Progesterone permeation from a new transdermal therapeutic system

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Purpose of the Work

The purpose of this work was to evaluate in vitro the transdermal delivery of progesterone from a new bioadhesive film called Patch-non-Patch® (PnP), in comparison with Crinone 8® (Industria Farmaceutica Serono, Italy), a commercial formulation of the drug.

PnP is a single layer film – bioadhesive only in the presence of water – thin transparent and mechanically resistant (1). PnP films were prepared by mixing a film-forming polymer (aqueous solution of PVA), an adhesive (aqueous solution of PVP K90 and PEG 400) and a w/o isopropyl myristate-based microemulsion in which progesterone was solubilized. The mixture was then spread on siliconized paper and oven-dried at 80 °C for 30 minutes.

Methodology

Permeation Experiments

Franz type diffusion cells (0.63 cm^2)

Barrier: Rabbit ear skin

Receptor: 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. Drug loading of the formulations tested and relative amount of progesterone delivered after 24 hours

Formulation	Drug Applied (mg/cm^2)	Progesterone permeated after 24 h (µg/cm^2)
Crinone® 8	0.8	25.10 ± 2.94
PnP 1	0.12	23.96 ± 2.63
PnP 2	0.12	49.43 ± 6.43

Table 2. Composition of the films PnP1 and PnP 2 (% w/won dry basis)

Composition	PnP1	PnP2
PVA	42	15
Adhesive	30	40
Microemulsion	26	43,5
Progesterone*	2	1,5

*The total amount of progesterone added in the preparation of the film PnP1 exceeded the solubility of the drug in the ME, leading to a supersatured system. Optical microscopy examination in the presence of polarized light showed the presence of several crystals of progesterone in PnP1 (figure 2), while few crystals were observed in PnP 2 (figure 3).

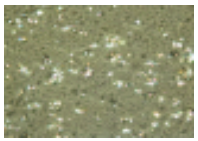

Figure 2. PnP1

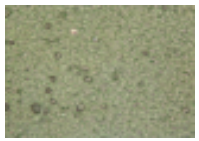

Figure 3. PnP2

Crystals of progesterone observed in the films by optical microscopy in the presence of polarized light

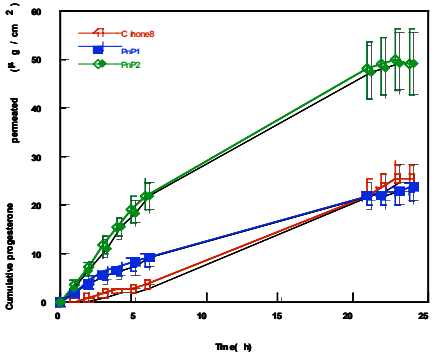

Figure 1. Permeation profiles of progesterone from the films and from the commercial gel

The amounts of progesterone delivered from PnP 1 and from Crinone® 8 were comparable after 24 hours, while PnP 2 showed a higher permeation profile. This behaviour probably depends on two factors:

1. The higher content of microemulsion in PnP 2, because isopropyl myristate – the main component of microemulsion – is known to be a permeation enhancer (2).
2. The absence of crystals in PnP 2, because precipitation of progesterone determines a reduction in the permeation of the drug across the skin.

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.

2. Effectiveness and mode of action of isopropyl myristate as a permeation enhancer for naproxen through shed snake skin, H. Suh, H.W. Jun, J. Pharm. Pharmacol., 48 (8), 812-816, 1996.

Conclusions

The bioadhesive films proposed are promising therapeutic systems for the transdermal delivery of progesterone, able to compete with a marketed product. The presence of a microemulsion is a critical parameter of the formulation of the film, both for the stabilization of the drug and for the amount of progesterone delivered in vitro across the skin.

Acknowledgments

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