Transdermal Delivery of Progesterone from Isopropyl Myristate-based Microemulsions

Vincenzo Aversa, Paolo Colombo, Gina Massimo, Patrizia Santi

Department of Pharmacy, Parco Area delle Scienze 27/A, 43100 Parma, Italy

Aim of the Work

The aim of this work was to investigate in vitro the transdermal permeation of progesterone from an isopropyl myristate (IPM) based water in oil microemulsion (ME) and from the Patch-non-Patch® film (PnP), in which the microemulsion was included. The Patch-non-Patch® system is a single layer film – bioadhesive only in the presence of water – thin, transparent and mechanically resistant (1). Permeation profiles obtained were compared with those shown by a commercial formulation of progesterone, Crinone® 8 (Industria Farmaceutica Serono, Italy)

Methodology

Permeation Experiments

Franz type difusion cells (0.63 cm^2)

Barrier: Rabbit ear skin

Receptor: 4 ml of saline solution containing 0.4% of HP-β-CD

HPLC Analysis of Progesterone

Column Nova-pak™ C18 (Waters)

Mobile phase: CH_3CN:H_2O (62:38 v/v)

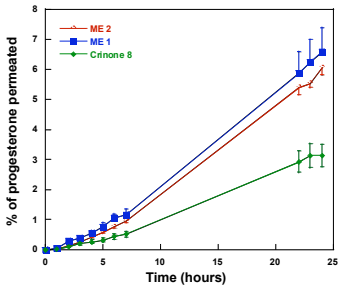
Flow rate: 1ml/min

Uv detection: 241 nm

Results and Discussion

Table 1. Composition (% w/w) of the MEs

Component	ME	ME 1	ME 2
IPM	36.30	36.25	35.20
Isobutanol	4.50	4.50	4.35
Tween® 80	20.50	20.47	19.90
Span® 20	20.50	20.47	19.90
Water	18.20	18.18	17.65
Progesterone	-	0.13	3.00



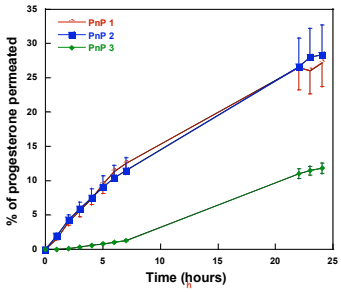


Table 2. Drug loading of the formulations tested and relative degree of supersaturation (DS)

Formulation	Drug Loading (% w/w)	DS
ME 1	0.13	-
ME 2	3.00	-
Crinone® 8	8.00	-
PnP 1 *	1.75	2
PnP 2 *	3.00	5
PnP 3 *	4.50	10

* The total amount of progesterone added in the preparation of the films exceeded the solubility of the drug in the ME, leading to supersatured systems.

The percentage of progesterone permeated from the microemulsion is about twice the percentage permeated from Crinone® 8, probably because of the presence of IPM, the main component of ME, which acts as penetration enhancer.

The highest permeation profiles were obtained with the bioadhesive films, which were supersatured systems and showed an higher thermodynamic activity. When the DS is very high, as in the case of PnP 3, the percentage of drug delivered is lower, because of the low stability of the system, which tends to crystallize. Crystals of progesterone were present in all the films realized; the greater the DS, the higher was the extent of crystallization.

Conclusions

The water in oil microemulsion prepared was able to increase in vitro the transdermal flux of progesterone. The microemulsion can be included in a transdermal therapeutic system, such as the bioadhesive film proposed.

However, the films showed to be metastable systems, which underwent crystallization of the drug.

References

1. Bioadhesive film for the transdermal delivery of lidocaine: in vitro and in vivo behavior, C. Padula, G. Colombo, S. Nicoli, P.L. Catellani, G. Massimo, P. Santi, J. Control. Release, 88 (2), 277-285, 2003

Acknowledgments

Lisapharma S.p.A. (Como, Italy) is gratefully acknowledged for supporting this work