

NIA24TM

Niacin-Powered Skin Therapy

Rebuilds
Skin Integrity
Three Ways

Photodamage leads to visible and invisible structural changes in the skin.

- Sun damaged skin loses elasticity, becomes wrinkled and mottled.
- Damaged DNA in skin cells causes the loss of genomic integrity resulting in the development of abnormal cell populations.¹
- The process of repairing DNA damage and maintaining genomic integrity induces photo-immune suppression.²

Scientific studies demonstrate the healing effects of Niacin.

Niacin is emerging as a key factor in protecting the skin from sun damage and aging. The bioactive form of Niacin, Nicotinamide Adenine Dinucleotide (NAD), serves as a substrate in a number of biochemical reactions and plays a central role in energy metabolism. The beta-N-glycosylic bond of NAD can be cleaved by three types of enzymes, including poly (ADP-ribose) polymerase or PARP-1.³

- PARP-1 is involved in DNA repair.⁴
- The unique molecule, Pro-Niacin™ transports Niacin in the form of Nicotinic Acid across the skin barrier deep into the cellular structure.
- Nicotinic Acid is converted to NAD which
 - Repairs damaged DNA⁴
 - Stimulates energy metabolism and promotes skin turn over⁴
 - Stimulates the release of leptin⁵

Pro-Niacin™ facilitates dermal delivery of Nicotinic Acid.

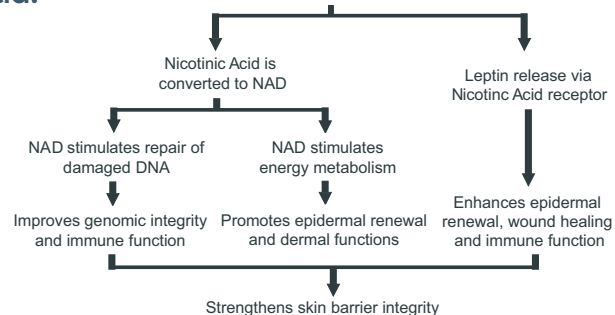


Figure 1. Mechanisms of action by which Nicotinic Acid treats and prevents photodamage.

Repairs DNA

PARP-1 plays an important role in cell responses involving NAD.⁴

- When cell damage is minor, PARP-1 activation enhances cellular recovery by stimulating DNA repair and allowing the cell to recover from genotoxic stress.⁴
- When cell damage is higher, PARP-1 affects apoptosis that can lead to necrosis.⁴

Stimulates energy metabolism and skin cell turnover

Living organisms derive most of their energy from oxidation-reduction reactions.

- NAD is a coenzyme containing Niacin and is responsible for a number of redox reactions involving numerous enzymes.⁷
- One of the primary roles of NAD is to produce energy. Most often it is involved with the catabolism of carbohydrates, fats, and proteins.⁷
- After Pro-Niacin™ is applied to the skin, it is converted to NAD and enhances the turnover of skin cells.⁴

Stimulates the release of leptin

- Topically delivered Niacin via Nicotinic Acid receptor stimulates leptin release and accelerates wound healing without vasodilation typically associated with oral administration.⁵
- Leptin exerts numerous protective effects including the enhancement of skin re-epithelialization.⁵

The unique properties of Pro-Niacin.™

Prior to the discovery of Pro-Niacin,™ efforts to transport Niacin, either in the form of Nicotinic Acid or Nicotinamide (Niacinamide) have failed due to their hydrophilic properties. In order to penetrate the lipophilic stratum corneum, a carrier molecule was needed.

Pro-Niacin™ is a lipophilic molecule that can penetrate the lipid-rich stratum corneum. Its dermal delivery system is a breakthrough in transporting Niacin across the skin barrier into the epidermis where it is converted to Nicotinic Acid.

NIA 24,™ a topical cream containing Pro-Niacin,™ allows for the continuous delivery of Nicotinic Acid which is then converted to NAD. The key to the therapeutic benefits of NIA 24™ is providing sustained Nicotinic Acid to skin cells so that the damage can be healed and the skin barrier can be strengthened.

Pro-Niacin™ — a patented molecule

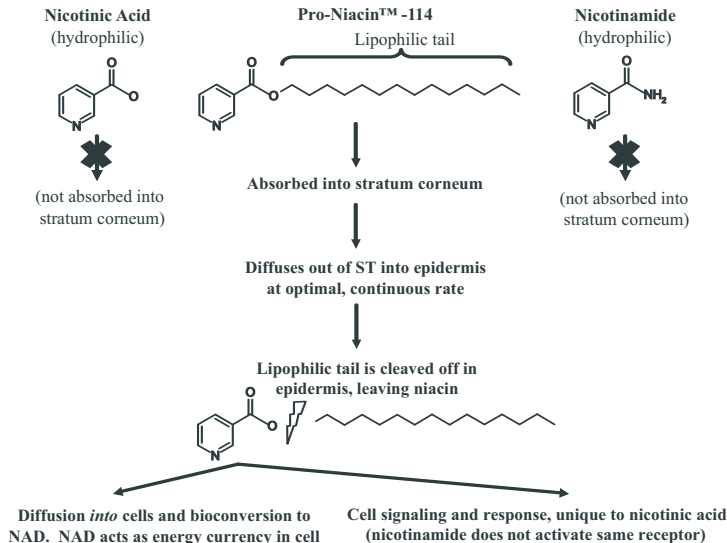


Figure 2. Structure, delivery and function of Pro-Niacin.™

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Delivery of Pro-Niacin.™ 6

Pro-Niacin™ rapidly separates from cream/lotion and is absorbed into the stratum corneum

Pro-Niacin™ is absorbed at an optimal rate from the stratum corneum into the epidermis

Pro-Niacin™ is converted to nicotinic acid by enzymes in the epidermis and dermis

Nicotinic Acid is converted to NAD by skin cells

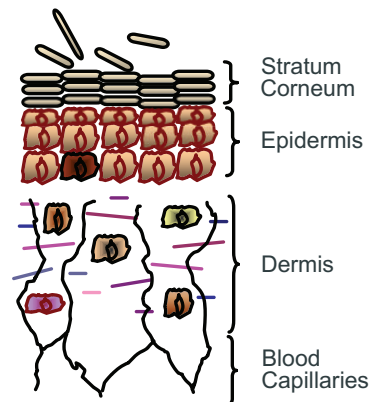


Figure 3. Delivery of Pro-Niacin.™

Pro-Niacin™ – increases skin NAD content. ⁶

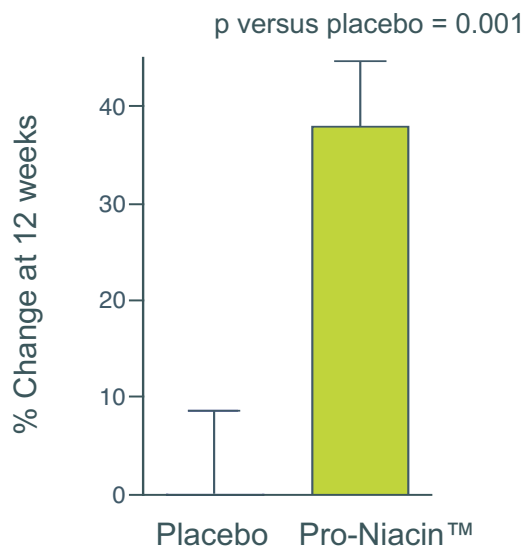


Figure 4. In a double-blinded study measuring NAD content in skin, subjects received either placebo or Pro-Niacin™ formulations for 12 weeks. ⁸

Clinical Efficacy of Pro-Niacin™

Pro-Niacin™ increases skin cell turnover and skin barrier integrity.

Studies using 1% Pro-Niacin™ and 5% Pro-Niacin™ vs. placebo demonstrated an increase in stratum corneum turnover and skin barrier integrity. ⁶

Table 1. Pro-Niacin™ stimulates skin cell turnover. ⁶

Pro-Niacin™		Placebo		Pro-Niacin™ increase	t-test
T _{1/2} (days)	n	T _{1/2} (days)	n		p value
Study 1 (1%) 17.2 ± 0.44	16	19.4 ± 0.41	16	11.3%	0.001
Study 2 (5%) 13.4 ± 0.18	34	14.3 ± 0.23	34	6.3%	0.003

The effectiveness of Pro-Niacin™ on the integrity of the skin barrier can be further measured by looking at the rates of transepidermal water loss (TEWL). Rates of TEWL were observed before and after following a standard regimen of stratum corneum removal by tape stripping.

Pro-Niacin™ decreases TEWL and strengthens skin barrier integrity. ⁶

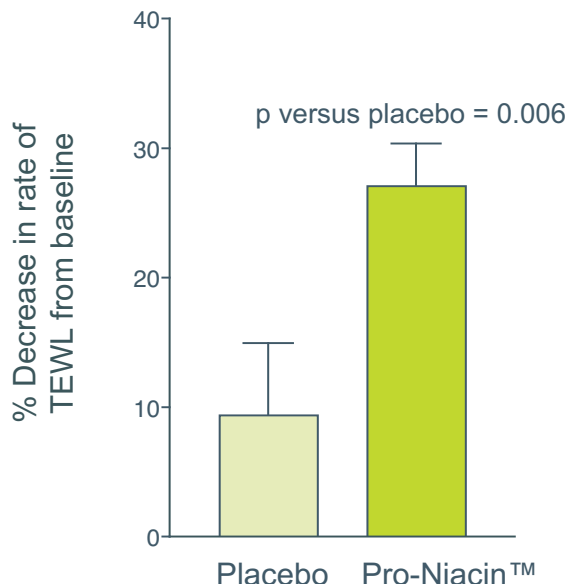
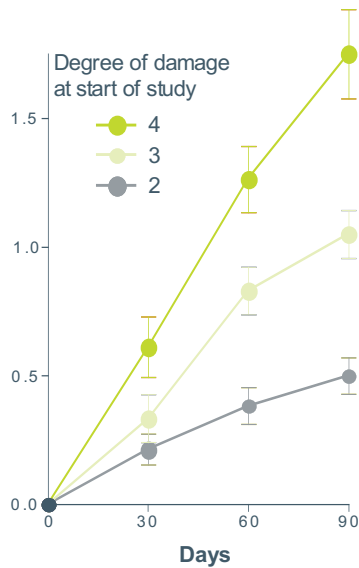


Figure 5. Rates of TEWL on the cheeks using 5% Pro-Niacin™. ⁶

Skin texture improved in 82% of study subjects. 6

Improvement was significant by 30 days and progressed over the 90-day trial period. The degree of improvement correlated with the degree of photodamage.

Figure 6. Physician evaluation of improvements in cheek texture with different levels of photodamage.



Day 0

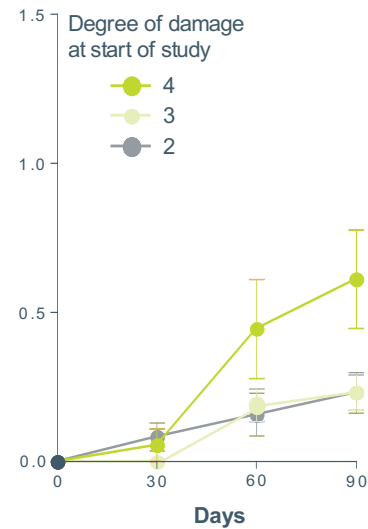
Day 90

Figure 7. Improvements in skin smoothness and texture and reduction in solar lentigines in a trial subject treated with 5% Pro-Niacin.™ 6

Skin firmness improved in 53% of study subjects. 6

The greatest improvements in skin firmness were also seen in subjects with severe photodamage. Significant improvements were observed in the cheek and periorbital regions at 30 days, and greater improvement in all regions was achieved at 60 days.

Figure 8. Physician evaluation of improvements in chin/jaw firmness with different levels of photodamage. 6



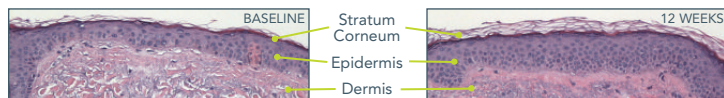
Day 0

Day 90

Figure 9. Improvements in chin and jaw firmness in a trial subject treated with 5% Pro-Niacin.™ 6

Cross Section of Cheek Biopsy

Patient I Biopsy



Patient II Biopsy



Jacobson, M.K., Jacobson, E.L., Kim, H., Kim, M., Rizer, R.L. and Trookman, N.S., Enhancement of human skin barrier integrity by nicotinic acid derivatives. (2004) Journal of Investigative Dermatology, Vol. 122: No. 3, A58.

Skin biopsy analysis shows a dramatic thickening of the stratum corneum and epidermal layers of Pro-Niacin™ patients, which results in improved skin barrier integrity. In addition, the lower dermal layer shows a healthier, tighter cellular matrix after 12 weeks of Pro-Niacin™ treatment. ⁸

At a seven-site, 90-day physician-directed trial, 140 patients with mild to severe sun damage used Pro-Niacin™ daily. The following changes observed by physicians represent the percent of patients who experienced improvement:

- 90% reduced hyperpigmentation
- 82% improved skin texture
- 81% improved skin tone
- 80% increased skin smoothness
- 68% reduced fine lines and wrinkles
- 53% improved firmness

Pro-Niacin™ offers photoprotection.

Erythema following UV exposure is a result of DNA damage. Pro-Niacin™ mitigates the development of this type of erythema by delivering Nicotinic Acid to the skin cells where DNA can become damaged. ⁶

Table 2.
Pro-Niacin™ confers photoprotection as determined by Minimal Erythema Dose. (MED) ⁶

Untreated		Placebo		Placebo Increase	t-test	Pro-Niacin™		Pro-Niacin™ Increase	t-test
MED (sec)	n	MED (sec)	n		P value	MED (sec)	n		P value
40.0	56	44.3	24	10.7%	0.011	48.2	24	20.5%	0.001

Pro-Niacin™ restores sun damaged skin in just 30-90 days ⁶, depending on the degree of damage.

- Research funded by the National Cancer Institute (NCI) is investigating whether Pro-Niacin™ may be effective in preventing skin cancer. ⁶

NIA 24™ is the perfect complement to other rejuvenating therapies.

With its unique power to heal and repair damaged DNA, Niacin should be top of mind as complementary therapy for patients undergoing serious skin care or procedures:

- Microdermabrasion
- Peels
- Laser therapies
- Cryo therapy
- Using retinols or other skin care products containing AHAs.

References

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3. Jacobson MK and Jacobson EL. Discovering new ADP-ribose polymer cycles: protecting the genome and more. *Trends in Biochemical Sciences*. 1999;24:415-417.
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7. Higdon, J. Niacin. The Linus Pauling Institute's Micronutrient Center. <http://lpi.oregonstate.edu/infocenter/vitamins/niacin/printniacin.html>, accessed 11/7/05.
8. Jacobson MK, Jacobson EL, Kim H, Kim M, Rizer RL and Trookman NS. Enhancement of human skin barrier integrity by nicotinic acid derivatives. *Journal of Investigative Dermatology*. 2004;122:58(A345).

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