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 (Permgeear, Bethlehem, PA) [2]. To assure the integrity of each skin section, permeability to tritiated water was determined before application of the vehicles. (Permegear, Bethlehem, PA) [2]. To assure the integrity of each skin section, 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/cm², 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 of the epidermis. The drug was extracted from the surface washing materials, epidermis and dermis using acetonitrile. Quantification of drug content was performed by liquid scintillation.

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.

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.

Table 1: Percentage of applied dose of drug accumulated in the receptor during 24-hour time period after application of 0.05% clobetasol propionate in foam or other formulations to split thickness human skin.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>±</th>
<th>Std.Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foam</td>
<td>5.9%</td>
<td>±1.1%</td>
<td></td>
</tr>
<tr>
<td>Solution</td>
<td>2.8%</td>
<td>±0.3%</td>
<td></td>
</tr>
<tr>
<td>Emollient cream</td>
<td>2.7%</td>
<td>±0.3%</td>
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<tr>
<td>Cream</td>
<td>2.1%</td>
<td>±0.2%</td>
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<tr>
<td>Lotion</td>
<td>1.3%</td>
<td>±0.1%</td>
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References