol 97:3

RESULT(S)

Permeation profiles

- A correlation between the applied dose and the cumulative amount of PE permeated in the skin PAMPA model was observed (r^2 = 0.99).
- The highest permeation of PE was observed for WP2, the formulation that most closely resembles actual baby wipe formulations. This finding was consistently observed in the skin PAMPA model and in Franz cell studies using porcine skin and human skin (Fig. 2-4).
- Permeation of CPC was not detected in the three models, but the presence of CPC enhanced the permeation of PE significantly ($p < 0.05$) compared to formulations without CPC (Fig. 5).

Comparative evaluation of the permeation data

- The rank orders for PE permeation were WP2>PG3>WP3>PG2>WP1>PG1 in the skin PAMPA model and WP2>PG3>PG2>WP3>WP1>PG1 in the Franz cell studies.
- A correlation between the skin PAMPA data and the porcine skin data for cumulative amount of PE permeated was observed (r^2 = 0.84, Fig. 6a).
- A good correlation was also observed between the skin PAMPA and human skin data for cumulative amount of PE permeated (r^2 = 0.89, Fig. 6b).

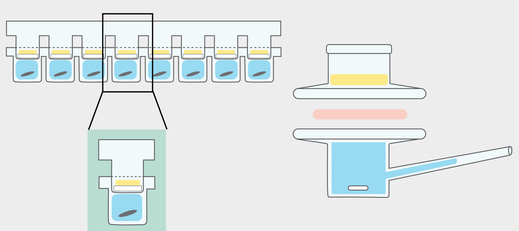

Figure 1. Assay setup for the skin PAMPA model (left) and Franz diffusion cells (right).

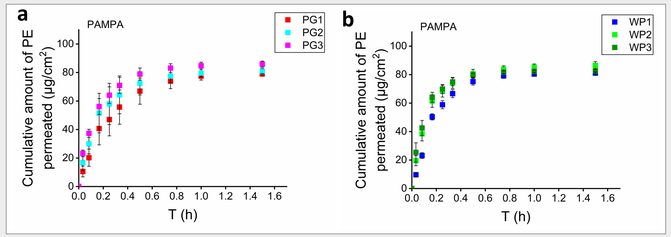

Figure 2. Permeation profiles of PE from various formulations in the skin PAMPA membrane. Data (mean ± SD, n = 6) grouped based on solvents: (a) PG and (b) WP.

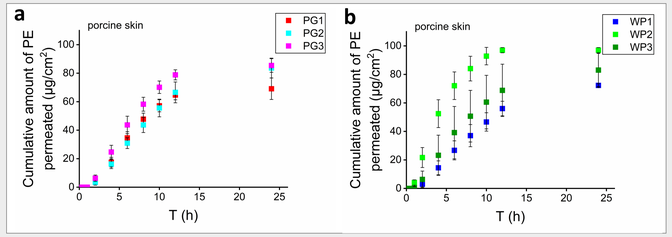

Figure 3. Permeation profiles of PE from various formulations in the skin PAMPA membrane. Data (mean ± SD, n = 6) grouped based on solvents: (a) PG and (b) WP.

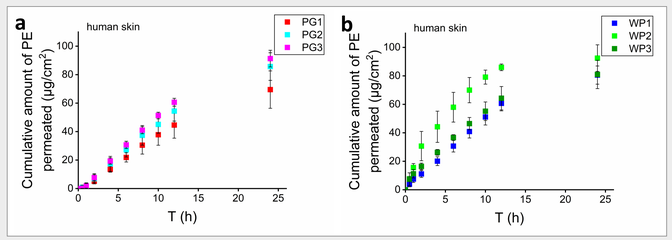

Figure 4. Permeation profiles of PE from various formulations in the skin PAMPA membrane. Data (mean ± SD, n = 6) grouped based on solvents: (a) PG and (b) WP.

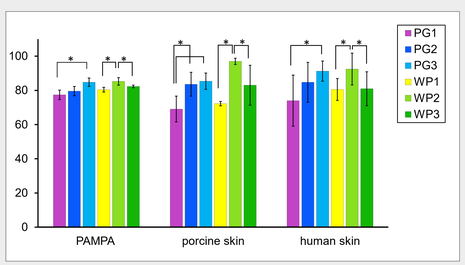

Figure 5. Cumulative amounts of PE that permeated through the membranes (mean ± SD, n = 4-6). *: $p < 0.05$

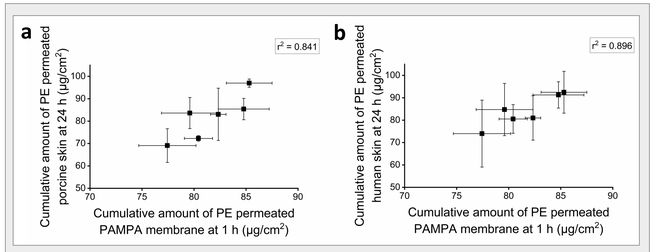

Figure 6. Correlation between cumulative amount of PE that permeated through skin PAMPA and (a) porcine skin and (b) human skin. Mean ± SD (n = 3-6).

CONCLUSION(S)

•This work confirms the potential of the PAMPA model as a predictive tool for skin permeation.

•An excellent correlation between the applied dose and cumulative amount of PE that permeated in the skin PAMPA model was observed (r^2 of 0.99).

•Good correlations between the skin PAMPA model and Franz cell studies using porcine and human skin, respectively, were observed for cumulative amount of PE permeated (r^2 = 0.84, r^2 = 0.89).

FUNDING/GRANT/ENCORE/REFERENCE OR OTHER USE

We thank our colleagues from the UCL Skin Research Group who provided insight and expertise that greatly assisted the research. A.R. is grateful for studentship funding from the Ministry of Finance of The Republic Indonesia (Grant Ref: S-1778/LPDP.4/2019).

References

1. Sinkó B, Garrigues TM, Balogh GT, Nagy ZK, Tsinman O, Avdeef A, et al. Skin-PAMPA: A new method for fast prediction of skin penetration. Eur J Pharm Sci. 2012;45(5):698-707.
2. Zhang Y, Lane ME, Hadgraft J, Heinrich M, Chen T, Lian G, et al. A comparison of the in vitro permeation of niacinamide in mammalian skin and in the Parallel Artificial Membrane Permeation Assay (PAMPA) model. Int J Pharm. 2019;556:142-9.