Topical nanocrystalline silver cream inhibits expression of matrix metalloproteinase-9 in animal models of allergic contact dermatitis.

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INTRODUCTION

Matrix metalloproteinase's (MMPs) are zinc-and calcium-dependent endopeptidases that are capable of degrading most components of the extracellular matrix (ECM) and are implicated in the pathogenesis of inflammatory diseases. MMP-9, also known as gelatinase B, is a zinc-dependent, calcium-requiring metalloproteinase capable of degrading type IV and V collagens, as well as gelatins. MMP-9 has been implicated in the pathogenesis of inflammatory diseases.

Increased expression of MMP-9 in psoriatic skin and during challenge phase of allergic contact dermatitis (ACD) patients has been reported (1, 2).

NPI 32101 (nanocrystalline silver) has been demonstrated to have exceptional anti-microbial properties (3). Acticoat ™ dressings coated with nanocrystalline silver are successfully used in the treatment of burns and wound healing. Our recent studies demonstrated that topical nanocrystalline silver in an emollient cream exhibited anti-inflammatory activity in guinea pig and mouse models of ACD (4,5), and nanocrystalline silver significantly suppressed pro-inflammatory cytokines and induced apoptosis of inflammatory cells (5). It has also been reported that, nanocrystalline silver in Acticoat™ dressing, suppressed MMP-9 in a porcine model of wound healing (6).

The objective of this study was to determine the expression of MMP-9 in animal models of allergic contact dermatitis and to examine the role of nanocrystalline silver cream on modulation of MMP-9.

Methods:

Allergic contact dermatitis was induced in guinea pig skin and mouse ear with dinitrochlorobenzene and dinitrofluorobenzene, respectively. Topical treatments, including vehicles and cream with 1% NPI 32101, were applied once a day for four days to mice and five days to guinea pigs. Erythema and edema were evaluated daily. Skin biopsies were collected after treatment and processed for immunohistochemistry and the intensity of the immuno-peroxidase staining was graded as described previously (7). Skin homogenates were used in Western blotting to detect binding of antibody to MMP-9.

RESULTS

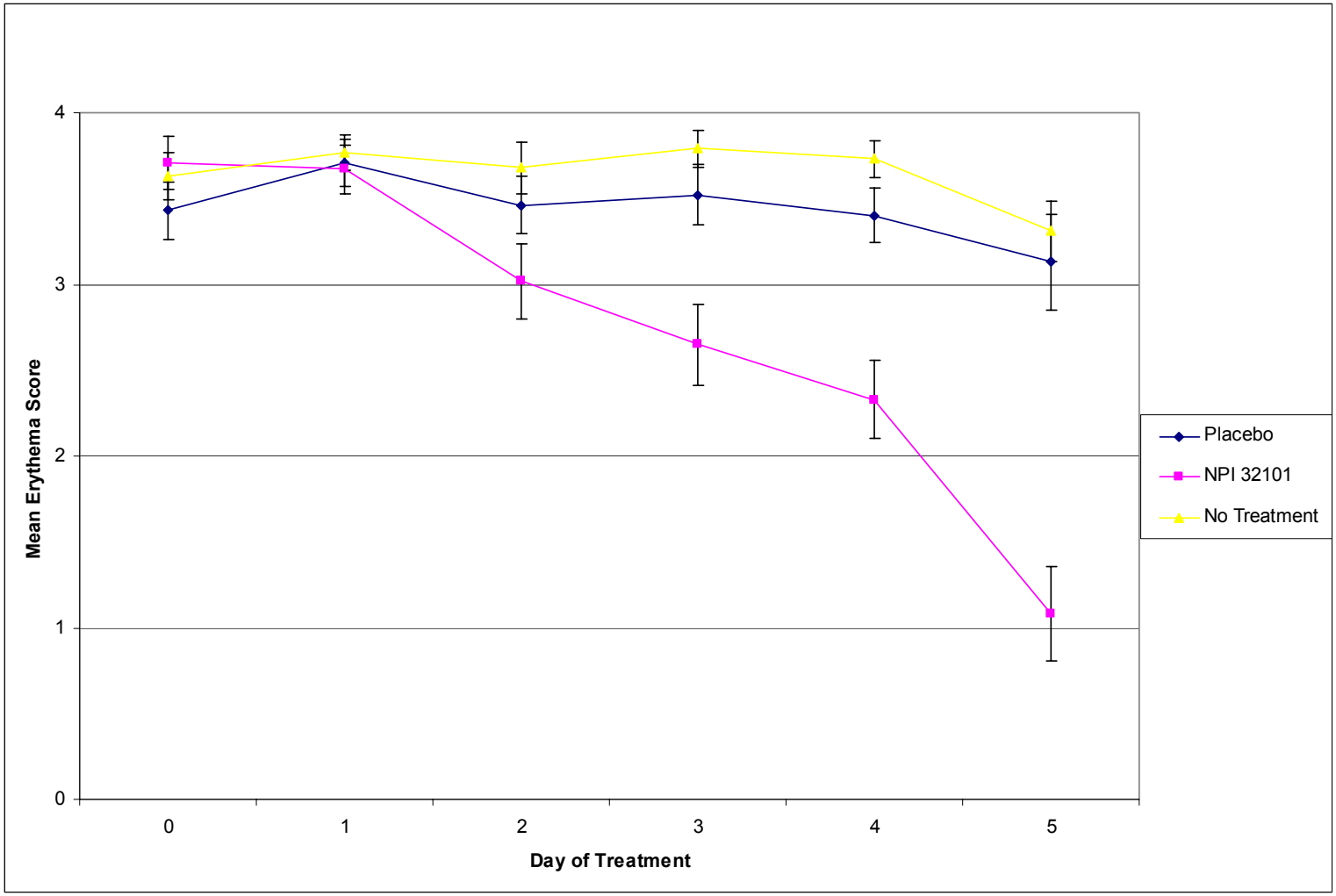

Fig. 1 Mean Erythema Scores (± SE; n=12) of Guinea Pigs with Allergic Contact Dermatitis (where 0 = none and 4 = very severe)

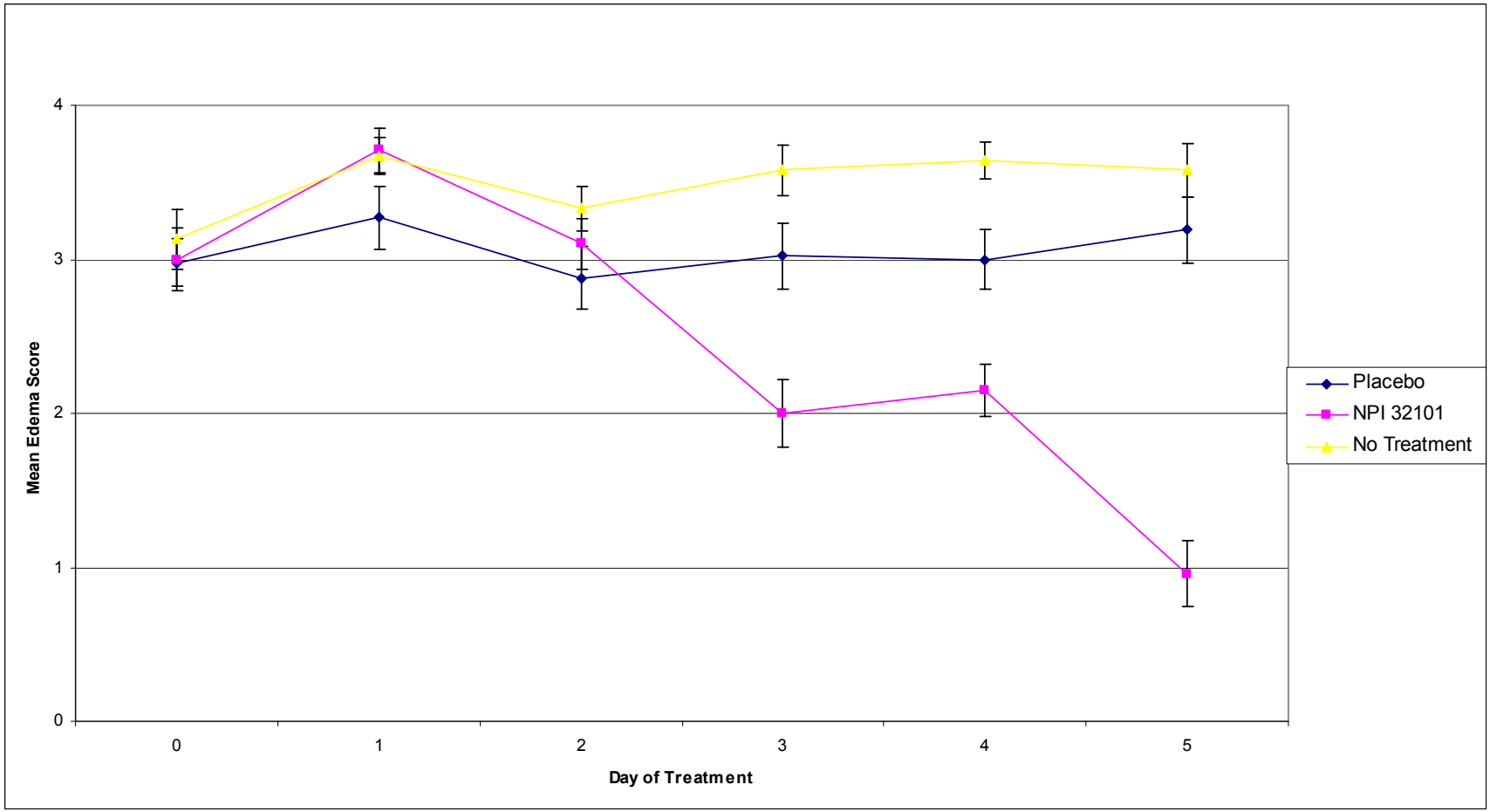

Fig 2 Mean Edema Scores (± SE; n=12) of Guinea Pigs with Allergic Contact Dermatitis (where 0 = none and 4 = very severe)

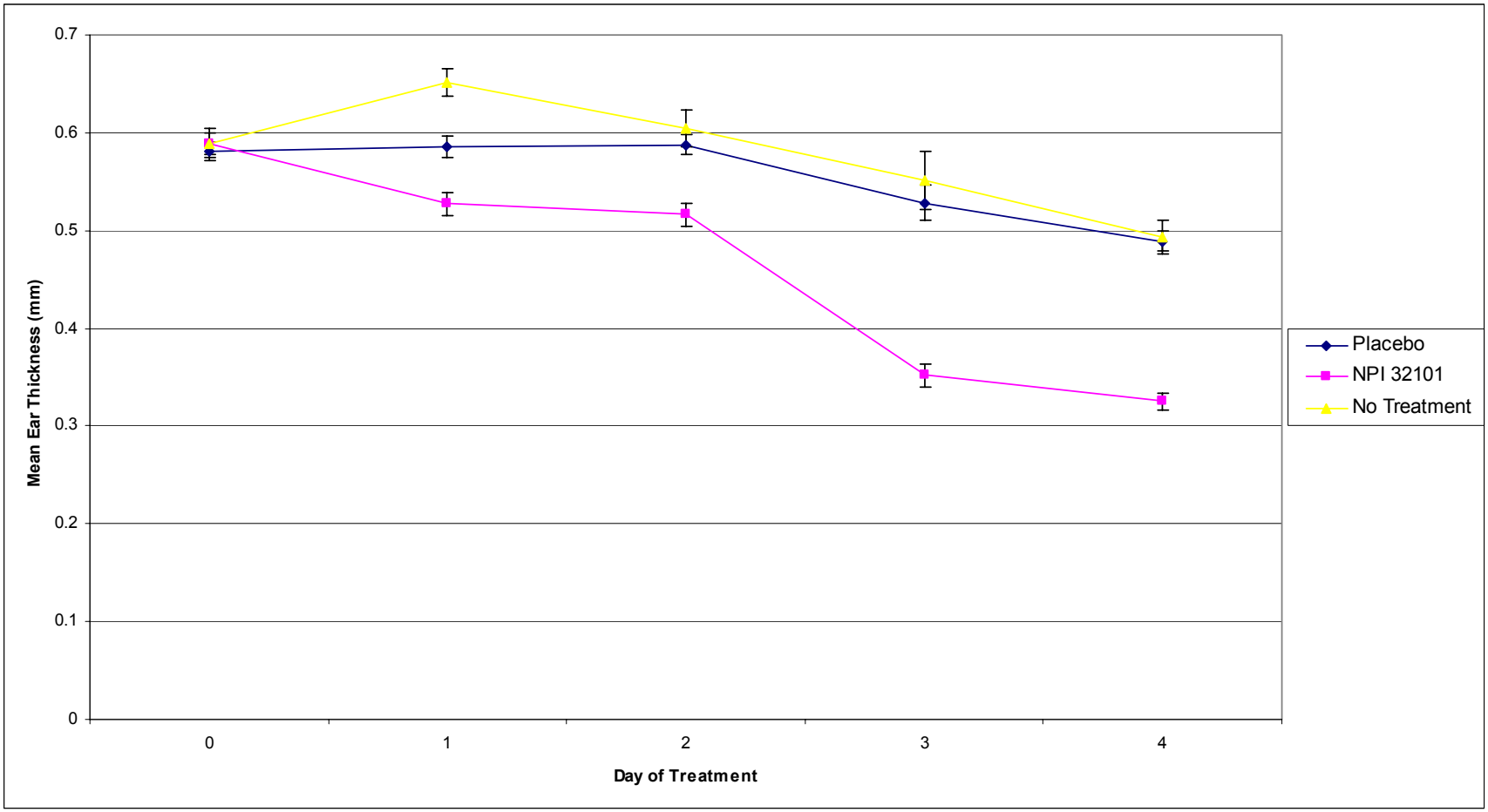

Fig. 3 Mean Ear Thickness Scores (± SE; n=15-30) of Mice with Allergic Contact Dermatitis

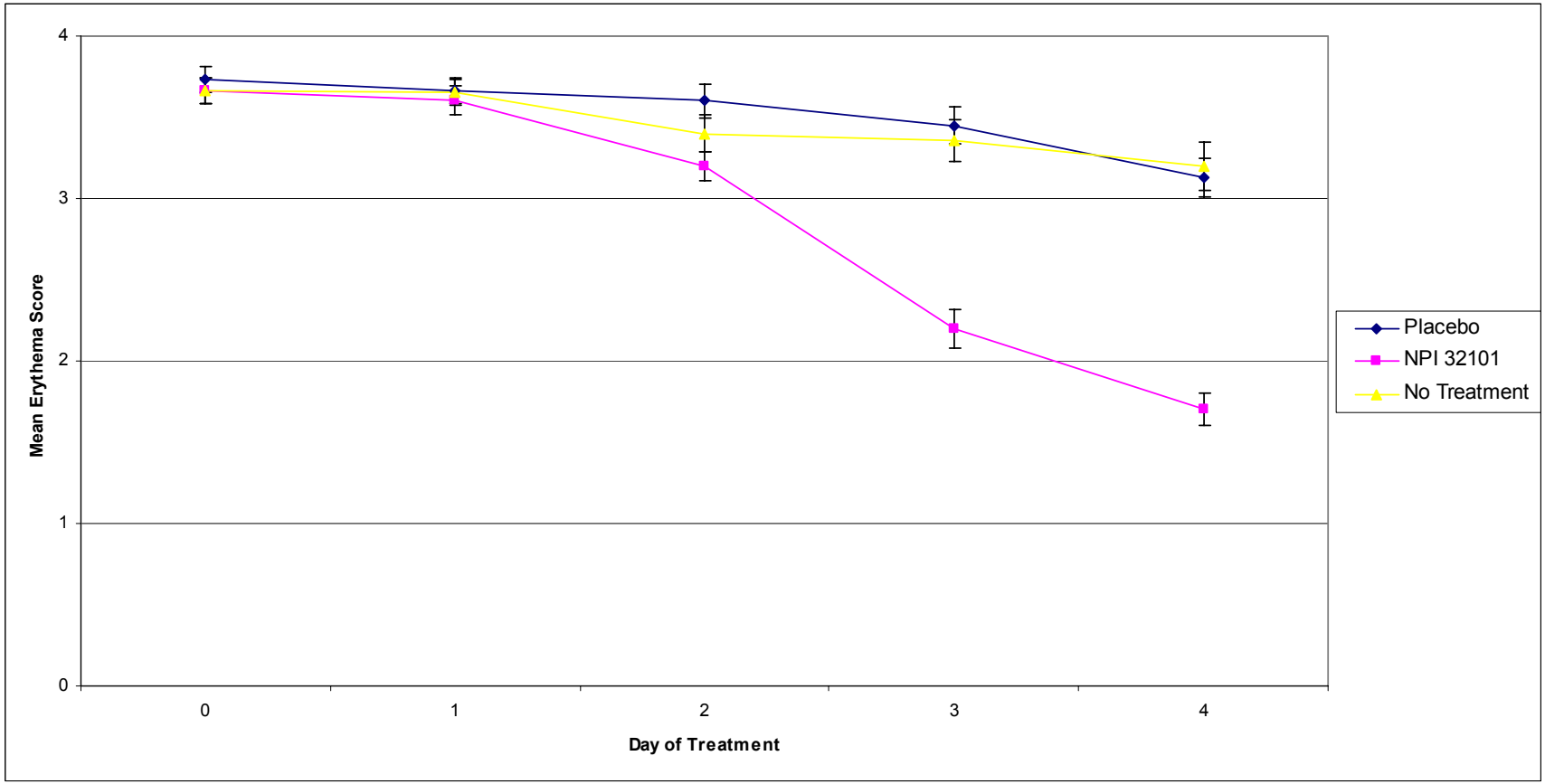

Fig. 4 Mean Erythema Scores (± SE; n=15-30) of Mice with Allergic Contact Dermatitis (where 0 = none and 4 = very severe)

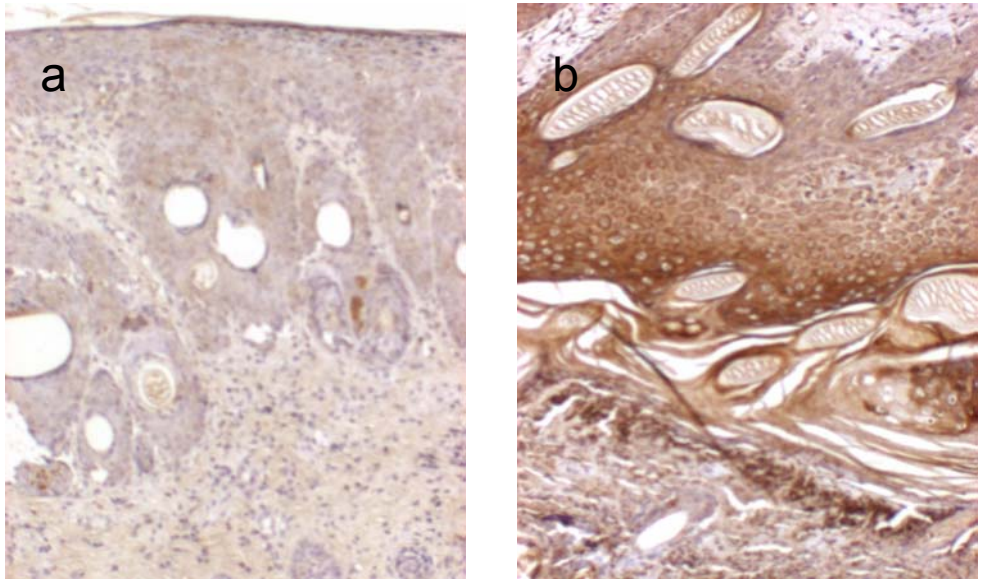

Fig. 5 Immuno-Peroxidase Staining of skin biopsies from guinea pigs with allergic contact dermatitis. (*a*) Treated with NPI 32101, (*b*) No Treatment

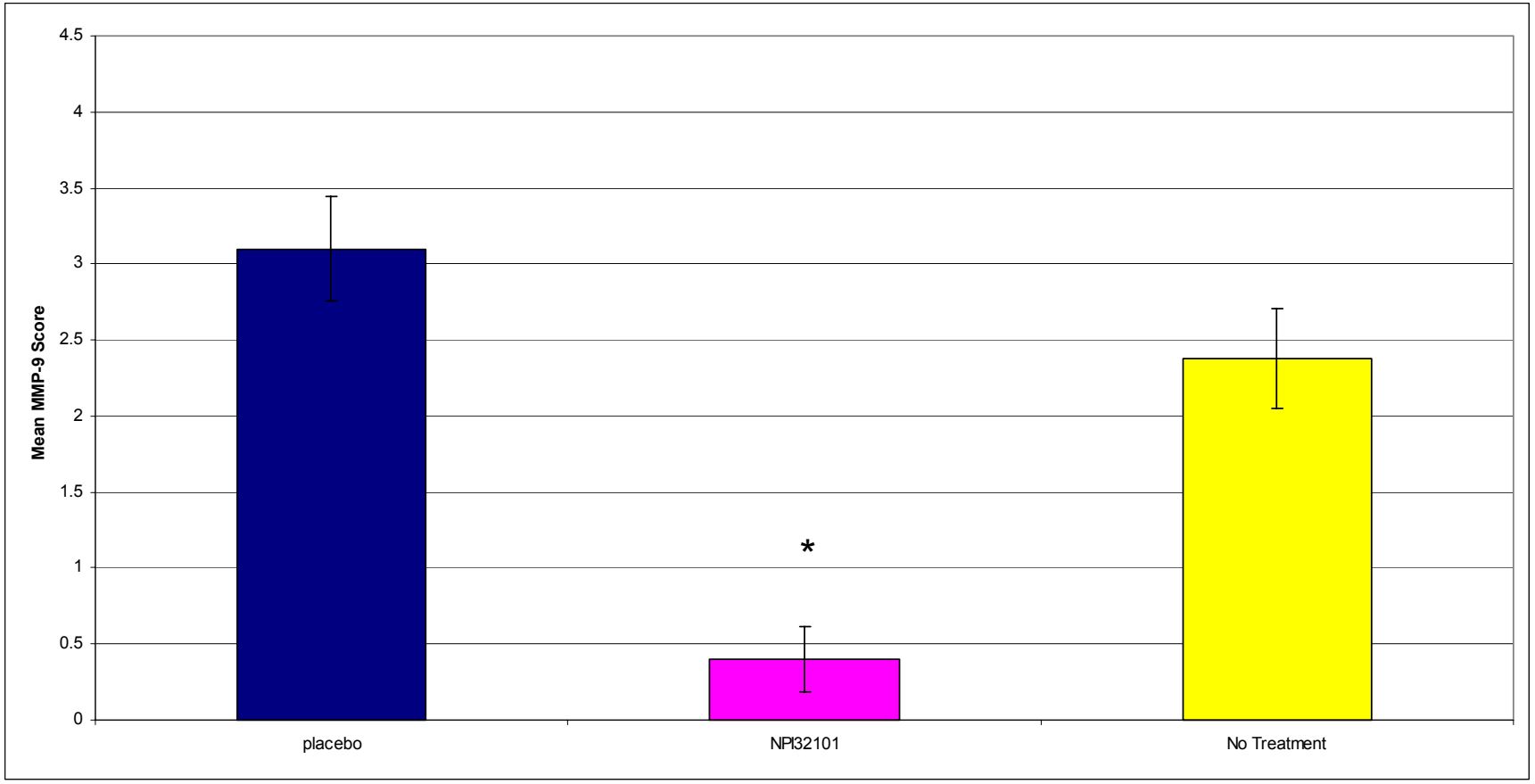

Fig. 6 Mean MMP-9 Scores (± SE; n=12) of Guinea Pigs with Allergic Contact Dermatitis after four days of treatment.
*P<0.05, compared to placebo and no treatment.

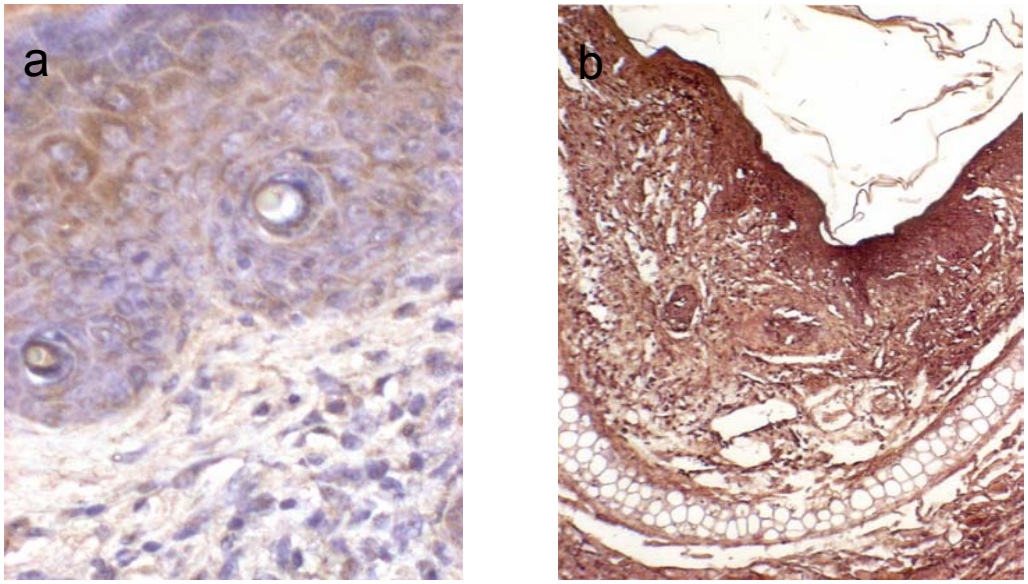

Fig. 7 Immuno-Peroxidase Staining of skin biopsies from mice with allergic contact dermatitis. (*a*) Treated with NPI 32101, (*b*) No Treatment

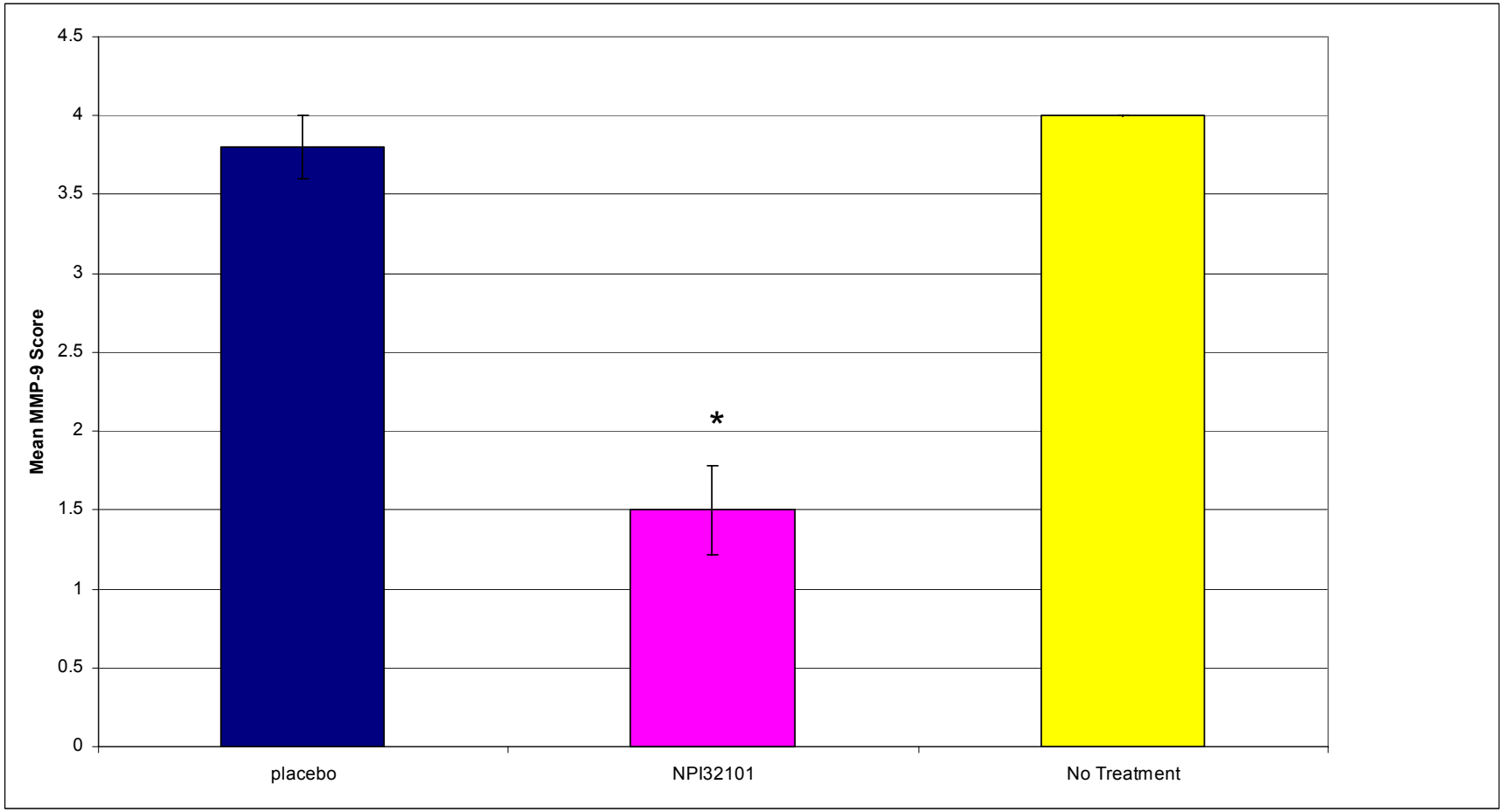

Fig. 8 Mean MMP-9 Scores (± SE; n=15-30) of Mice with Allergic Contact Dermatitis after five days of treatment.
*P<0.05, compared to placebo and no treatment.

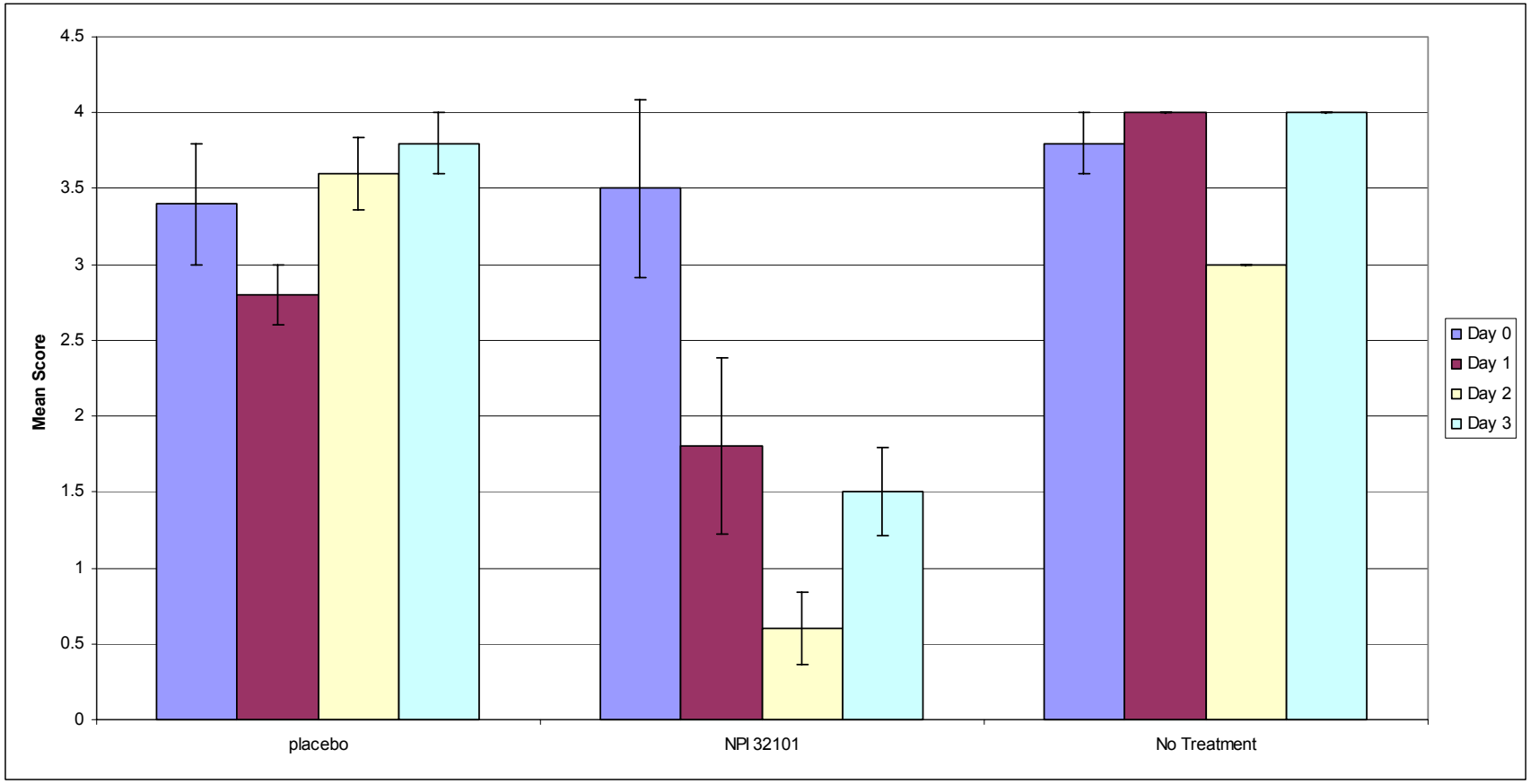

Fig. 9 Mean MMP-9 Scores (± SE; n=15-30) of Mice with Allergic Contact Dermatitis on each day of treatment

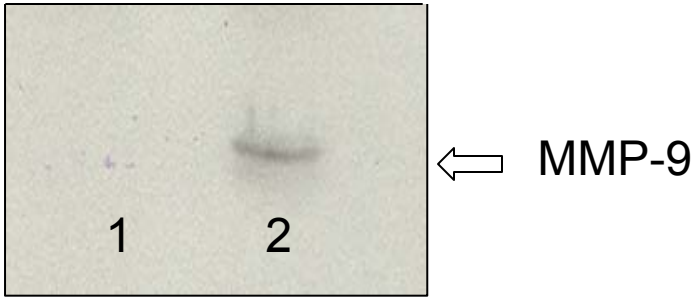

Fig. 10 Western blotting assay showing expression of MMP-9 in the ACD skin of untreated guinea pig (lane 2) and reduced or absent in the skin after treatment with NPI32101 (lane 1).

CONCLUSION:

Compared to placebo groups, significant ($P < 0.05$) reductions of erythema and edema were observed in both mice and guinea pigs with allergic contact dermatitis treated with 1% NPI 32101 cream.

Immunohistochemical staining of the biopsies and immunoblotting studies using the skin homogenates demonstrated that 1% NPI 32101 treatment significantly suppressed the expression of MMP-9.

This study suggests that increased expression of MMP-9 may contribute to the pathogenesis of allergic contact dermatitis and the suppression of MMP-9 expression may be one of the mechanisms by which 1% NPI 32101 cream exerts its anti-inflammatory activity in allergic contact dermatitis.

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