THE TREATMENT OF RHUS DERMATITIS (Poison Ivy) WITH MANGANESE SALTS

A PILOT STUDY

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INTRODUCTION

Poison Ivy cases are estimated at over 5 million per year in the United States. The information provided by the FDA monograph indicates that no remedy has proven to be totally effective although palliative treatments are helpful in most cases.

The toxic agent present in poison ivy, poison oak and poison sumac is urushiol – a catechol having a side chain of 15 or 17 carbons with zero, one or three points of unsaturation. Of special significance are the two hydroxyl groups that characterize catechols because these reactive sites are adjacent on the organic ring. With the structure of urushiol and the reactivity of the hydroxyl groups, metal ions such as divalent manganese may be expected to replace the reactive hydrogens to form a metallo-organic ring:

\[ \text{O} \quad \text{OH} \quad + \quad \text{Mn}^{**} \quad \rightarrow \quad \text{O} \quad \text{O} \quad \text{Mn} \]

Where \( R \) is the organic side chain.

The reaction product is called a chelate. A term derived from the clawlike appearance of the function group arrangement responsible for the “grabbing” of a polyvalent metal ion, in this case, manganese (**)..

Many reactive functional groups are known to be involved in chelate formation including hydroxyl, keto, thioketo, oxime, primary, secondary and tertiary amines. Of specific interest in regard to the toxicity of urushiol and its possible neutralization in the presence of the reactive hydroxyl groups is the fact that the reaction product has a ring structure consisting of five members.

In this regard, four member rings are quite rare and five and six member rings comprise most of the chelate structures (*). Rings with more than six members tend to induce structural stress although very large rings having 12-24 members can be very stable because of the lack of bond angle stresses between the atoms that make up the molecular structure (2). Adjacent hydroxy groups on aliphatic as well as aromatic structures react almost universally with polyvalent metal ions to form stable chelates.
Thus, it can be expected that a metal such as manganese (**) will react with urushiol, changing its identity, its behavior and thus its toxicity.

MATERIALS & METHODS

Manganese sulfate, is a solid which is usually a hydrate of divalent manganese and sulfate ions. The monohydrate, MnSO₄. H₂O has a molecular weight of 169.01 of which 89.39 percent is the anhydrous form associated with 10.66% water. The detoxifying agent is the manganese ion, Mn ++ or ore properly MnII., which is present as 32.50% of the monohydrated solid of MnSO₄. Manganese II sulfate crystalizes also with five moecules of water and may be purchased as a mixture of the four and five hydrates.

Sterile solutions of manganese sulfate were prepared and the pH of the solution was in the range of 5.5 to 7.0 as determined by the base to acid transition color of the methyl orange indicator or by pH meter.

The topical solution was administered as a two percent aqueous solution of MnSO₄ and H₂O. Topical application was achieved by spraying the solution to the area of

CLINICAL STUDIES

Patients were selected at random over a two-year period as they presented to be treated for Rhus dermatitis. Those patients wishing to particapate in the pilot study with manganese sulfate solution were given the opportunity to use this novel treatment. All patients were assured that alternative treatment with systemic and/or topical corticosteroids would be available to them if they were not responsive to the treatment with Manganese sulfate within 2 to 3 days.

A total of 33 patients have been treated to date using the Manganese sulfate solution. The patients were seperated into three categories:

- **Group I** – subjects had no prior treatment except for over-the-counter (OTC) remedies.
- **Group II** – subjects had no prior treatment but were given a short action steriod intramuscularly (betamethasone) because of severe edema.
- **Group III** – subjects had typical, acute Rhus dermatitis and had ben treated elsewhere with either systemic ste-roides and/or topical steroids and were still experiencing severe symptoms (itching and dermatitis).

The responders were classified as subjects reporting rapid relief of symptoms (mainly itching) and improvement of the derma-titis (marked decrease in vesication, crusting and erythema) within 2 to 5 days.

The nonresponders were classified as persons who requested cortisone or other treatment. (Two of the six nonresponders in Groups I and III were pleased with the manganese sulfate solution but found that applying the solution to large areas of the body while at work was not practical and preferred the convenience of cortisone pills.)
RESPONSE OF PATIENTS USING MANGANESE SULFATE FOR TREATMENT OF POISON IVY DERMATITIS

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<th>Group I</th>
<th>Group II</th>
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<tr>
<td>Responders</td>
<td>16</td>
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<tr>
<td>Nonresponders</td>
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<td>Lost to Follow-up</td>
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**Group I** – Patients with no prior treatment of the Rhus dermatitis except for over-the-counter (OTC) remedies.

**Group II** – Patients with Rhus dermatitis with severe edema who were given a short acting parenteral steroid Bethamethasone.

**Group III** – Patients already being treated for Rhus dermatitis with systemic and/or topical corticosteroids that were still experiencing severe itching and dermatitis.

**DISCUSSION**

The usual course of Rhus dermatitis varies significantly with the degree of exposure and the sensitivity level of the individual involved. The dermatitis is characteristically very pruritic even with limited skin involvement and the dermatitis remains on the involved skin for at least 1 to 2 weeks.

Most of the treatments for Rhus dermatitis are directed toward the relief of the itching, edema, and the vesiculation – i.e. cool compresses, colloidal baths and lotions, topical anesthetics, antihistamines and corticosteroids (both OTC and prescribed). Serious and extensive cases of poison ivy dermatitis are usually treated with high dose oral and/or parenteral corticosteroids for at least two weeks in addition to palliative medicaments.

The manganese sulfate treatment does not appear to be a miraculous cure for poison ivy dermatitis; however, it does appear to promptly diminish itching. Relief of itching has been the most significant finding reported by most of the patients treated with the manganese sulfate solution and this has been the impetus for stimulating further studies into mechanisms involved in this treatment.

We propose that the manganese sulfate solution probably acts as a chelating agent for urushiol in Rhus contact dermatitis although we recognize that other mechanisms may also be possible.

The effect of chelation should always result in the detoxification of some urushiol molecules, but the success of the treatment as used on a given patient will always have many variables which affect a given response, i.e.:

1. The amount of urushiol in the skin.
2. The ability of detoxicant to reach the urushiol.
3. The amount of detoxicant applied to the affected area.
4. The possible effect between time of exposure and application of the manganese sulfate solution.

Since Rhus dermatitis may develop over several days after exposure, many affected individuals may not anticipate skin surface areas that have been sensitized (treatment of the total body surface may not always be practical unless a bath solution could be developed to use after exposure).
Most of the treatments available for poison ivy dermatitis are somewhat effective for treating the symptoms of the dermatitis. Strong corticosteroids seem to be the most effective medication for edema, erythema and dermatitis of severe cases of poison ivy and do seem to shorten the course somewhat, but severe Rhus dermatitis continues to remain a dreaded condition in spite of the available treatments.

In 1958, Albert Kligman suggested that chemical inactivation of the antigen in Rhus dermatitis would be the most logical approach for topical prophylaxis of poison ivy rashes. We do not yet know if the manganese sulfate solution fulfills a role in prophylaxis but we have been impressed with its effect on curtailment of the symptoms of the dermatitis (especially the itching) rather promptly in most of the individuals treated. There may be a rational chemical basis for this prompt response. Inactivation of the Rhus antigen via chelation may have occurred on the skin surface and within the skin. It is also possible that the chelating effect has displaced some aspect of the antigen/antibody reaction cascade within the skin itself via several unknown mechanisms.

It is also well known that as little as 5% concentration of water in a solution Rhus extract can deteriorate the urushiol's potential for creating a dermatogenic effect. The combination of manganese sulfate in an aqueous solution could possibly have multiple effects since the manganese and the water can both react with urushiol.

Although there are other divalent and trivalent metals which would work equally well as a chelating agent to deactivate the urushiol, such as aluminum, iron, lead, calcium, magnesium, cadmium, zinc, nickel, and beryllium; manganese is preferred because it appears to be most effective and carries no known side effects. For example, if aluminum chlorohydrate were used as a chelating agent, the astringent properties of this compound would probably prevail. While this compound may be useful in preventing the urushiol toxin from entering the skin, it might not work well as a treatment method. Also, aluminum chlorohydrate and other trivalent metal salts must typically have a pH of less than 5 to prevent the metal from hydrolyzing and precipitating. Once precipitation takes place, the products are non-reactive with the urushiol. Therefore, because of the high-acidity required to keep it in solution, aluminum chlorohydrate is ill-suited for use on sensitive areas of the skin and around the eyes.

Salts of iron and lead, such as ferric chloride and lead nitrate, may also be used as chelating agents, but these also tend to be acutely toxic. Furthermore, the use of iron salts can create a brown lesion or "tattoo" in the affected skin area making it unacceptable. Possible toxicity also preclude the use of zinc and cadmium. Calcium and magnesium salts could be used, but would not form stable complexes.

Manganese, on the other hand, is an element whose trace amounts are a necessary part of good human nutrition. There are no known adverse health effects of using this element for topical applications, and its possibility for use as an over-the-counter medication becomes feasible. Also, soluble salts of manganese can be compounded at a pH close to that of the skin (but typically no greater than pH 7 to prevent hydrolyzation) so that it can be used on sensitive skin areas (i.e. around the eyes).

CONCLUSION

Manganese sulfate solution – a simple and inexpensive treatment – seems to be very effective in relieving the itching and hastening the resolution of Rhus dermatitis in the small group of patients studied. Controlled double blinded studies could further define its role in the treatment of mild and severe cases of Rhus dermatitis as compared to other therapies presently being used.

REFERENCES