

**Enhancement of human skin barrier integrity by nicotinic acid derivatives**

MK Jacobson,<sup>1</sup> EL Jacobson,<sup>1</sup> H Kim,<sup>1</sup> M Kim,<sup>1</sup> RL Rizer<sup>2</sup> and NS Trookman<sup>3</sup> *1 University of Arizona and Niadyne, Inc., Tucson, AZ, 2 TJ Stephens & Associates, Colorado Springs, CO and 3 Rocky Mountain Laser Center, Colorado Springs, CO*

A weakened skin barrier is characteristic of numerous dermatology conditions including atopic dermatitis. In addition, evidence suggests that certain treatments for skin photodamage may result in decreased barrier integrity and heightened photosensitivity. Derivatives of nicotinic acid tailored for topical delivery of nicotinic acid to the cellular compartments of skin have been shown to increase NAD content to support genomic integrity and energy metabolism functions and to stimulate the release of leptin to stimulate epidermal differentiation. In the present study, a double-blinded protocol was used to compare placebo and myristyl nicotinate (MN) formulations for effects on skin barrier integrity. Formulations containing 5% MN increased skin NAD content by an average of approximately 40% ( $p=0.001$  vs. placebo) and epidermal turnover by 6.3% ( $p=0.003$ ). Skin barrier assessment was made by determination of rates of trans-epidermal water loss (TEWL), effects on minimal erythema dose (MED), and analysis of skin biopsies. Over a period of 12 weeks, the placebo formulation decreased the rates of TEWL by approximately 9% while MN formulations decreased TEWL rates by nearly 30%, demonstrating a strong effect of MN on barrier integrity ( $p=0.006$ ). Even greater effects of MN on reduction of TEWL were observed in atopic subjects. The presence of MN also resulted in a photoprotective effect on MED of approximately 9% ( $p=0.08$ ). Skin biopsies showed that the presence of MN resulted in an increased thickening of the granular and spinous layers and also dramatically increased cellular layers of the stratum corneum. These results indicate that skin delivery of nicotinic acid may provide clinical benefit to skin conditions that are characterized as having a partially compromised skin barrier, and may be useful either alone or in combination with other treatments for such conditions.