

Bioadhesive film for the transdermal delivery of progesterone



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Introduction

The aim of this work was to investigate *in vitro* the transdermal permeation of progesterone from a new bioadhesive film, called Patch-non-Patch®(1).

Since progesterone is poorly water soluble, it has been introduced in the films in the form of two inclusion systems: a saturated water solution containing 0.4% of hydroxypropyl- β -cyclodextrin (HP- β -CD) and an isopropyl myristate-based microemulsion. Therefore, two types of film were realized, according to the system employed: they are coded respectively PnP-CD and PnP-ME. The results obtained were compared with those shown by a commercial formulation of the drug (Crinone® 8, Industria Farmaceutica Sirono, Roma, I).

Experimental Methods

Permeation experiments:

Franz type diffusion cells (0.63 cm²)
Rabbit ear skin as barrier
4 ml of saline solution containing
0.4% of HP- β -CD as receptor.

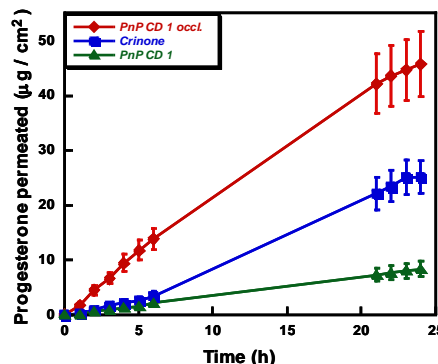
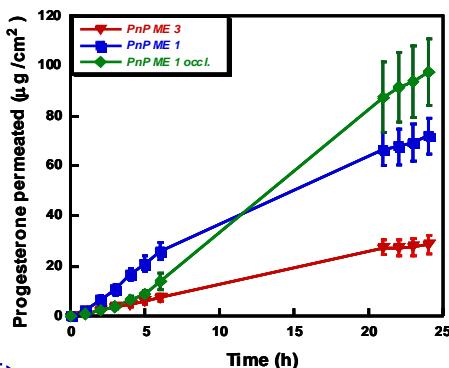
HPLC Analysis of Progesterone:

Column Novapak™ C18 (Waters, Milford, USA)
Mobile phase: acetonitrile and water (62:38 v/v)
Flow rate: 1ml/min
Uv detection: 241 nm

Results

Composition of the films realized and relative amount of progesterone delivered *in vitro* across the skin.

Formulation	Drug Loading (% w/w)	Progesterone permeated at 24 h ($\mu\text{g}/\text{cm}^2$)	
		Not occluded	Occluded
PnP CD 1	2	8	45
PnP CD 2	3	8.5	-
PnP CD 3	10	12	52
PnP ME 1	3	72	98
PnP ME 2	4.5	28	-
PnP ME 3	10	29	120
Crinone®	8	25	-



Optical microscopy examination of the films showed the presence of crystals of progesterone in all films prepared. The greater the drug loading the higher was the extent of crystallization.

Crystals of progesterone inside the film PnP ME 1

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, I) is gratefully acknowledged for supporting this work.

Conclusions

- the bioadhesive film proposed is a promising therapeutic system for transdermal delivery of progesterone, able to compete with the commercial formulation of the drug;
- the inclusion of a microemulsion containing progesterone is able to produce better performances than the use of cyclodextrins. The use of occlusive conditions further improved the performance of the system;
- drug crystallization in the films produced a reduction of progesterone permeation but might be avoided with the use of an inhibitor.