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The Effects of Topical Triptolide in an Animal Model of Contact Dermatitis

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Background: Topical corticosteroids remain the first-line treatment for inflammatory skin disorders such as atopic dermatitis. However, extensive use of potent corticosteroids may lead to substantial local and systemic adverse effects. This study examines the use of a novel immunosuppressive compound for the treatment of inflammatory skin disorders.

Tripterygium wilfordii is a poisonous perennial liana of the *Celastraceae* family used since antiquity in traditional Chinese medicine (TCM) for the therapy of fever, chills, edema and inflammation. Crude extracts from its xylem have been used to treat rheumatoid arthritis (RA), chronic nephritis and various skin disorders. Triptolide is one of the main diterpene lactone epoxide compounds found to have immunosuppressive and antiphlogistic activities. In vitro data from our laboratory showed that triptolide has potent T cell immunosuppressive effects at doses that do not cause cytotoxic effects. Based on the proposed mechanism of Triptolide, we speculate that this compound should be highly active against T cell-mediated inflammatory skin disorders such as atopic dermatitis. We therefore used a well-established animal model of contact dermatitis to determine the immunological effects of triptolide on cutaneous inflammation.

Methods: The dorsal surfaces of the ears of BALB/c mice were sensitized to 1% oxazolone. 2 weeks later, the animals were treated with topical triptolide at various concentrations from 0.001% to 0.1% or vehicle whilst being rechallenged with oxazolone for 2 consecutive days. 24 hours after the second oxazolone treatment, cervical lymph nodes and ears were removed for analysis.

Results: Oxazolone treatment alone resulted in considerable hypertrophy of the draining lymph nodes and cutaneous inflammation marked by intense infiltration of the dermis by mononuclear cells, and disruption of the epidermis. Treatment with 0.1% triptolide reduced the number of lymph node cells by >50%, and completely abrogated the cutaneous inflammatory response. Flow cytometry analysis of the lymph node cells revealed a reduction in CD69 expression on CD8 cells from 35% to 27%, and on Ia+ cells from 52% to 18%. Cytokine analysis revealed a reduction in IFN-γ and an increase in IL-4 production by lymph node cells.

Conclusion: Triptolide appears to exert potent immunosuppressive effects when administered transcutaneously, and deserves further study as a potential treatment for inflammatory skin disorders.