

Thiocolchicoside Concentration in the Stratum Corneum after Application of a Dermal Patch

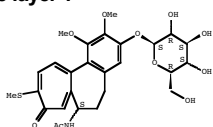


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Introduction

Thiocolchicoside is a muscle-relaxant agent administered by the oral, intra-muscular and topical routes. The physico-chemical properties of thiocolchicoside are not favourable for its permeation across the skin.

The Patch-non-Patch® platform is a bioadhesive film in which the constituents of (trans)dermal patches have been condensed in one layer¹.



m.w. 563
logP -0.35

Aim of the work

The aim of this work was to determine the distribution of thiocolchicoside in the stratum corneum to evaluate the feasibility of Patch-non-Patch® containing thiocolchicoside.

Objectives

To compare the stratum corneum accumulation obtained with the Patch-non-Patch® with that from commercial formulations.

Experimental Methods

Tape Stripping:

- 5 healthy volunteers (25-30 y old).
- Application time: 2 h.
- Amount applied:
 - Muscoril cream and ointment (0.5 % w/w): 28 mg/cm²
 - Patch-non-Patch® (11% w/w): 650 µg/cm²
- Thiocolchicoside extraction from tape strips with mobile phase.

Thiocolchicoside HPLC analysis:

- C8 column (Nova-Pak®, Waters, USA).
- UV detection @ 370 nm.
- Mobile phase: acetonitrile: water (15:85) @ 1 ml/min.

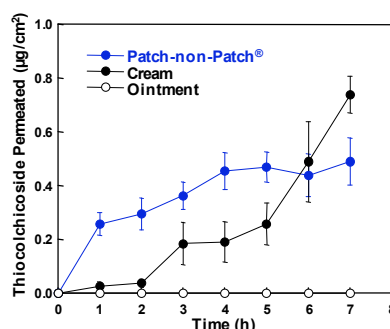
Results & Discussion

Patch-non-Patch® Characteristics

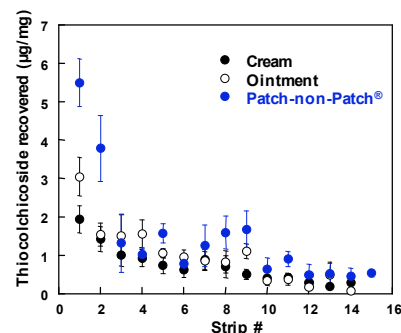


- Not self-adhesive
- Adhesive only on wet skin
- Flexible, transparent
- Water permeable
- Electrically conductive

Permeation across Rabbit Ear Skin in Vitro



Tape Stripping in Vivo



Discussion

Permeation across the skin

- Patch-non-Patch® and cream gave rise to measurable amounts permeated, whereas ointment was not effective. The diffusive parameter (D/L^2) from cream resulted $0.055 \pm 0.021 \text{ h}^{-1}$.

Stratum Corneum Concentration

- The two commercial formulations gave similar profiles, while the new dermal patch produced a higher accumulation in the more external layers of the stratum corneum.
- The partition coefficient was significantly higher for cream and ointment compared to the patch ($p < 0.01$), while the diffusive parameter did not change.

Conclusions

- Thiocolchicoside permeation and accumulation was improved using the new dermal patch.
- The Patch-non-Patch® platform can be useful for the topical administration of thiocolchicoside.

Acknowledgements

Sanofi-Synthelabo is acknowledged for providing thiocolchicoside.

Parameters

Stratum corneum profiles fitted according to Eq.²

$$C_x = KC_v \left(1 - \frac{x}{L} - \frac{2}{\pi} \sum_{n=1}^{n-6} \frac{1}{n} \sin \left(n\pi \frac{x}{L} \right) \exp \left(-\frac{D}{L^2} n^2 \pi^2 t \right) \right)$$

	K	$D/L^2 (\text{h}^{-1})$
PnP	0.071 ± 0.010	0.026 ± 0.013
Cream	0.457 ± 0.078	0.045 ± 0.010
Ointment	0.666 ± 0.109	0.048 ± 0.012

References

1. C. Padula, G. Colombo, S. Nicoli, P.L. Catellani, G. Massimo, P. Santi, Bioadhesive film for the transdermal delivery of lidocaine: in vitro and in vivo behavior, J. Control. Release, 88 (2), 277-285, 2003.
2. C. Curdy, Y.N. Kalia, A. Naik, R.H. Guy, Piroxicam delivery into human stratum corneum in vivo: iontophoresis versus passive diffusion, J. Control. Release, 76, 73-79, 2001.