Impact of vehicle on clobetasol propionate skin permeation and drug distribution in vitro

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Introduction

Topical glucocorticosteroids are among some of the most frequently used medications in dermatological practice. Over the years, research has focused on strategies to optimize potency and, in particular, the anti-inflammatory and immunosuppressive capacity of these drugs, while also minimizing adverse effects. Commonly the delivery vehicle is modified to achieve these purposes. Clobetasol propionate, a fifth generation corticosteroid, is a typical example of a potent molecule for dermatoses [1], which is available in various formulations and delivery vehicles (such as foam, lotion, cream, ointment, spray, and shampoo) that have been employed in clinical practice.

Objective

To compare the impact of vehicles on clobetasol propionate skin permeation and distribution profile in vitro

Methods

Diffusion setup

In vitro permeation through human split-thickness skin (~0.25mm) was measured using flow-through diffusion cells. Skin from each donor was cut into multiple smaller sections, large enough to fit on the diffusion cells (Permegear, Bethlehem, PA) [2]. To assure the integrity of each skin section, its permeability to tritiated water was determined before application of the test products [3]

Dosing and Sampling

All formulations were radiolabeled and applied to the skin sections using a positive displacement pipette set to deliver a target dose of 5 µL/0.64 cm^2, and then spread over the entire surface with the Teflon tip of the pipette. Topical steroid formulations were applied on three or four replicate sections from each of three human skin donors. Receptor fluid was collected at 4 hour intervals for 24 hours. At 24 hours after dosing, following the last receptor solution sample collection, the skin surface was washed, wiped and tape-stripped twice consecutively. The epidermis was then carefully peeled off the dermis. The drug was extracted from the surface washing materials, epidermis and dermis using acetonitrile. Quantification of drug content was performed by liquid scintillation .

Cumulative Amount in the Receptor

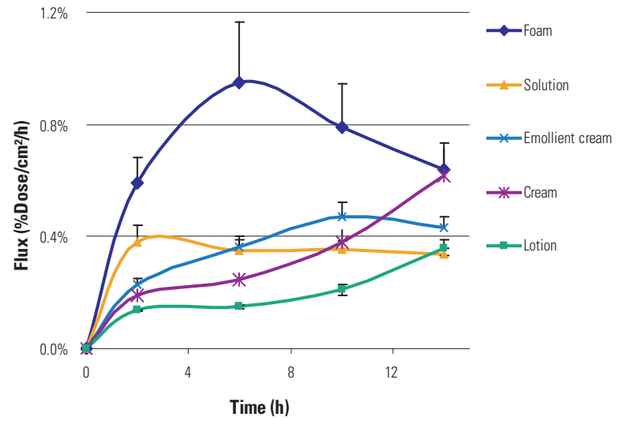

Figure 1: Cumulative amount of clobetasol propionate (CP) after topical application of CP in 5 different vehicles.

Amount in Skin Layers at 24 h

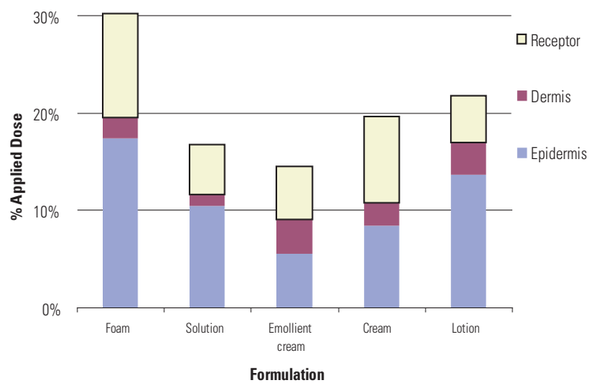

Figure 2: Skin distribution profile of clobetasol propionate (CP) 24 hours after topical application of CP in 5 different vehicles.

Results and Discussion

Immediately after application the foam vehicle delivered clobetasol propionate faster than the other formulations tested. The distribution profile results demonstrated that, compared to other commercially available clobetasol propionate vehicles, foam can deliver clobetasol propionate more efficiently because it follows a vehicle-skin non-interactive pathway.

* *non-interactive pathway:* pathway with little or no interaction with skin components.

Table 1: Percentage of applied dose of drug accumulated in the collection fluid at 12-hour time point after application of 0.05% clobetasol propionate in foam or other formulations to split thickness human skin.

	Mean	±	Std.Error
Foam	5.9%	±	1.1%
Solution	2.8%	±	0.3%
Emollient cream	2.7%	±	0.3%
Cream	2.1%	±	0.2%
Lotion	1.3%	±	0.1%

Conclusions

The results from this study indicate that foam is the most efficient drug delivery vehicle for permeation and distribution of clobetasol propionate in comparison to solution, lotion or creams.

References

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