Thyroxine Skin Accumulation from Bioadhesive Film

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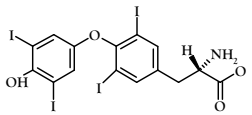
Introduction

Levothyroxine (T4) is the main product of thyroid secretion employed topically for cosmetics purposes, to reduce deposits of subcutaneous adipose tissue.



MW: 776.86 LogP: 4.1

Patch-non-Patch® (PnP) (1) is an innovative dermal/transdermal drug delivery system recently developed in our laboratory. It is a monolayer film, water based and adhesive only when applied on wet skin.

Aim of the work

The aim of this study was to **formulate** T4 in the Patch-non-Patch® film, to evaluate its **skin retention** and penetration and to verify if **occlusion** can affect T4 permeability. Somatoline®, a commercial formulation containing T4 for topical application, was used as reference. Rabbit ear skin was used as barrier since it was been shown to be a reasonable model for human skin (2).

Methodology

In vitro diffusion experiments

- Franz type diffusion cells (0.63 cm^2)
- Rabbit ear skin as barrier
- PBS pH 7.4 as receptor phase
- Room temperature

	%
Isopropyl mirystate	36.3
Tween 80	20.5
Span 20	20.5
Water	18.2
Isobuthanol	4.5

Films composition

	PnP	PnP2	PnP ME	PnP ME2
PVA[a]	62.00	62.00	55.94	55.94
PVP[b]	27.00	27.00	24.36	24.36
Sorbitol[c]	4.00	4.00	3.61	3.61
Water	6.90	6.25	6.32	6.00
T_4	0.10	0.75	0.75	1.00
Microemulsion	-	-	9.02	9.02
T4 content in the dried products				
µg/cm^2	19±1	181±23	169±8	226±11
% w/w	0.2	2.3±0.3	1.72±0.1	2.4±0.1

[a] 20 % w/w water solution
[b] 21 % w/w in water:PEG400 (85:15 % w/w) solution
[c] 70 % w/w water solution

T4 skin extraction

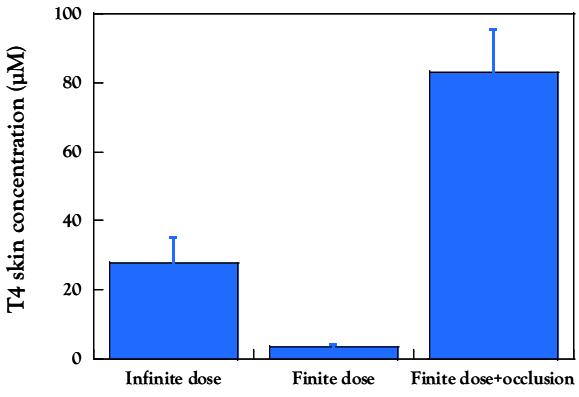
- 100 µl methanolic sodium hydroxide
- 900 µl HPLC mobile phase
- 40°C for 30 min

HPLC analysis

Column: Spherisorb® Cyano (Waters, 2.1x250 mm)
Mobile phase: H_2O: CH_3CN:H_3PO_4 (70:30:0.1, v/v/v)
Flow rate: 0.3 ml/min
UV detection: 225 nm

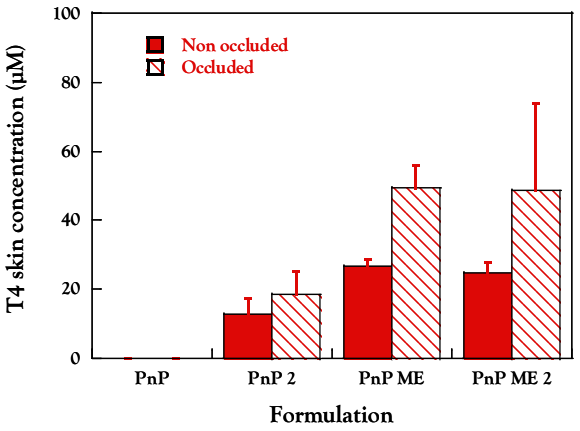
Results

Commercial formulation



The increased skin accumulation produced by infinite dose application (0.8 ml/cm^2) is probably due to the partially occlusive effect of applying a formulation as a thick layer.
Skin retention of T4 was significantly improved by occlusion, although no skin permeation was observed.

Patch-non-Pacth®



The film with a drug loading of 0.2% (w/w) did not produced any T4 accumulation in the skin. Increasing drug loading or introducing microemulsion in the film, produced modest increasing in skin retention.
All formulations tested in occlusive conditions gave superior results compared to the respective formulation in non occlusive condition.

Conclusions

TX was released from the polymeric film and was able to accumulate in the skin. Owing to the lipophilic nature of the drug, the presence of an occlusive backing increased T4 skin retention although in a non statistically significant way. The amount accumulated from films without microemulsion was comparable with that obtained from the commercial formulation. Introducing the microemulsion in the PnP formulation, the extent of accumulation was higher even if the increase is more evident in the presence of occlusion.

References

1. C. Padula, G. Colombo, S. Nicoli, P. L. Catellani, G. Massimo and P. Santi. Bioadhesive film for the transdermal delivery of lidocaine: in vitro and in vivo behavior. *J. Control. Release* **88**: 277-285 (2003).
2. S. Nicoli, M. Cappellazzi, P. Colombo and P. Santi. Characterization of the permselective properties of rabbit skin during transdermal iontophoresis. *J. Pharm. Sci.* **92**: 1482-1488 (2003).