Compositions for Prevention/prophylactic Treatment of Poison Ivy Dermatitis

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Abstract

Poison ivy (*Toxicodendron radicans*), poison oak (*T. diversilobum*), and poison sumac (*T. vernix*) are the primary causes of contact dermatitis in the United States, affecting 10-50 million Americans every year. Other genera of the plant family Anacardiaceae with dermatogenic constituents include *Anacardium* (cashew nuts), *Semicarpus* (India ink tree), *Metopium* (poison wood), and *Mangifera* (mango).

The prevalence of sensitivity to poison ivy and poison oak in the general adult population ranges from 50% to 70% with peak frequency for sensitization occurring between the ages of 8 and 14. Outdoor activities as well as outdoor occupations which relate to firefighting, forestry and agriculture are at high risk, costing significant medical expenses and worker's disability.

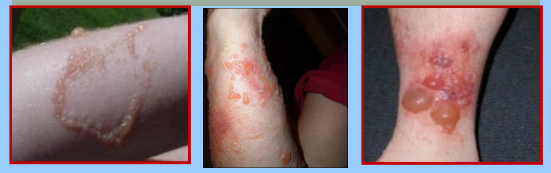
Each fire season, approximately one third of forestry workers in California, Oregon and Washington are disabled by poison oak dermatitis with treatment costs in California alone representing 1% of the annual worker's compensation budget.

During ongoing studies aimed at the discovery of an effective prophylactic treatment for Toxicodendron dermatitis, we have developed a series of novel agents and tested the efficacy of these agents in an *in vivo* animal model..

Introduction

Poison ivy is a weed found in just about every state of mainland USA. The leaves of poison plants release oily material urushiol which is a strong allergen. When urushiol contacts skin it causes dermatitis. Hence the name "Contact Dermatitis". Beside poison ivy, other plants that contain similar allergen include poison oak, and poison sumac. Only 1 ng (billionth of a gram) needed to cause rash while average is 100 ng for most people. Five hundred people could itch from the amount covering the head of a pin. One to 5 years is normal for urushiol oil to stay active on any surface including dead plants.

Twenty-five million to 40 million Americans require medical attention after being exposed to one of these plants. The symptoms of poison ivy dermatitis usually appear within one to two days of contact with the plant oils. They begin with intense itching and a rash that progresses to swelling and blistering. The inflammation is confined to the area that had contact with the plant, often the hands or face, and can occur on any part of the body.



These blisters are painful and sometimes can get worse if infected with secondary bacterial infection. Most of the treatments are aimed at reducing the itching until the self-limited rash runs its course. Topical lotions and creams are used to help relieve the itching and burning rash and blisters. Systemic steroids produce rapid resolution of both the itching and the rash. However, require a careful assessment of the individual before administering it orally or via the intramuscular injection. We have successfully developed drugs by using a poison ivy urushiol induced contact dermatitis model in guinea pigs, that when administered, protect against development of poison ivy contact dermatitis.

Methods and Project Design

The novel agents were synthesized, purified, and characterized by spectral analysis techniques [1]. A guinea pig contact dermatitis model was used for *in vivo* efficacy studies.

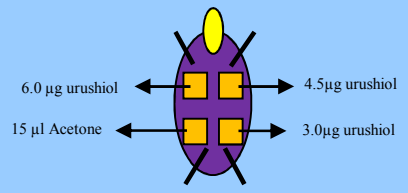


Figure 1. Sites on the abdominal surface of skin for application of urushiol challenge doses dissolved in 15ul acetone vehicle.

Animals: Twenty Hartley strain of guinea pigs (age approximately 6 weeks old) were purchased from Harlan Laboratories. They were housed in the vivarium facility, and fed food and water *ad libitum* according to the guidelines of IACUC at the University of Mississippi. The animals were numbered and divided into 5 groups as described under:

Group I and group II (n=8) were given PBS and 5% ethanol (the vehicle) respectively, while group III, IV and V were given (ELI-21-83, ELI-21-78-1 or ELI-21-57-3, respectively), (600µL containing 20 mg of the drug) via IM route (n=8). Two weeks later all the animals in all the groups were sensitized with urushiol (100µL containing 1.0 mg of urushiol) on the skin surface of the dorsal side of the neck. Two weeks later all the animals were challenged with urushiol (15µl volume acetone containing 3.0µg, 4.5µg and 6.0µg) on the abdominal skin as shown in figure 1.

Scoring skin reactions

The severity of erythema and edema were observed and scored according to Draize scoring system..

Results

Score of erythema and edema of each animal in a group was added to give a sum total score at 24, 48 and 72 hours. Figure 2A shows the sum of scores of skin reactions observed at 24 h post urushiol challenge in all groups. ELI-21-83, ELI-21-78-1 and ELI-21-57-3 treated animals showed no skin reaction compared to buffer or vehicle treated groups (figure 2A). At 48 h after challenge, the skin reaction in group IV was very mild (below the lowest score). No erythema or edema was observed in group III at either of the 3 challenge doses (figure 2B).

At 72 hours post urushiol challenge, the sum total score of groups III, IV and V remain under the lowest score in the Draize scoring scale compared to buffer or vehicle treated guinea pigs (figure 2C).

Stability

ELI-21-57-3 is stable as freeze dried material for 3 years. It is also stable in five aqueous formulations for 18 months at room temperature. Studies will be carried out for 24 months.

Acknowledgements:

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Reference:

[1] Mahmoud A. ElSohly, Waseem Gul, Mohammad Khalid Ashfaq, Susan P. Manly, "Compositions for Prevention/Prophylactic Treatment of Poison Ivy Dermatitis", International Publication Number WO 2009/146131 A2.

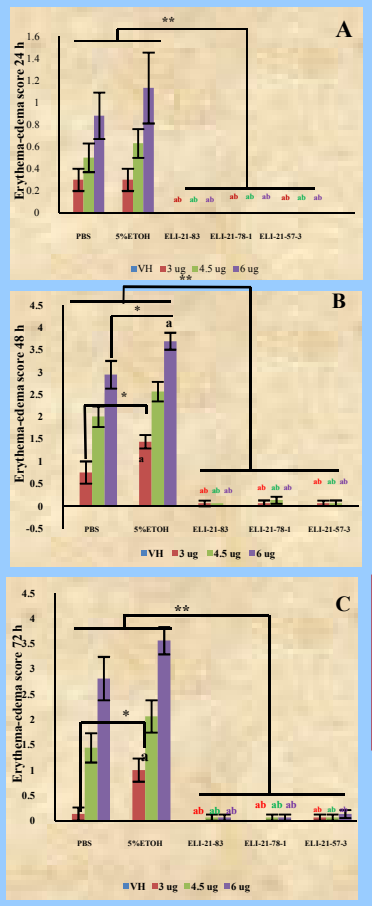

Figure 2. Erythema-Edema score 24 h (A), 48 h (B) or 72 h (C) after challenge with or without ELI-21-83, ELI-21-78-1 or ELI-21-57-3 injection. Data represent mean ± SEM. *P < 0.05, **P< 0.01 and ***P <0.001 considered significant compared to vehicle treated group.

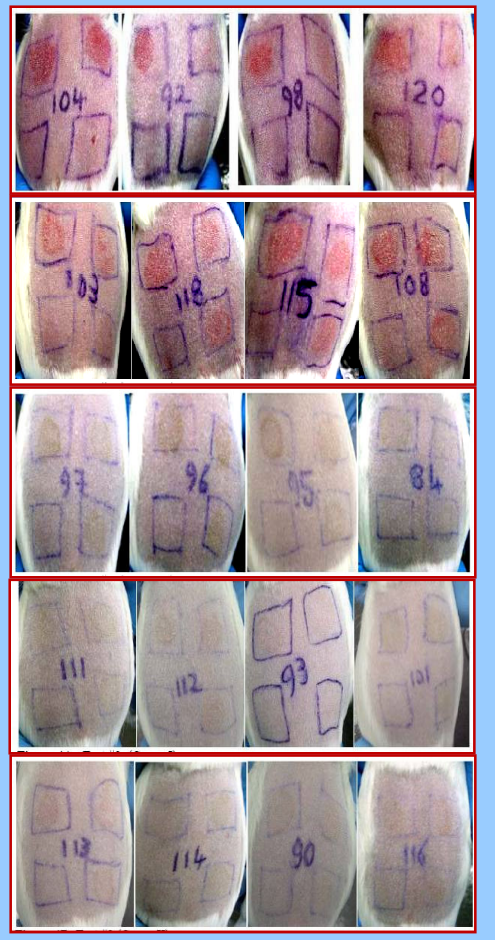

Figure 3. Guinea pigs in Group I and II showing intense skin lesions after 24 h of Urushiol challenge (not treated with any drug). The guinea pigs in Group III, IV and V do not show skin lesions after 24 h of Urushiol challenge. These animals were treated with ELI-21-83, ELI-21-78-1 or ELI-21-57-3 IM respectively (only 4 animals are shown for each group because of space limitations).

Conclusion

- The novel agents were shown to be effective *in vivo* in a guinea pig contact dermatitis model at preventing sensitization, when administered pre-exposure to poison ivy (tolerance).
- Skin reaction to urushiol challenge was dose dependent.
- Pretreatment with ELI-21-83, ELI-21-78-1 or ELI-21-57-3 showed a protective effect against dermatitis caused by urushiol.