ANTI-INFLAMMATORY EFFECT OF TOPICAL NANOCRYSTALLINE SILVER CREAM ON ALLERGIC CONTACT DERMATITIS IN A GUINEA PIG MODEL

Kailash C. Bhol¹, Joseph Alroy², Paul J. Schechter¹

¹ NUCRYST Pharmaceuticals Inc., Wakefield, MA, USA,
² Tufts University, Boston, MA, USA

© 2003 NUCRYST Pharmaceuticals, Inc.
Introduction

- Incidence of inflammatory skin diseases, including atopic dermatitis and psoriasis, is increasing in adults and children. Several established topical and systemic therapies, including steroids and immunomodulators are available. These existing therapies do not meet patient and physician expectations due to the lack of durable efficacy and are associated with adverse effects. Hence, there is a need for the development of a safe alternative treatment for inflammatory skin diseases.

- Nanocrystalline silver has been demonstrated to have exceptional anti-microbial properties, and has been successfully used in wound healing. The objective of this study was to determine the anti-inflammatory effects of nanocrystalline silver using a guinea pig model of allergic contact dermatitis (ACD).
Materials and Methods

- Eighty female Hartley guinea pigs were sensitized with 5% dinitro-chloro benzene (DNCB) in acetone on four test sites on the back of each animal. The test sites were treated for five days beginning one day after elicitation of ACD. Erythema and edema were evaluated on a scale of 0-4 (absent to very severe). Prior to treatment and after five days of treatment, skin biopsies were taken from one of the test sites. The biopsies were processed, the stained slides were blindly examined and histological changes in epidermis, superficial dermis, deep dermis and subcutis were graded on a 0-4 scale (absent to very severe changes).

- Scores for erythema, edema and histopathological changes in different group of animals were compared using Tukey-Kramer’s multiple comparison tests following one-way analysis of variance.
Results
Mean Erythema Score of Guinea Pigs with Dermatitis

Figure 1: Graph showing the erythema scores (Mean±SE) in guinea pig dermatitis (n=10). Scoring: 0=No visible erythema; 4+=Very severe erythema and crusting.

© 2003 NUCRYST Pharmaceuticals, Inc.
Mean Edema in Guinea Pigs with Dermatitis

Figure 2: Graph showing the edema scores (Mean±SE) in guinea pig dermatitis (n=10). Scoring: 0=No edema; 4+=Extensive edema.
Histopathological Changes in Guinea pigs with Contact Dermatitis

Figure 3: Histogram showing the histopathological inflammation (Mean±SE; Quantified by five points scoring procedure in each of four regions) prior to treatment and after five days of treatment. 0=No changes, scattered cells; 4+=Very severe changes, numerous inflammatory cells in masses in almost all microscopic fields.
Histological Analysis of Inflammatory Response in Guinea Pigs (HE Stain)

**Figure 4:** Histological sections illustrate distinctly different degrees of inflammatory changes in untreated or in vehicle treated skins and close to normal or mild changes in Tacrolimus and Nanocrystalline silver treated skin.
Concentration—Response of Nanocrystalline Silver Cream on Allergic Contact Dermatitis in the Guinea Pig

Figure 5: Dose Response
Conclusions

- Macroscopic and microscopic observations revealed that topical application of Nanocrystalline silver cream (0.5%, and 1%) and Tacrolimus ointment produced significant suppressive effects on allergic contact dermatitis in a guinea pig model.

- The effects of 0.5% and 1% nanocrystalline silver cream were equivalent to tacrolimus ointment.

- Cream with 0.1% or 0.25% nanocrystalline silver did not show significant reduction in inflammation.

- There was a clear concentration-response relationship to the decrease of inflammation.

- This study suggests that nanocrystalline silver cream may have therapeutic potential for treating inflammatory skin diseases.