LOGAN INSTRUMENTS CORP.

Application Note

Comparison of Synthetic Membranes to Skin

Introduction

In order to evaluate the response of skin to topical preparations a suitable substrate is required that mimics the behavior of skin in an in vitro environment. Actual samples of human skin can be used but there are several problems associated with this practice.

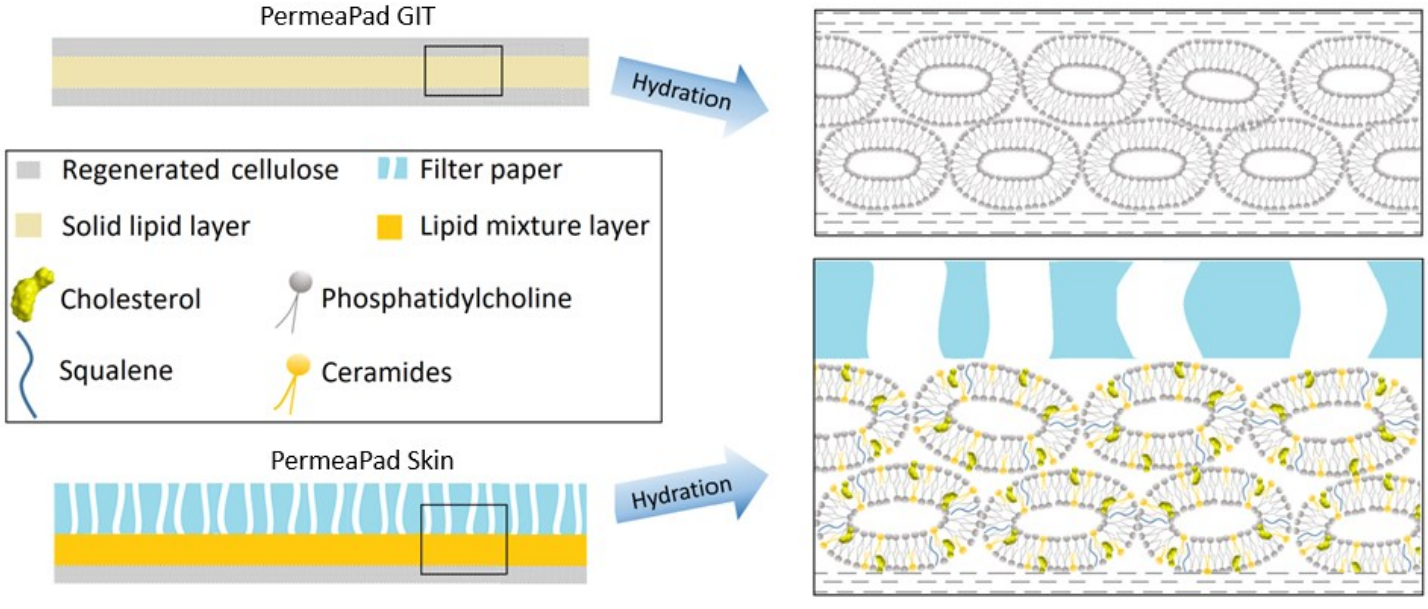
- Human skin exhibits high intra and inter donor variability. This makes comparing results of replicates, and inter-laboratory comparison challenging.
- Human skin is difficult to handle, stored samples require significant care and preparation before testing.
- There are safety issues associated with potential pre-existing infection of samples and contamination during handling. Safety concerns require treatment of the samples that may influence the results of the testing.
- Ethical issues prohibit use of human skin in some countries.
- The cost of procuring samples, skilled handling requirements and prolonged preparation protocols make the use of human samples expensive.

Because of these challenges various synthetic alternatives have been proposed. In this Application Note we describe three experiments comparing the results of in vitro transdermal release testing experiments comparing human skin to biomimetic membranes.

Experiment 1. Comparison of permeation of two topical therapies through: human skin, Strat M and PermeaPad Skin.

Materials

For this study two biomimetic, synthetic membranes were chosen: Strat M®, a synthetic, non-animal membrane (Millipore), PermeaPad™ Skin, a synthetic, skin mimicking, non-animal lipid, sandwiched between 2 layers of regenerated cellulose. [1]



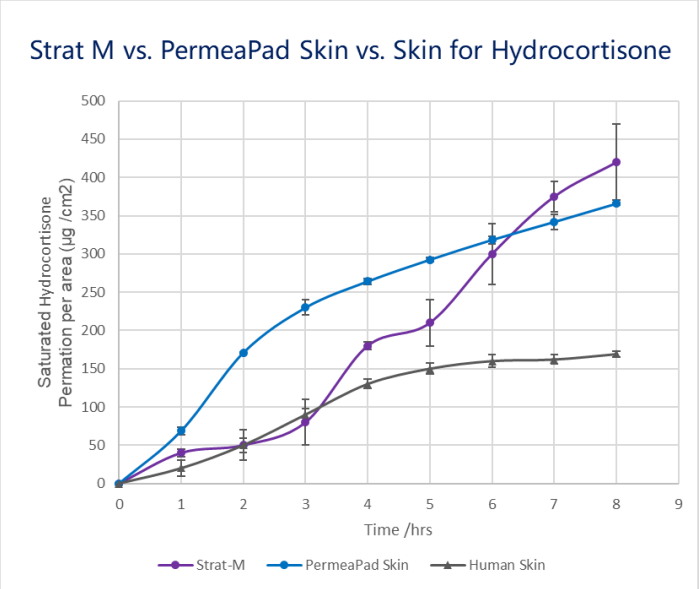
Dermatomed (~500 µm) human cadaver skin samples from posterior leg of three different donors, (2 males at the age of 16, 53 and one female at the age of 57) which were obtained from The New York Firefighters Skin Bank (New York, NY, USA), were cut into appropriate size, slowly thawed and then soaked in filtered PBS (pH 7.4) for 30 min.

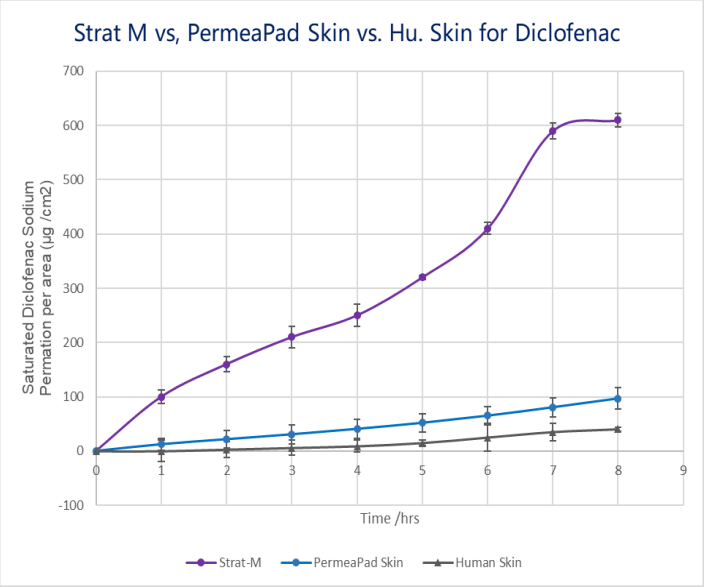
The test compounds were Diclofenac sodium, a commonly available topical treatment for arthritis. An excess amount of diclofenac sodium salt powder (Sigma Aldrich, USA) was dissolved in 1 mL of propylene glycol (PG) (BASF, USA) and sonicated at 37 °C for 6 hours to obtain a saturated solution.

The second test compound was Hydrocortisone. 20 mg of USP grade hydrocortisone powder (Sigma Aldrich, USA) was dissolved in 1 mL PG and sonicated at 37 °C for 6 h to obtain a saturated solution.

Permeation assay

- The permeation test was conducted using static vertical glass Franz diffusion cells with a donor area of 0.64 cm^2 and a receptor volume of 9.0 mL (Logan Instruments, System 913-24).
- All formulations were tested in 6 replicates.
- The receptor compartment of each cell was filled with filtered PBS (pH 7.4) and maintained at 37°C, , the surface of the skin was left un-occluded at ambient room temperature.
- The receptor chamber was stirred continuously using a magnetic stirrer.
- Prior to applying the formulations, the diffusion cells were allowed to equilibrate for 30 min.
- PermeaPad Skin membrane was used immediately with no pretreatment.
- 1.5 mL of receptor solution was collected hourly for 8 h. Receptor cells were refreshed with PBS media.
- All receptor samples were analyzed using validated HPLC methods.





PermeaPad Skin represents the closest comparison to human skin.

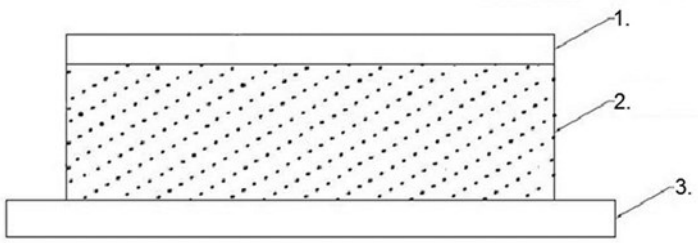
Experiment 2. Comparison of 7-day permeation of contraceptive patches tested through Human Skin, PermeaPad Skin and PermeaPad GIT.

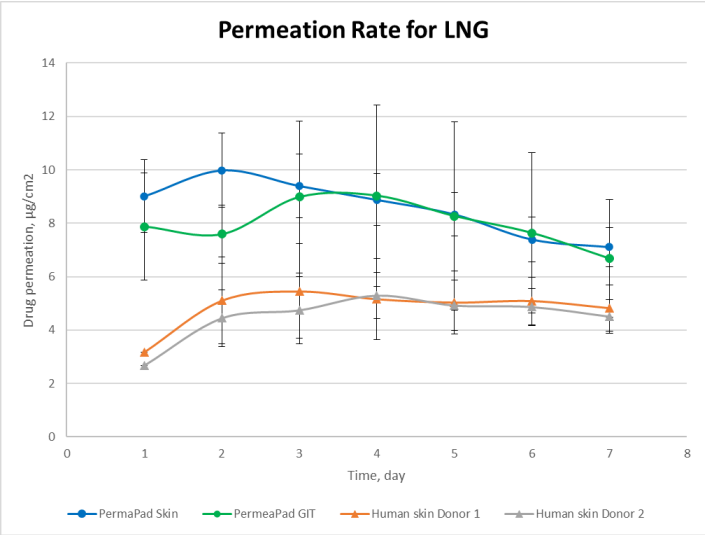
For this study permeation of matrix transdermal patches of Levonorgestrel (LNG) and Ethinyl Estradiol (EE) were tested against:: human skin, PermeaPad Skin and PermeaPad GIT. [2]

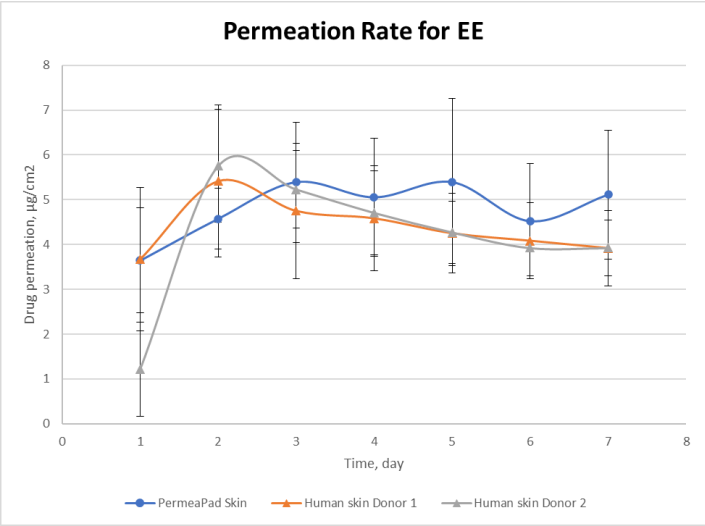
Materials

Drug-in–adhesive monolith.

1. Impermeable backing
2. Drug-Adhesive matrix.
3. Release Liner.







PermeaPad Skin represents the closest comparison to human skin and the least variability.

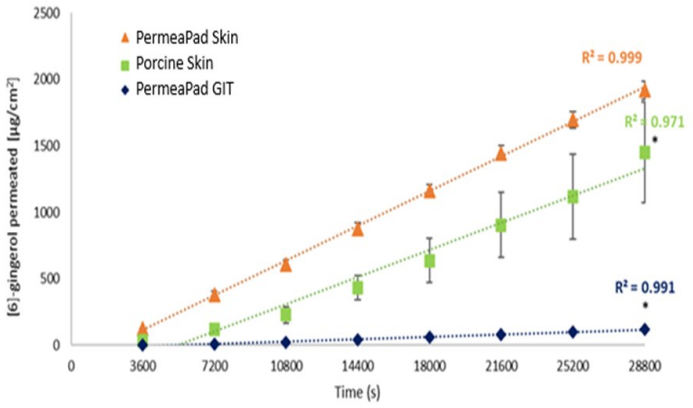
- PermeaPad Skin has the least variation compared to other test materials (Human skin > PermeaPad GIT >PermeaPad Skin for LNG
- The permeability of PermeaPad Skin was closer to that of human skin (PermeaPad GIT > PermeaPad Skin > Human skin)
- There was no permeation observed using PermeaPad GIT for EE
- Using PermeaPad Skin the permeation profile was very close to human skin.

Results demonstrated that the resistance measured with the intact human skin and the PermeaPad Skin are in the same order of magnitude, ranging from 0.9 x 105 ± 0.60 x 105 s/cm to 1.04 x 105 ± 0.10 x 105 s/cm.

Experiment 3. Comparison of permeability of ginger extract for PermeaPad Skin, Porcine skin and PermeaPad GIT

Permeation studies of [6] gingerol from ginger lipophilic extract were conducted using vertical Franz diffusion cells. Full thickness porcine skin was used with the stratum corneum facing the donor chamber, PermeaPad Skin and PermeaPad GIT were used following the manufacturer's directions.

Permeation of [6]-gingerol through PermeaPad Skin was comparable to that observed in porcine skin samples. Permeation observed with permeation of [6]-gingerol with PermeaPad GIT was not comparable to porcine skin.



Conclusions

In vitro permeation studies show that:

- **PermeaPad Skin more closely resembles human skin than Strat M.**
- PermeaPad Skin, a biomimetic barrier membrane, has **less variation, and closer permeability to human skin.**
- PermeaPad Skin is a **better substitute for human skin** than PermeaPad GIT.
- Permeation studies of [6] gingerol indicate PermeaPad Skin will give **results comparable to porcine skin.**

References

1. Haq, A.; Goodyear, B.; Ameen, D.; Joshi, V.; Michniak-Kohn, B. Strat-M® synthetic membrane: Permeability comparison to human cadaver skin. Int. J. Pharm. 2018, 547, 432–437
2. Pressure-sensitive adhesives for transdermal drug delivery systems. Tan H, Pfister W.R. Pharm Science Technology Today 2: 60-69
3. Magnano, G.C.; Sut, S.; Dall'Acqua, S.; Di Cagno, M.P.; Lee, L.; Lee, M.; Filon, F.L.; Perissutti, B.; Hasa, D.; Voinovich, D. Validation and testing of a new artificial biomimetic barrier for estimation of transdermal drug absorption. Int. J. Pharm. 2022, 628, 122266.

Logan Instruments System 913-24

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