Cristallization of Mometasone Furoate: influence of polymers on *in vitro* permeation studies

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Introduction

Atopic dermatitis is a chronic (long-lasting) disease that affects the skin. In atopic dermatitis, the skin becomes extremely itchy and inflamed, causing redness, swelling, cracking, weeping, crusting, and scaling.

Mometasone furoate, a synthetic 16 alpha-methyl analogue of beclomethasone, is classified as a class 3 glucocorticoid for dermatological use. It is an anti-inflammatory and anti-pruritic corticosteroid, witch is a very useful molecule in the atopic dermatitis treatment.

Many topical formulations have poor bioavailability with only a few percent of the applied dose reaching the target site.

Significant improvements can be made by optimizing the thermodynamic activity of the drug in the formulation.

Aim

The present study was conducted in order to correlate the permeation of mometasone furoate (MF) from two different gels through silicone membranes.

Conclusion

These results suggest that the corticosteroid is polymer dependent concerning the crystallization of mometasone furoate.

Nevertheless, these preliminary results may find other expression during stability tests, which is currently being investigated.

References

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Matherial and Methods

Gels Processing:

Two gels of 0,1% mometasone furoate were prepared, differing on the cellulose polymer used: Hydroxypropyl methylcellulose (HPMC) and Hydroxypropyl cellulose (HPC). Formulations were prepared with cellulose polymer 1,5% in water, isopropylic alcohol and propylenoglycol USP (40:40:20).

Physicochemical properties

Rheology: A Brookfielfd viscometer (Model DV II, SSA, SPD nº 21 at 25 ºC) was used to determine the apparent viscosity and rheograms;

Assay: The analysis was performed by HPLC (Merck-Hitachi, set at a flow rate of 1.5 ml/min; a Merck Diod Array UV detector set at 248 nm). The column was a Inertsil C8 – 5mm – 4.6x150mm (GL Sciences). The mobile phase was methanol:water (70:30, v/v).

***In vitro* studies:**

In vitro permeation profile was determined using vertical Franz diffusion cell apparatus (Fig. 1) through silicone membranes with a diffusion area of 1cm^2, with a receptor phase of water/ethanol (1:1). The amount applied was 200 mg of either formulations. At pre-determined time, several samples of 0,2 ml were collected and the same volume replaced with fresh solution. Repeated measures design using six replicated cells for each formulation was used. The concentration of mometasone furoate in the receptor phase was analysed by HPLC using an UV detector (λ=248nm). Data was expressed in cumulative amount of mometasone furoate permeated per cm^2 in order to time.

Figure 1 - Support with Franz diffusion cells (n=6) in a heat water bath (32ºC)

Results and Discussion

Rheology

The results of rheological data are shown on figure 2 and 3.

Both formulations presented a pseudoplastic behaviour, indicating good applicability onto skin and HPC gel showed higher apparent viscosity.

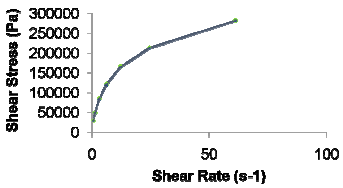

Figure 2: Rheogram of HPC gel

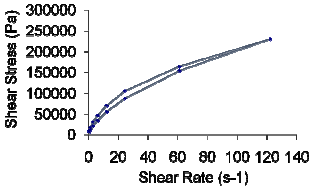

Figure 3: Rheogram of HPMC gel

***In vitro* studies**

Five days after gel preparation, the amount of MF released was similar in both gels. (Fig.4) The analysis of variance (ANOVA) showed that no significant differences were found among the two formulations (p>0,05 and $F_{exp} < F_{crit}$).

Assay

Concerning the assay after 15 days, the results obtained were significantly different for both gels (HPMC gel- 103% and HPC gel - 90%).

These results can be explain because cristals were observed, macroscopically, 2 weeks after the preparation in HPC gel but no crystals appeared in the presence of HPMC.

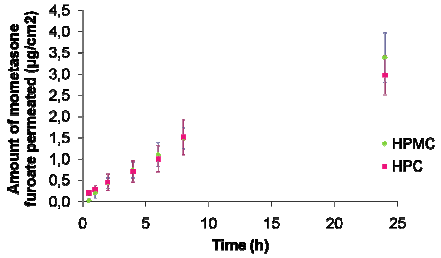

Figure 4: Amount of mometasone furoate permeated (n=6)