Compounding for Atopic Eczema and Psoriasis

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Introduction/Background

The incidence of atopic eczema is rising in Australia with one in four children developing the disease before the age of two. Psoriasis, on the other hand, is a chronic, immune-mediated inflammatory skin disease estimated to affect 6.6% of the population[1-2]. Psoriasis is characterized by red, scaly, and well-defined lesions (Figure 1) that form as a result of hyperproliferation of keratinocytes (cells within the epidermal layer of the skin). Though the exact mechanism is poorly understood, it has been proposed that cytokines such as interleukin (IL)-2, IL-6, IL-8, and tissue necrosis factor (TNF)-α play a vital role in facilitating the inflammatory response and the hyperproliferation of keratinocytes[3]. Topical corticosteroids (e.g. mometasone furoate) and vitamin D analogues (e.g. calcitriol) are often used in the management of psoriasis due to their anti-inflammatory and/or antiproliferative properties. While topical corticosteroids help to reduce inflammation and itching in both skin conditions, nevertheless they are not without side effects. As a result, many patients and caregivers are searching for more "natural" products, with fewer side effects which can be used on a regular basis.

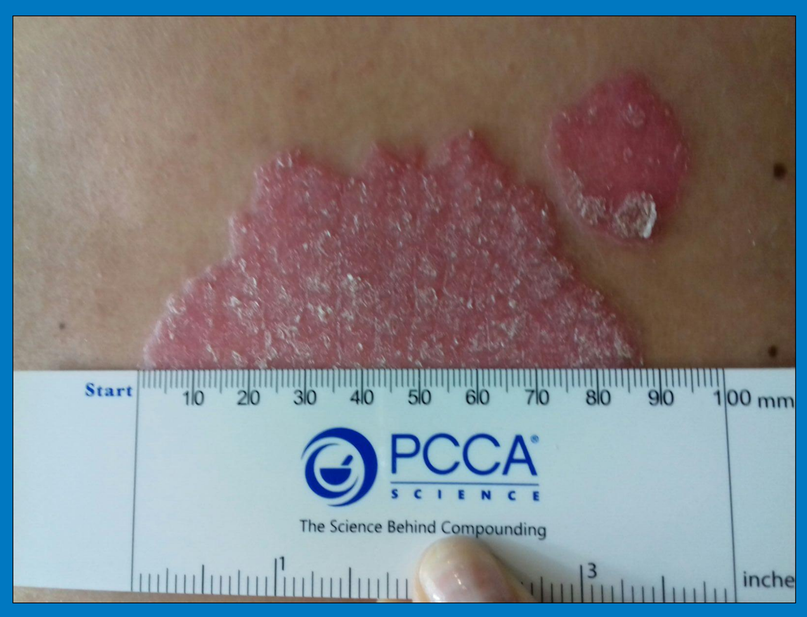

Figure 1. Example of a psoriasis skin lesion.

Methods/Materials

The *in vitro* anti-inflammatory and antiproliferative properties of 4 different formulations were assessed using the enzyme-linked immunosorbent assay (ELISA) for detecting interleukin (IL)-6 production in a reconstructed psoriatic tissue model (Figure 2).

The formulations tested included 2 commercial medicines and 2 compounded medicines, as follows: Mometasone Furoate Ointment USP 0.1% (Perrigo®); Vectical® Ointment Calcitriol 3 mcg/g; Mometasone Furoate 0.1% in XemaTop; and Calcitriol 3 mcg/g in XemaTop. The commercial medicines selected are commonly prescribed in psoriasis and were used in this study as positive controls; untreated tissue samples were used as negative controls. XemaTop is a proprietary base developed to be used in compounded topical formulations for patients with common skin disorders, such as atopic eczema and psoriasis.

An aliquot of 50 µL of each test formulation (4 replicates) was applied to reconstructed psoriasis tissue samples (MatTek Corporation[4]), on day 0 and on day 2 of the study. Culture media were collected on day 5 and applied to the antibody coated plates. The levels of IL-6 were quantified based on the absorbance level at 450 nm.

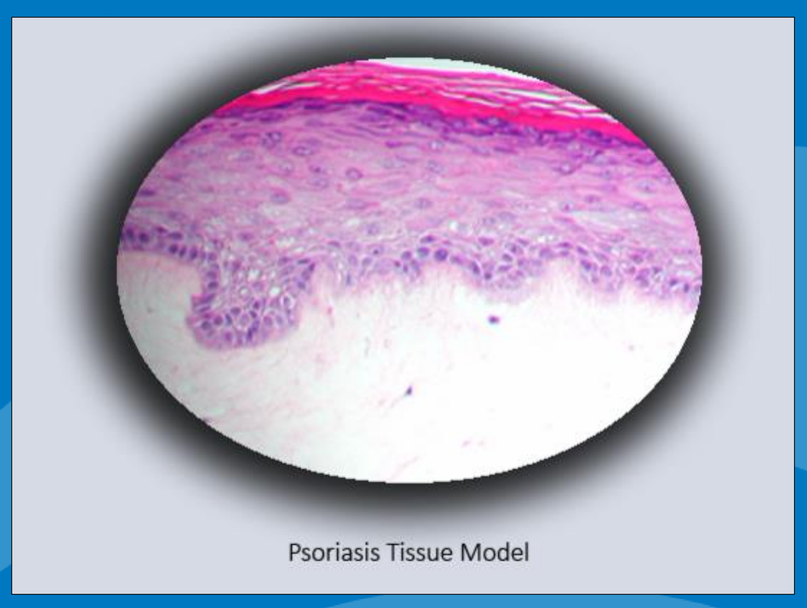

Figure 2. Illustration of the psoriasis tissue model (*adapted from* MatTek Corporation[4]).

Results and Discussion

Mean IL-6 concentrations (pg/mL) in the psoriasis tissue samples treated with the 4 test formulations were significantly lower than in the untreated tissues, with $p < 0.05$ (statistically significant), which shows that all formulations inhibited the production of IL-6 (Table 1 and Figure 3). Considering that cytokines facilitate the inflammatory response and the hyperproliferation of keratinocytes[3], a reduction of IL-6 in the psoriasis tissue suggests that all test formulations presented anti-inflammatory and antiproliferative properties. When Mometasone Furoate 0.1% in XemaTop and Calcitriol 3 mcg/g in XemaTop are compared to the corresponding commercial medicines, it is demonstrated that the compounded medicines inhibited the production of IL-6 to a greater extent (79.713 pg/mL vs 113.902 pg/mL, p=0.040; 54.023 pg/mL vs 106.898 pg/mL, p=0.001). These results suggest that the proprietary base facilitates the delivery of active substances to psoriatic skin and hence the better performance of the base when compared to the commercial medicines of reference.

Table 1. Mean IL-6 concentrations (pg/mL) following *in vitro* application of the test formulations.

Test Formulations	Mean IL-6 (pg/mL) ± SD	*P*-value (negative control)	*P*-value (positive controls)
Negative control (untreated tissues)	528.864 ± 12.153	____	____
Mometasone furoate 0.1% in XemaTop	79.713 ± 9.596	$1.763E^{-09}$	0.040
Calcitriol 3 mcg/g in XemaTop	54.023 ± 7.096	$7.125E^{-10}$	0.001
Mometasone Furoate Ointment USP 0.1%	113.902 ± 15.439	$5.200E^{-06}$	____
Vectical® (calcitriol) Ointment 3 mcg/g	106.898 ± 15.212	$1.009E^{-08}$	____

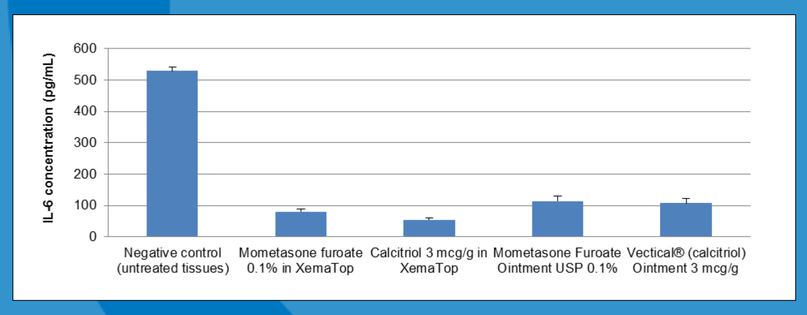

Figure 3. Mean IL-6 concentrations (pg/mL) following *in vitro* application of the test formulations.

Conclusions

Nonmalignant skin conditions are common in Australia and represent a considerable burden to both the patients and the healthcare system[2]. Pharmaceutical compounding may then offer a more 'natural' and effective approach therapeutic alternative in atopic eczema and psoriasis.

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2. Plunkett, A., Merlin, K., Gill, D., Zuo, Y., Jolley, D. and Marks, R. (2001) 'The frequency of common nonmalignant skin conditions in adults in central Victoria, Australia', *International Journal of Dermatology*, 38 (12), p. 901-8.
3. Baliwag, J., Barnes, D.H. and Johnston, A. (2015). Cytokines in psoriasis. *Cytokine*, 73, p. 342-50.
4. MatTek Corporation (2016) *Psoriasis*. Available at: https://www.mattek.com/products/psoriasis/ (Last accessed: 29 March 2016).