Alternating the sequence of application of Elocon cream with emollients: The impact on drug delivery to the skin

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Background

Topical corticosteroids (TCSs) and emollients are frequently prescribed as a first line treatment package for inflammatory skin conditions; however, current guidance for the application of both TCSs and emollients lacks consensus and an evidence base.

The clinical need to address the uncertainties surrounding the effects of applying these two products on clinical efficacy has been highlighted as a key research priority by both patients and clinicians[1].

When developing TCS formulations, the choice of excipients are carefully considered as they have the potential to alter drug delivery across the skin. However, in clinical practice it is common for the TCS formulation and emollient preparations to be applied at similar times, potentially altering the TCS formulation on the surface of the skin and affecting drug absorption.

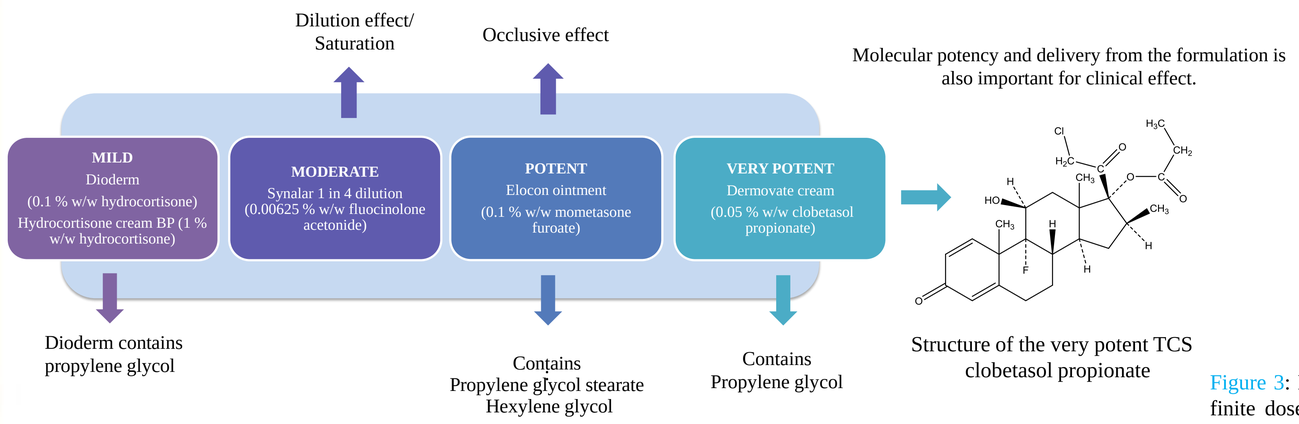

Figure 1: The UK topical corticosteroid potency groups and formulation factors which may influence drug absorption to the skin.

Aim

The aim of the present study was to determine the effect of altering the sequence of application of the potent TCS Elocon cream (mometasone furoate, 0.1 % w/w) and 3 emollients on mometasone furoate absorption across human skin. The selected emollients were Diprobase cream, Diprobase ointment and Hydromol Intensive.

Methodology

- Franz cells (Soham Scientific, UK) were employed to conduct *in vitro* drug absorption studies across human skin.
- A finite dosing model was employed and donor chambers were dosed with products according to the application regimens detailed in Figure 2.

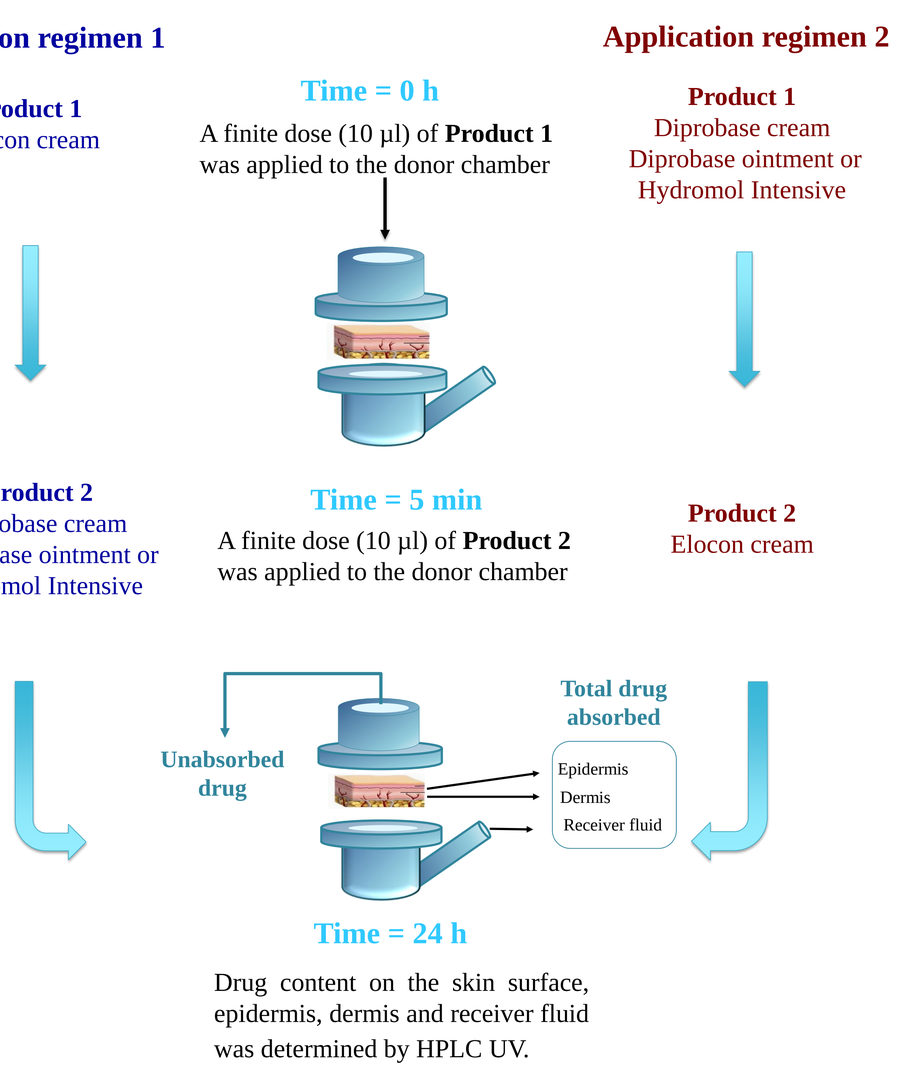

Figure 2: Methodology for the *in vitro* finite dose, drug absorption, experiments conducted using Franz cells. Replicate cells (n = 6) were used for each application regimen.

Reference

1.Batchelor JM, Ridd MJ, Clarke T, Ahmed A, Cox M, Crowe S *et al.* The Eczema Priority Setting Partnership: a collaboration between patients, carers, clinicians and researchers to identify and prioritize important research questions for the treatment of eczema. *Br J Dermatol*. 2013;**168**(3):577-582.

Results and Discussion

Alternating the sequence of application of Elocon cream with the 3 selected emollients altered the extent of drug delivery to the epidermal and dermal layers of human skin and the receiver fluid, to varying extents (Figure 3).

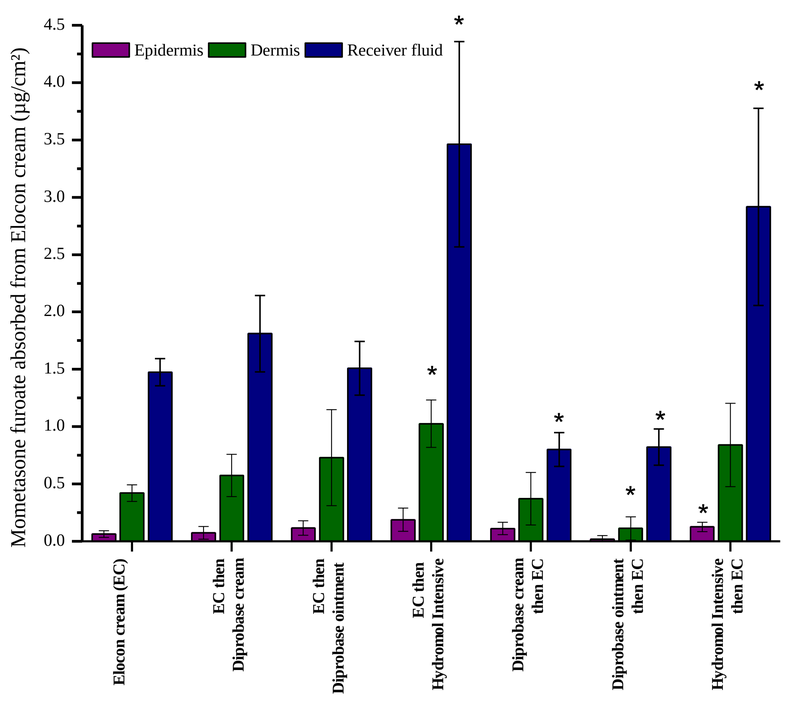

Figure 3: Mometasone furoate content (µg/ cm²) in the epidermis, dermis and receiver fluid following the application of a finite dose of Elocon cream (EC) alone and EC applied 5 minutes before, or after, either Diprobase cream, Diprobase ointment or Hydromol Intensive. Data shown as mean ± SD (n=6). * Denotes a significant difference when compared to Elocon cream alone.

The application of Elocon cream before Diprobase cream or Diprobase ointment appeared to increase the total amount of drug delivered to the skin (epidermis, dermis and receiver fluid) by up to 1.3 fold, when compared to the application of Elocon cream alone (Figure 4).

Conversely, the application of these two emollients prior to the TCS significantly decreased total drug delivery to the skin up to 2 fold, when compared to Elocon cream alone ($p < 0.05$). The magnitude of this alteration was greatest in the case of Diprobase ointment, where a significant 2.5 fold increase in total drug delivery was observed when Elocon cream was applied prior to the emollient compared to the reverse application regime of Diprobase ointment applied prior to the TCS.

In the presence of Hydromol Intensive however, total drug delivery to the skin was significantly increased up to 2.4 fold irrespective of the sequence of application, when compared to the application of Elocon cream alone ($p < 0.05$).

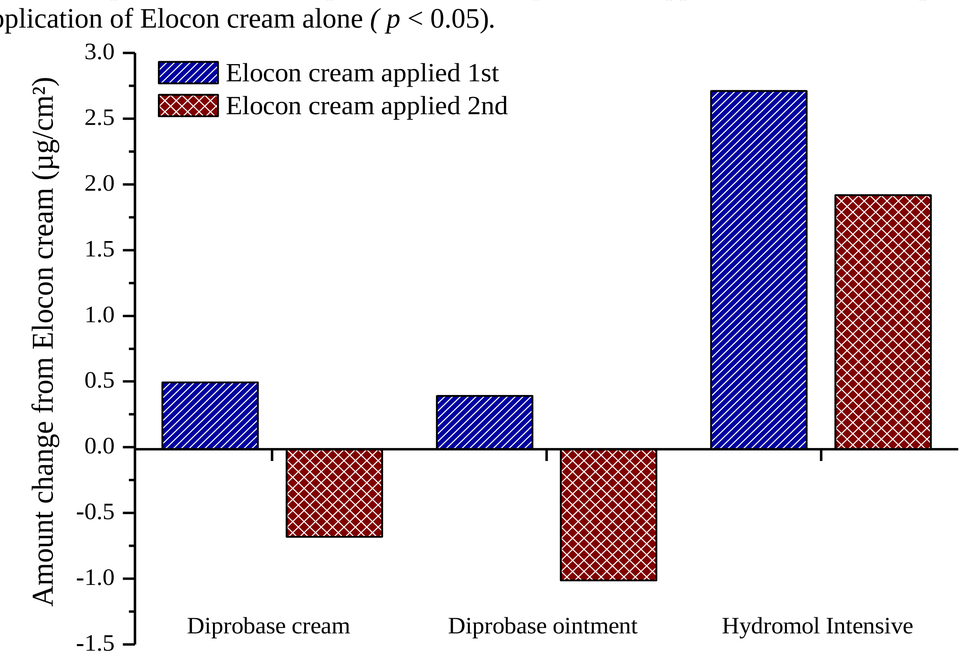

Figure 4: Comparison of the amount change in total drug absorbed (total of epidermis, dermis and receiver fluid; µg/ cm²) from Elocon cream alone (1.96 µg/ cm² ± 0.17 SD) when Elocon cream was applied 5 minutes before or after either Diprobase cream, Diprobase ointment or Hydromol Intensive.

Conclusion

These initial *in vitro* findings suggest that altering the sequence of application of Elocon cream and particular emollients has the potential to alter drug absorption to the skin. The extent of this change appears to be emollient specific; in some cases, applying the emollient prior to the Elocon cream lowers drug absorption to the skin. Such findings suggest that allowing several minutes to elapse before applying a TCS, as recommended by current NICE guidance, may not be sufficient to mitigate against changes in drug absorption. Furthermore, the application of particular emollients such as Hydromol Intensive with a TCS, irrespective of the application regimens, has the potential to impact on the extent of drug absorption and side effect profiles.

Future Work

Further *in vivo* studies are required to determine the clinical impact of these findings.

Acknowledgments

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