NAD+ For Skin Care



SCIENCE-BASED SKIN CARE

NAD⁺ is an effective strategy to reverse the dermal and epidermal signs of photo and chronological aging.

Technological advancements, such as liposomal delivery, have improved the potential of NAD⁺ to renew the deepest layers of skin strata and replenish the skin's NAD⁺ pool. 9

"NAD⁺ is changing the landscape of the skincare industry and it's our most promising anti-aging strategy yet." – Dreama Pilcher, MD



AGE DEFYING POWER

NAD⁺ precursors such as niacinamide, have a long heritage in dermatology due to their ability to increase oxidized nicotinamide adenine dinucleotide (NAD⁺). $\frac{6.9}{2}$

"The systemic and topical use of niacinamide in the case of medical and cosmetic problems has proved effective." 9

Skin Aging

"Niacinamide, as a precursor of NAD / NADP, had a stimulatory effect on collagen synthesis, epidermal biopolymers (proteins) and keratin."

Wound healing

"It was possible to reduce the time to wound healing from 15–17 days to 7–10 days."

Anti-inflammatory

"In total, 82% of those treated showed an improvement in overall disease condition after 8 weeks."

Hyperpigmentation

"Significant lightening of hyperpigmentation as a result of niacinamide lightening of the skin."

Rosacea:

"In addition to an improvement in horny layer moisture, there was also a reduction in the reddening of the skin."

UV Damage

"On aging skin, niacinamide improves the surface structure of the skin, shows a wrinkle-smoothing effect and has an inhibitory effect on photocarcinogenesis."

SHIELDS UV DAMAGE

NAD⁺ deficiency in the skin leads to UV sensitivity, DNA damage and may contribute to wrinkles by weakening the bond between dermis and epidermis of extrinsically age skin.²

It's making its way into dermatologist's anti-aging arsenal because of its critical role in the aging process.

According to researchers,

"It may prevent dermal matrix degradation by inhibiting the enzymes that break down collagen and promote an optimal physiologic environment: the enhancement of cell activity, hydration, and the synthesis of collagen, elastin and HA (hyaluronic acid)."



PROTECTS THE GENOME

The importance of replenishing and maintaining cellular NAD⁺ levels has gone mainstream thanks to recent scientific findings. $\frac{3}{2}$

NAD⁺ has been identified as the key to overall skin health and its status is critical in preserving genomic stability. A *genome* is an organism's complete set of DNA, including all of its genes.

Tissues with a high cellular turnover, such as the skin, require higher doses of NAD⁺ to counteract daily genomic threats. $\frac{4.5}{5}$



IMPROVED SKIN ELASTICITY

Scientists are now discovering the NAD⁺ compound itself can provide antiaging skin health benefits similar to niacinamide, such wrinkle reduction, collagen production and improved skin elasticity. ^Z

INCREASED MOISTURE CONTENT

The topical application of B3 also reduces transepidermal water loss (TEWL) and improves the moisture content of the stratum corneum. 8



RESTORES CELL FUNCTION

Over the past few years, there's been a tremendous interest in boosting NAD⁺ levels due to its central role in maintaining and restoring cellular health.

Cells rely on NAD⁺ to carry out over 500 critical metabolic functions, including a vast array of processes ranging from energy creation to maintaining healthy DNA. 10

In the first study to show NAD $\!\!\!^+$ levels decrease with age in human tissue, researchers found,

"The observed correlation between NAD⁺ levels and aging adds weight to the idea that NAD⁺ may play a role in cell

senescence and longevity and not simply as an electron carrier." ¹¹



REJUVENATES SKIN

As chronic oxidative stress and chronological aging can cause NAD⁺ breakdown in the skin, from the outermost layer to the deepest

layer, the NAD⁺ metabolic pathway has been implicated as a potential therapeutic target to promote cellular health. $\frac{12}{2}$

Recent studies have shown that enhancing NAD⁺ levels can reduce global oxidative cell damage, replenish total NAD⁺ stores and restore optimal skin cell function.

According to scientists,

"Chronic accumulation of oxidative stress and inflammation during advanced age represents a major driver of NAD⁺ decline. Promotion of NAD⁺ anabolism using NAD⁺ precursors may represent a clinically relevant therapeutic strategy to ameliorate age-related decline in cellular energy." ¹³



In a study examining the effectiveness of topical NAD⁺ in 37 patients suffering from psoriasis, researchers reported remarkable antipsoriatic performance of topical NAD⁺.

"Topical NAD⁺ therapy can be viewed as a potential alternative to the conventional treatment of psoriasis and without the side effects." $\frac{14}{14}$

Skin aging is driven by a combination or external and internal factors such as sun exposure (UV), stress, environmental toxins and the natural mechanisms of aging occurring in all cells and tissues.

Raising NAD⁺ levels may help inhibit several mechanisms of aging at once and is a promising approach to skin rejuvenation. $\frac{15}{15}$



ACTIVATES LONGEVITY GENES

Much of the renewed interest in NAD⁺ over the last decade can be attributed to the sirtuins—the "guardians of the genome."

Sirtuins are a family of seven proteins in humans (SIRT1-SIRT7) that are involved in multiple cellular processes relevant to dermatology and can only function in the presence of NAD⁺.

Now, everyone in the skincare world seems to be talking about these longevity-linked proteins, which are intricately involved in photoaging, collagen synthesis, ultraviolet radiation damage response, oxidative stress and wound repair.

Sirtuins are key modulators of cellular pathways implicated in maintaining overall skin health.

Supplying the skin with NAD⁺+ may help activate sirtuins in skin cells and ameliorate the damaging effects of UV exposure, DNA damage and aging. $\frac{16}{}$

NAD⁺ LEVELS DECLINE WITH AGE





Source: Zhu, Xiao-Hong, et al. "In Vivo NAD Assay Reveals the Intracellular NAD Contents and Redox State in Healthy Human Brain and Their Age Dependences." Proceedings of the National Academy of Sciences, vol. 112, no. 9, 2015, pp. 2876–2881., doi:10.1073/pnas.1417921112. Source: Massudi, Hassina, et al. "Age-Associated Changes In Oxidative Stress and NAD+ Metabolism In Human Tissue." PLoS ONE, vol. 7, no. 7, 2012, doi:10.1371/journal.pone.0042357.

SKIN MAY SUPPLY NAD⁺ TO OTHER TISSUES

Previous research has shown that during exercise, NAD+ levels decrease, while NADH levels increase in muscle tissue. (White and Schenk, 2012)

"NAD⁺ content in human muscles decreased after moderate (75% of VO₂max) and high intensity (100% of VO₂max) exercise."

"Exercise until exhaustion alters the NAD+/NADH ratio."

This 2019 study shows that NADH levels increase and NAD⁺ decrease in skin. $^{\underline{8}}$

"NADH increases within two minutes after exercise initiation and it remains elevated during and immediately after the exercise completion."

"Skin cells at this depth have a vivid metabolism of NADH and react in a dynamic way to ischemia-triggered hypoxia and then to re-oxygenation during reperfusion."

(NADH was used as a proxy, as NAD⁺ decreases proportionally with an increase in NADH).

CONCLUSION

Skin cells depleted of NAD⁺ accumulate DNA strand breaks, increase reactive oxygen species (ROS) and apoptotic cell death. Resupplying cells with NAD⁺ can prevent oxidative stress, DNA damage, senescence and tissue inflammation.

The topical use of NAD⁺ is a clinically relevant therapeutic strategy to ameliorate age-related conditions, replenish the NAD⁺ reservoir in the skin for utilization by other cells and tissues. $\frac{18}{10}$

The efficacy of enhancing skin NAD⁺ concentrations with pure NAD⁺ sets the stage for future formulations of science-based products.

Resveratrol

"The Longevity Molecule"

Resveratrol is a stilbenoid polyphenol synthesized by plants in response to stressful stimuli and is protective in aging. $^{9, 10, 6}$

Its broad-spectrum properties (antimicrobial, anti-inflammatory, antioxidant and antiaging) make it a potent bioactive for dermatological application by limiting the effects of cellular aging. ¹¹

Its antioxidant activity (95%) is higher than vitamin E (65%) and C (37%) and has been shown to be active in neutralizing and inhibiting the formation of reactive oxygen species. $^{6, 12}$

Apocynin

The Skin Cell Tonic"

Apocynin, a natural vanilloid compound, has emerged as a bioactive phytochemical with potent anti-inflammatory properties for the skin. ¹³

A new paper published in *Nature*, found that declining levels of a collagen protein called COL17A1 (Collagen 17), cause our skin to develop wrinkles, sag and lose elasticity. ⁴

Apocynin was able to restore levels of Collagen 17 and repair damaged skin, leading scientists to believe it's possible to reverse our skin's timeline at the cellular level. ¹⁴

NAD+

"The Youth Molecule"

May Improve Rosacea

According to research Topical NAD+ has been shown to improve metabolism of skin cells. Its profound antioxidant properties can lessen inflammation that is associated with the damaging effects of free radicals.

May Improve Psoriasis

According to this study, it's as effective as the leading pharmaceutical at treating psoriasis, and without side effects. NAD+ mitigates cellular damage and lessens inflammation, which leads to a visible improvement in the skin.

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Renue[™] Age Defying Face Serum with Liposomal NAD+ and NMN

Renue[™] – Age Defense Day Cream

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15. Environmental Stressors on Skin Aging

16. <u>Slowing Aging by Design: The Rise of NAD⁺ and Sirtuin-Activating</u> <u>Compounds</u>

17. <u>The Effect of Exercise on the Skin Content of the Reduced Form of</u> <u>NAD and Its Response to Transient Ischemia and Reperfusion in Highly</u> <u>Trained Athletes</u>

18. NAD⁺ in Skin: Therapeutic Approaches for Niacin

NAD+ Levels in Aging Skin

"Tissues with high cellular turnover, such as skin, require higher doses of NAD+ to counteract genomic insults."

As you age, your skin is exposed to an array of environmental insults, which cause cellular dysfunction and over time it becomes difficult for the repair mechanisms to work efficiently. Your skin requires higher levels of NAD+ to combat damage and keep your skin in a youthful and healthy state. Aging is directly associated with lower NAD+ levels in the skin.

"With aging, both the epidermis and dermis undergo thinning and lose their regenerative capacity, which manifests as wrinkling, dryness, and mottling."

UV radiation through sun exposure is associated with skin photo-aging, inflammation and oxidative damage. Photo-aged skin often has textural issues, wrinkles, uneven pigmentation and a leathery appearance. When the repair mechanisms can't keep up, and NAD+ levels are low, it increases your susceptibility to further damage.

"NAD+ deficiency increases skin sensitivity to UV radiation, impairs DNA damage response, increases genomic instability." Delivery of NAD+ through transdermal liposomal serums and lotions, is an optimal way to safely raise levels of NAD+ in the skin. In dermal fibroblasts (cells within the dermis), nicotinamide protects against oxidative stress, glycolysis, oxidative phosphorylation and increases mitochondrial efficiency.

"Bioactive compounds targeting the mitochondria have proved effective against age-related as well as UV-induced skin damage, in addition to different skin diseases with mitochondrial involvement."

The Renue Skincare line offers potent ingredients, a scientifically advanced formulation and a superior mode of delivery. Liposomes safely carry the active ingredients, which include our NAD+ Complex (NAD+ and NMN) and Apocynin, past the outer skin barrier and deep into your cells. The potent delivery system offers a deeper penetration of key ingredients into the skin's surface to combat the most visible signs of aging and promote vibrant, youthful looking skin.