Permeation analysis of novel steroid vehicles to deliver and retain steroid in skin layers associated with psoriasis

Leon Kircik, MD[1]; Franklin Okumu, PhD[2]; Sateesh Kandavilli, PhD[2]

[1]DermResearch, PLLC, Louisville, KY; [2]Promius Pharma, a subsidiary of Dr. Reddy's Laboratories, Princeton, NJ

Introduction

- It is possible to tailor the formulation of topical treatment vehicle to facilitate delivery of active drug to the site of skin disease pathology.
- Psoriasis is a condition primarily affecting the epidermal layers of the skin. Developing a vehicle that optimizes steroid delivery to the affected psoriatic skin layers, while reducing permeation of the steroid into the systemic circulation could be beneficial in the treatment of psoriasis.
- This study was designed to evaluate various vehicle formulations on the penetration and retention of betamethasone dipropionate in the skin to identify the formulation with the best balance of penetration into the epidermis and low systemic absorption.

Methods

- A base vehicle formulation containing water, sorbitan monostearate, polyoxyl 20 cetostearyl ether, cetostearyl alcohol, mineral oil, propylparaben, methylparaben, butylated hydroxyl toluene, and hydroxyethyl cellulose was developed.
- All formulations contained betamethasone dipropionate, 0.05%. Vehicle formulation variants included eladiyl alcohol (F-A), hexanol (F-B), dodecanol (F-C), octadecanol (F-D), docosanol (F-E), or oleyl alcohol (F-10).
- Test agents were applied to human cadaver skin in static Franz-cell chambers containing receptor fluid (4% BSA and 0.01% gentamicin). Permeation of betamethasone into the receptor fluid was measured at 0, 2, 6, 10, 12 and 24 hours. At 24 hours, the distribution of betamethasone and its metabolites in the stratum corneum, epidermis, and dermis was analyzed using LC-MS/MS.

Results

- The F-C formulation had the highest retention of betamethasone in the skin and the highest 12-hour and 24-hour permeation of betamethasone through the skin into the receptor fluid.
- The F-10 formulation had the second highest retention of betamethasone in total skin and relatively low permeation of betamethasone into the receptor fluid (Figure 2).
- The F-10 formulation had skin layer betamethasone concentrations of 33 ng, 18 ng, and 14 ng in the stratum corneum, epidermis, and dermis, respectively (Figure 1).
- The skin layer concentrations of the F-C formulation were 37 ng, 43 ng, and 34 ng, and those of the F-A formulation were 5 ng, 17 ng, and 14 ng in the stratum corneum, epidermis, and dermis (Figure 1).
- The formulation with the best balance of penetration, permeation, retention, and low absorption (F-10/DFD-01) was selected for additional evaluation.

Figure 1. Penetration of Total Betamethasones after 24 Hours

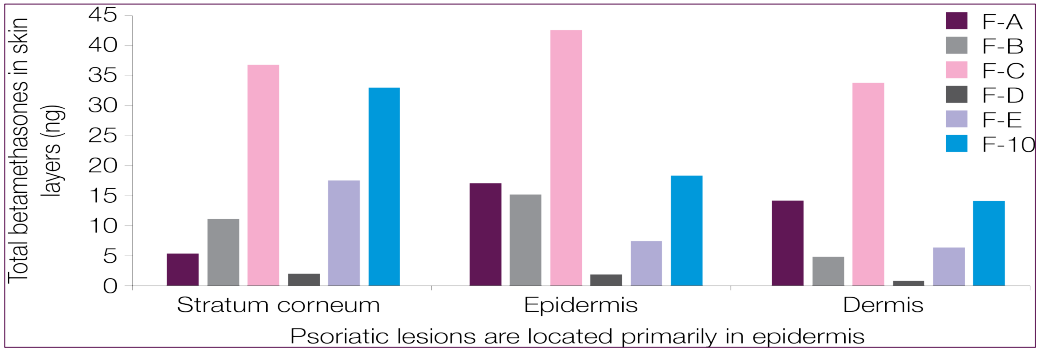
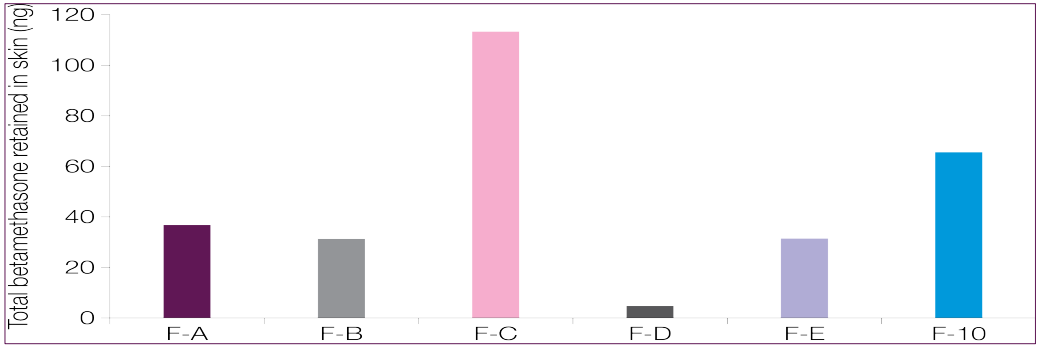


Figure 2. Retention of Total Betamethasones after 24 Hours



Conclusions

- The F-10 (DFD-01) formulation containing oleyl alcohol, sorbitan monostearate, polyoxyl 20 cetostearyl ether, cetostearyl alcohol, and mineral oil, demonstrated a good balance of betamethasone retention in the skin, with low systemic absorption.
- This vehicle is designed to achieve retention of steroid in skin layers to maximize local efficacy while minimizing systemic absorption of steroid.

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