Permeapad™
A new biomimetic tool for drug permeability studies

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Introduction

Permeability properties of new chemical entities are decisive in drug development. However none of the currently available permeability assays (e.g. Caco-2 cells and PAMPA) are able to match the requirements of R&D in industry in terms of high throughput, robustness and ease of use.

A novel biomimetic permeation barrier "Permeapad™" has been developed and permeability of drugs studied.

Aim

- The aim of this work was to validate Permeapad™ in passive permeability studies using Franz diffusion cells.
- The functional stability of the barrier against pH changes and the presence of excipients, e.g. surfactants has also been investigated [2,3].

Fig. 1, Franz cell diffusion chambers

Conclusion

- Permeapad™ barriers can be used to predict the passive permeability of a range of compounds.
- The Permeapad™ barrier proved to maintain its functionality over time, in different pH environments and in the presence of solvents and surfactants.
- Furthermore comparison with the literature indicated a good correlation between the P_{app} measured with Caco-2 cell and PAMPA assays in relation to Permeapad™.

Permeapad™ is a promising tool for fast, cost effective, and reliable screening of passive permeability of drugs and chemical entities

Results

The apparent permeability coefficients of each drug was measured through Permeapad™. Results showed good correlation to reference values for Caco-2 and PAMPA [2].

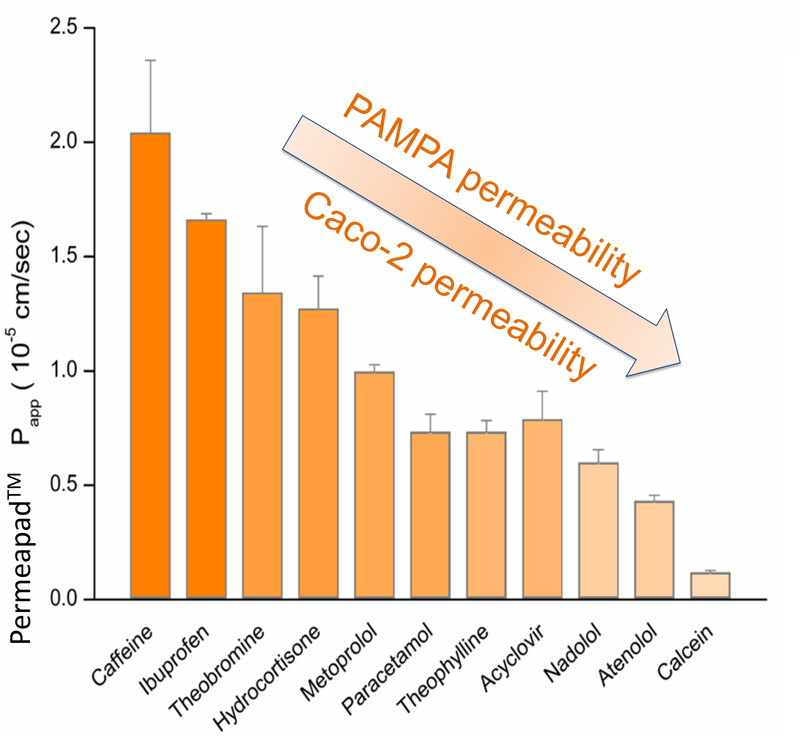


Fig. 2, *Apparent permeability coefficients (P_{app}) measured through Permeapad™ barrier. Results are reported as mean value ± SD (n=3).*

The compatibility of Permeapad™ with solvents and surfactants was tested using calcein, a hydrophilic marker. The results show good compatibility enabling Permeapad™ to be used with formulations. [3]

		Concentration (%)	Permeability (Papp) (10^{-5} cm/s)
	Barrier support	-	**1.65 (0.10)**
	PBS	-	0.12 (0.01)
Surfactants and co-solvents	Triton-X	1	0.12
	Ethanol	4	0.12
	Tween 60	4	0.15
	Tween 80	5	0.06
	Cremophor ®	5	0.12 (0.01)
	SDS	5	0.21
	DMSO	10	0.15

Table 1, *Permeability for calcein in PBS through barrier support and Permeapad™ respectively in the presence of surfactants and solvents in the donor medium; (mean ± std.dev., n=3-6) or as single values.*

The functional stability of the barrier at different pH values was investigated using the pH independent drug Hydrocortisone. Results showed no change in permeability at pH values between 1 and 9 indicating that the integrity of Permeapad™ is still maintained. [2]

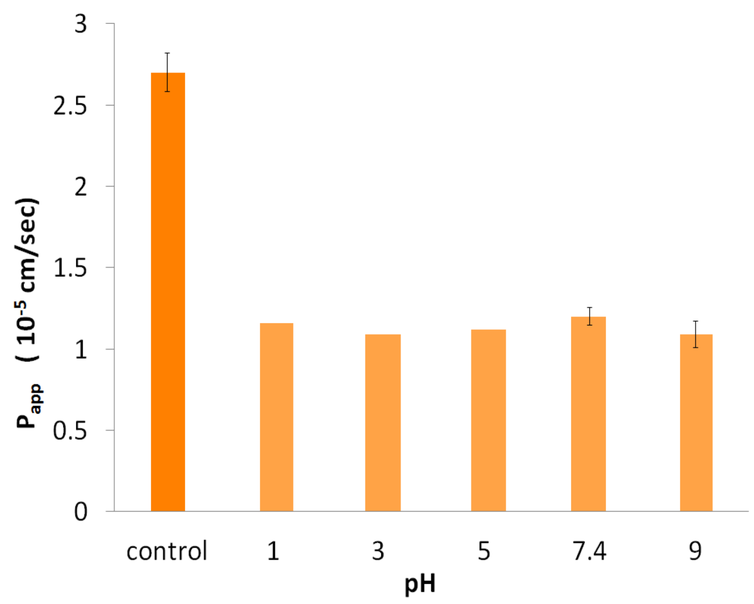
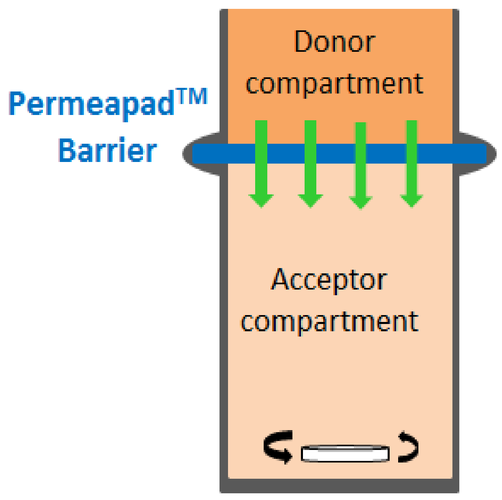


Fig. 3, *Permeability of hydrocortisone (HC) measured employing Permeapad™ barriers at different pH. Control is represented by the permeability of HC measured through support layer. Results are reported as mean ± SD (n=3) or as single values.*

Method

10 different drugs of different permeation properties and log *P* values, and calcein, a hydrophilic marker were tested on Permeapad™. Studies were carried out under sink conditions.

Franz cell diffusion system



Samples were withdrawn every 30 minutes for 5 hours and the flux (J) was calculated:

$$\mathbf{J} = \frac{\mathbf{1}}{\boldsymbol{A}} * \frac{\boldsymbol{dQ}}{\boldsymbol{dt}}$$

The apparent permeability coefficient (P_{app}) was calculated by normalizing the flux (*J*) measured by the concentration of the drug in the donor compartment (C_0):

$$\mathbf{P_{app}} = \frac{\mathbf{J}}{\mathbf{C_0}}$$

References

[1] di Cagno, M., Bauer-Brandl, A., Danish Patent Office, Filed November 2014;
[2] di Cagno, M., Bibi, H.A., Bauer-Brandl, A., 2015. Eur. J. Pharm. Sci. 73, 29-34
[3] Bibi, H.A., di Cagno, M., Holm, R., Bauer-Brandl, A., 2015 Int. J. Pharm. Sci. 493, 192–197

Acknowledgements

SDU Erhverv at University of Southern Denmark