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Skin Health & Beauty Nutrition

REJUVENATION

from within

Scientific Review

Reviewed for accuracy by HealFast Medical Team
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INTRODUCTION

The Skin is the largest organ in the human body. Adults carry an average of 8 pounds (3.6 kilograms) of skin for a rough average total of 22 square feet (or 2 square meters). As an organ, skin is complex and contains almost 500 genes with unique patterns of expression. Unlike most other organs, the skin is directly exposed to the outside world, it maintains homeostasis, and acts as a wall of defense against outside threats.

To accomplish these tasks, the skin has a multifaceted barrier system which comprises of the: stratum corneum, tight junctions, microbiome, chemical barrier, and immunological barrier. For a substance to be absorbed through the skin, it must first bypass these barriers along with the skin's 7 different layers.

For generations, topical applications including skin creams have been utilized for the maintenance and improvement of skin health. However, the absorption and utility of many of these interventions have been questioned.

Current studies show that skin health is often a reflection of overall health, environmental factors, and stress.

Many metabolic and internal factors affect the skin, and new scientific research is emerging to characterize how skin regeneration and rejuvenation can be optimized through internal metabolic mechanisms.

This trend of maintaining skin health via internal metabolic means, is aptly named "*Beauty From Within*". The idea is that to truly optimize skin health, one must focus on their overall metabolism and physiology. Since skin regenerates roughly every 27 days, it's important to continuously nourish it with orally absorbed bioavailable ingredients to maintain skin health and vitality. "Orally absorbed" is key here. Our gastrointestinal tract is specifically made and optimized for absorption, while the skin is meant to be a barrier and prevent things from entering our body.

This white paper will review, generally, skin structure and function, and the concept of "Beauty from Within" ("BFW"). Its primary purpose is to discuss the most evidence-based, orally consumed, bioavailable ingredients shown to improve skin structure, function, and regenerative ability. Lastly, it will highlight some of the achieved results from using these interventions.

BACKGROUND

Generally, in order to understand how to improve skin and its appearance, one must understand the basics of skin structure and function.

1. SKIN STRUCTURE

Skin is composed of 3 main layers.



1. Epidermis: The outer layer. The epidermis is the thinnest layer of the three. It is responsible for protecting the body from the harsh outside environment. It is comprised of 5 layers and hosts different types of cells including:

- Keratinocytes: produces Keratin and the extracellular matrix; i.e., the main component of the epidermis that protects the skin and provides skin its texture and structure.
- Melanocytes: provides melanin, a skin pigment.
- Langerhans cells: which prevent particles from getting into the skin.

2. Dermis: The middle layer. The dermis layers provide the skin with its fullness and plumpness. Age and the Sun can damage the dermis and lead to wrinkles. The dermis is a complex layer, containing blood vessels, hair follicles, sebaceous (oil) glands, as well as the extracellular matrix.

One of the main synthetic cells located in this layer are the fibroblasts. These cells manufacture collagen, elastin, heparan sulfate, and hyaluronic acid. All of which play key roles in the health and appearance of the skin. As the skin ages, the number of functional fibroblast cells begins to decline, and the remaining cells typically slow down the production of collagen, hyaluronic acid and heparan sulfate.

These changes typically lead to skin thinning, fragility, fine lines, wrinkles, easy bruising and skin sagging.

Many topically applied skin creams attempt to address these changes but do not penetrate deep enough into this layer. This is true for most topically applied products on the market today. External stem cells, peptides, hyaluronic acid and other ingredients applied topically do not penetrate down into the dermal skin layer.

3. Hypodermis: is the fatty layer and also known as the subcutis. Within it are the sweat glands, fat and collagen cells, and it's responsible for conserving body heat and protecting the vital inner organs. The reduction of tissue volumes in this layer often contributes to skin sagging.

2. SKIN MATRIX – KEY COMPONENTS

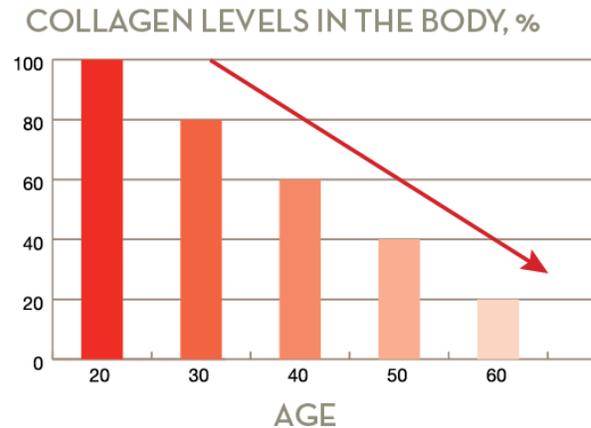
In these three layers, there are several cellular components that maintain skin structure. These components reside in the extracellular matrix. The Extracellular Matrix (“ECM”) is a three-dimensional network of extracellular macromolecules (such as: collagen, enzymes, glycoproteins, keratin, elastin, and hyaluronic acid) that provide structural and biochemical support of surrounding cells.

The main four to know and understand in detail are Collagen, Elastin, Keratin, and Hyaluronic acid.



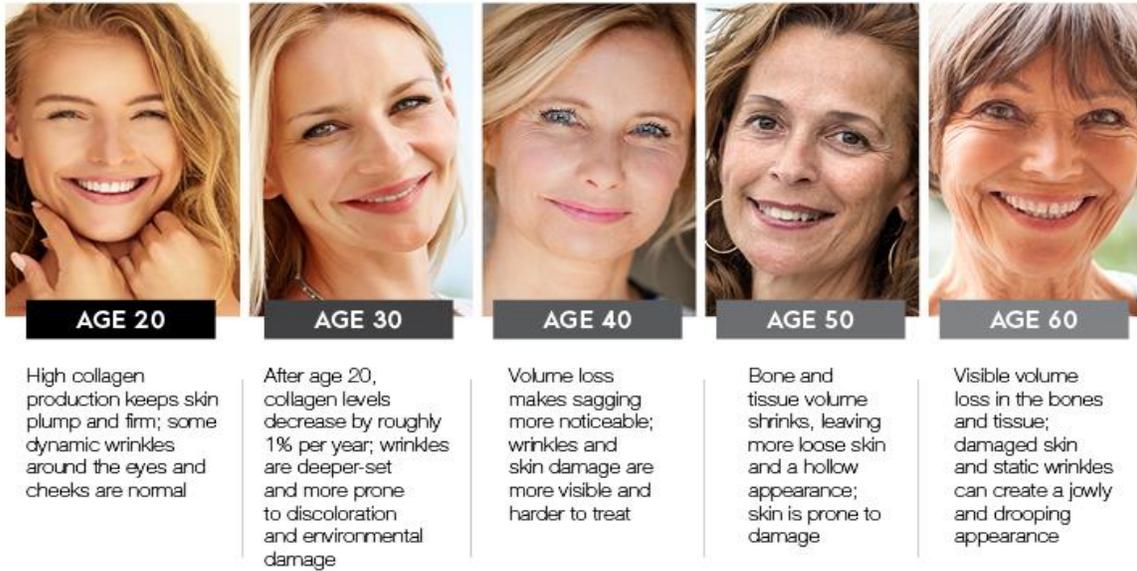
- **Collagen:** is the main structural protein in the extracellular space of various connective tissues including skin. As the main component of connective tissue, it's also the most abundant protein in mammals. Making 25% to 35% of the whole-body protein content and over 80% of *dry skin weight*.

There are many types of collagen, but over 90% of the collagen in the human body, is Type I collagen. It's the substance that holds the body together by forming a scaffold to provide strength and structure. In fact, some types of collagen fibrils, gram-for-gram, are stronger than steel. However, collagen production declines with age and exposure to factors such as smoking and UV light. Collagen is a very large molecule and thus does not penetrate the skin from the outside.



- **Elastin:** is the skin component responsible for elasticity or “bounce back”. The skin sags when elastin levels decrease. After puberty, the skin begins to produce less elastin, which is why older skin is not as supple and elastic as younger skin. Elastin is formed as a precursor, called tropoelastin, which then must be modified by the cell to form mature elastin, which is then complexed with other elastin fibers.
- **Hyaluronic Acid (HA):** is a specific type of sugar that is naturally present in the skin. It has the ability to bind to and retain up to 1,000 times its weight in water molecules. It plumps and gives volume to the skin. Although widely available, most formulations of topical hyaluronic acid do not actually penetrate into the skin as the molecule is too large.
- **Keratins:** are the major structural proteins of the vertebrate epidermis. Keratin confers rigidity to the skin and helps with its barrier protection. Together with Actin microfilaments and microtubules, Keratin filaments make up the cytoskeletons of epithelial cells.

These filaments give mechanical strength to Keratinocytes, without which the cells become fragile. And this fragility can make them prone to rupturing upon physical stress. In addition to skin, Keratins are also found in high concentrations in hair shafts, cuticles, and nails.



BEAUTY FROM WITHIN

As apparent from its structure and purpose, skin is an incredibly complex organ. However, its main function is to be a barrier to the outside world. The body synthesizes most of the key components found in the skin, hair and nails using substrates ingested through the Gastrointestinal Tract.

Although creams confer some benefit, the skin is not able to significantly absorb the nutrients required to maintain and regenerate its appearance and function.

Evolving scientific studies have depicted that in order to effectively regenerate and support the skin as an organ, nutrients must be taken orally and metabolized.

The below information will review some of the known skin repair mechanisms and detail the level of evidence for various orally-consumed ingredients.

1. COLLAGEN



Collagen, as reviewed above, is the main structural protein of the connective tissue including skin. In fact, it comprises about 80% of the skin's dry weight. It is commonly known that among other factors, collagen production



declines with age and exposure to smoking and UV light.

Specific collagen peptides contained in HealFast Rejuvenate's formulation, VERISOL (described below), have been shown to improve skin elasticity, reduce fine lines, wrinkles, maintain skin tone, and support skin healing in as little as 4 weeks.

1.1 ABSORPTION, BIOAVAILABILITY, AND MECHANISM OF ACTION

Collagen is a very large molecule and cannot be easily absorbed topically. In this large and intact form, it's also not absorbed by the gastrointestinal tract. Thus, collagen needs to be broken down into smaller components by a process known as *enzymatic hydrolysis*.

Studies show that hydrolyzed collagen, on the other hand, has a 90% rate of digestion/absorption and is available in the bloodstream within an hour. Collagen is absorbed in several ways, one via dipeptides and tripeptides, and also intact hydrolyzed amino acid peptide (up to 30 amino acids). From the bloodstream, these peptides are transported to tissue, including skin, bones, and cartilage. (1-7).

Once in the bloodstream, collagen peptides act via a dual mechanism in the skin. First, they stimulate fibroblasts via integrin and other receptors to produce more collagen and extracellular matrix (8) and they provide the ideal mixture of amino acids as building blocks for collagen production (8).

However, not all collagen is created equal. The process and result of the hydrolysis and enzymatic breakdown of collagen influences the bioavailability and stimulatory effect of the resulting peptide. Depending on the process used, molecular weight, amino acid composition and sequence play a role in bioavailability and ability to provide a stimulatory effect on the fibroblasts.

To date, the most effectively studied peptide is VERISOL, which contains a unique peptide profile, and average molecular weight of 2kDa. This unique collagen peptide has been shown to have the highest effect in triggering extracellular matrix formation (collagen and proteoglycans) among other collagen peptides of very similar specification. (9) These bioactive peptides have also been found to have an increased affinity towards connective-tissue cells, higher than individual amino acids (19)

Summarized Key Points on HEALFAST REJUVENATE'S VERISOL Collagen

- Bioactive Collagen Peptides® are polypeptides of unique shape and amino acid composition that are absorbed in an intact form, to some extent.
- The rare single helical structure of Bioactive Collagen Peptides®, formed by frequent Proline–Hydroxyproline–Glycine repeats, providing a favorable folding and stability that facilitate gut permeability.
- Bioactive Collagen Peptides® are remarkably rich in the amino acid Proline (1/4). It's known that Proline forms strong peptide bonds that are more resistant to being broken down by digestive enzymes. This improves the rate of remaining intact to be of use to the skin, hair, and nails.



- The true digestibility of Bioactive Collagen Peptides® is very high (98.4%) (18). Amino acids are important products to peptide digestion, since they're protein building blocks of new connective tissue. Approximately 10% of the Bioactive Collagen Peptides® stay intact during digestion (good bioavailability) and have a direct stimulatory impact on cell metabolism.

Verisol is made through an enzymatic hydrolysis process to produce Bioactive Collagen Peptides® from the parent collagen protein. The process is similar to human digestion, however it's much more specific and consistently produces precise bioactive sequences that have been shown to have the most stimulatory effect by in-vivo and in-vitro studies.

The results of a series of preclinical trials performed by manufacturer GELITA demonstrated that minimal differences in peptide molecular weight and structure ultimately have major effects on the efficacy of Bioactive Collagen Peptides®

Although gut digestion can break down collagen into peptides, the digestion is random and does not always cleave the collagen protein into the desired active sequences (10-12).

The absorption of HEALFAST REJUVENATE's VERISOL, is confirmed by a number of studies in-vivo which tested the concept that small, but physiologically significant quantities of polypeptides, ranging in chain length of 3 to 51 amino acids, or even small proteins of nearly 200 amino acids, can be absorbed intact through the adult gut and produce biologic effects at the tissue level. (13-14)

Specifically, Bioactive Collagen Peptides® ("BCP") comprising HEALFAST REJUVENATE's VERISOL are resistant to gastrointestinal degradation due to high levels of Proline-Hydroxyproline-Glycine repeats in the collagen. This gives the BCPs a functional shape and resistance to hydrolysis. Thus, the BCPs do not encounter the same permeability issues as the broader class of nutritional polypeptides.

Interestingly, the polypeptides that survive hydrolysis in the gut are usually high in the amino acid Proline. Proline and Hydroxyproline represent 1/4 of all the amino acids in collagen peptides, a remarkably high proportion not seen in any other protein sources. (15)

In fact, within the pharmaceutical industry, for example, the new generation of "Cell-Penetrating Peptides" – called the 'triple-helical' CPPs – are mimicking the native collagen folding in their structure for improved stability against enzymatic breakdown and provide for a safer and more efficient route for delivery of active substances across the intestinal barrier (16).

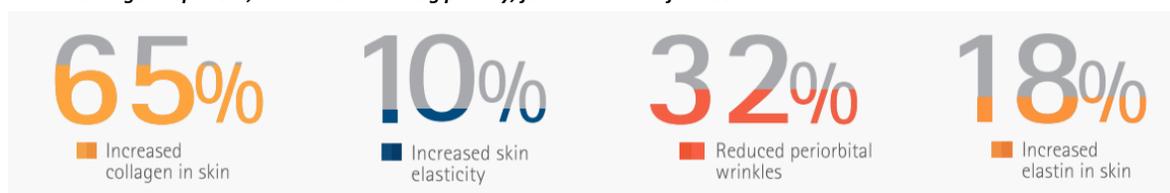


1.2 CLINICAL EFFICACY

Collagen, as an oral ingredient, has been scrutinized by the scientific community. This has largely been the case since little standardization was seen between the studies and individual peptides were not tested (with the exception of VERISOL peptides). Additionally, different peptides with different molecular weights and compositions were often used.

HEALFAST REJUVENATE focuses on a single peptide, VERISOL, as it has the most scientific merit out of all collagen peptides studied.

Please note: the results included herein may not apply to all collagen peptides, they are specific to VERISOL Bioactive Collagen Peptides®, administered at 2.5g per day, for a minimum of 4 weeks.



In one first study, 114 women aged 45–65 years, were randomized to receive 2.5 g of BCP or placebo, once daily for 8 weeks, with 57 subjects being allocated to each treatment group. Skin wrinkles were objectively measured in all subjects, before starting the treatment, after 4 and 8 weeks as well as 4 weeks after the last intake (4-week regression phase). (20)

Per the study:

The ingestion of the specific BCP used in this study promoted a statistically significant reduction of eye wrinkle volume ($p < 0.05$) in comparison to the placebo group after 4 and 8 weeks. Moreover, a positive long-lasting effect was observed 4 weeks after the last BCP administration ($p < 0.05$).

Additionally, after 8 weeks of intake, a statistically significantly higher content of procollagen type I (65%) and elastin (18%) in the BCP-treated volunteers compared to the placebo-treated patients was detected.

In conclusion, findings demonstrate that the oral intake of specific bioactive collagen peptides (Verisol®) reduced skin wrinkles and had positive effects on dermal matrix synthesis. (20)



In another study, a double-blind, placebo-controlled trial; 69 women aged 35–55 years were randomized to receive 2.5 g or 5.0 g of Collagen Hydrolysate (CH) or placebo once daily for 8 weeks, with 23 subjects being allocated to each treatment group. Results found skin elasticity in both dosage groups showed a statistically significant improvement in comparison to placebo. After 4 weeks of follow-up treatment, a statistically significantly higher skin elasticity level was depicted. (21)

Further BCPs have been shown to reduce cellulite.

A double-blind, placebo-controlled clinical study, 105 women aged 24–50 years with moderate cellulite were randomized to orally receive a daily dosage of 2.5 g BCP or a placebo over 6 months. In addition, skin waviness, dermal density, and the length of the subcutaneous borderline were assessed. BCP treatment led to a statistically significant decrease in the degree of cellulite and a reduced skin waviness on thighs ($P < 0.05$). Moreover, dermal density was significantly improved ($P < 0.05$) compared to the placebo. (22)

The Bioactive Collagen Peptides in VERISOL® have also been shown to improve the growth and health of fingernails.

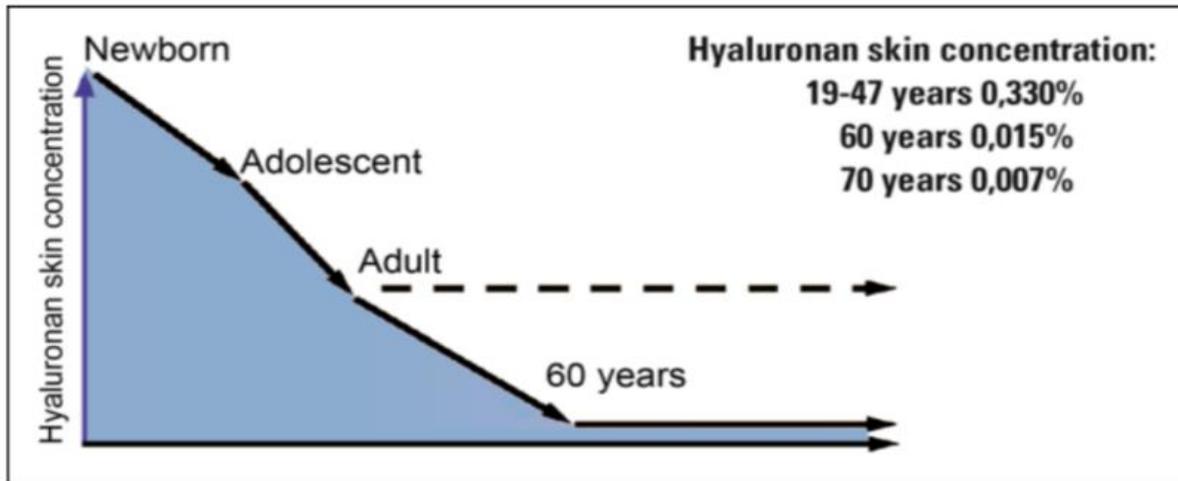
Research showed a decrease in cracked and/or chipped nails after 2 months of treatment, reaching a decrease of 42% after 6 months. Compared to the control group, the nail growth speed was increased, and simultaneously, there were notable improvements in nail peeling and clearly decreased nail edge irregularity. 80% of the patients were completely satisfied and satisfied with VERISOL® treatment. 75% of the women perceive their nails as longer, while 71% said their nails grew faster and became longer (66).



2. HYALURONIC ACID

Hyaluronic acid (“HA”) is a high-molecular-weight polysaccharide composed of repeated polymeric disaccharides of D-glucuronic acid and N-acetyl-D-glucosamine. (23) HA is a major component of the skin’s extracellular matrix and plays a key role in the metabolism of the dermis. It’s one of the most hydrophilic molecules in nature and has been described as “nature’s moisturizer”. (23, 24)

2.1 CLINICAL EFFICACY



With aging, the epidermal HA content decreases from 0.03% in women aged 19 to 47 years down to 0.015% in women aged 60 years and halves to 0.007% in women aged 70 years. (25)

One trial tested HAs with 2 different molecular weights improved the skin condition by increasing the moisture content. These trial involved Japanese women aged 35 to 60 years, who complained about dry and sagging skin or wrinkles around the outer canthus. (26)

Another study, tested 20 female subjects with healthy skin in the age group of 45 to 60 years. For the study, they took the product once daily for 40 days and found that intake of the HA solution led to a significant increase in skin elasticity, skin hydration, and to a significant decrease in skin roughness and wrinkle depths. (27) An increase in skin hydration was up to 37%, elasticity gained was up to 26%, skin roughness decreased by up to 30%, reduction of wrinkle depths was up to 37%. Participants also noted stronger hair and nails as part of the study, and 70% of patients would recommend the HA supplementation.





These findings have been echoed by multiple other studies as depicted in the table below:

Test method	Test design	Substance	Subjects	Results	References
Oral consumption of HA at 240 mg daily for 6 weeks	Randomized, double-blind, placebo-controlled trial	HA (M.W.: 80 K)	22 patients with dry skin (in Japan)	Improved dry skin on the face and whole body Significant increase of skin moisture	Kajimoto, O. <i>et al.</i> (2001) [15]
Oral consumption of HA at 120 mg daily for 4 weeks	Randomized, double-blind, placebo-controlled trial	HA (M.W.: 80 K)	35 patients with dry skin (in Japan)	Significant increase of skin moisture	Sato, T. <i>et al.</i> (2002) [16]
Oral consumption of HA at 120 mg daily for 6 weeks	Randomized, double-blind, placebo-controlled trial	HA (M.W.: 80 K)	39 female patients with dry skin (in Japan)	Significant increase of skin moisture	Sato, T. <i>et al.</i> (2007) [17]
Oral consumption of HA at 120 mg daily for 6 weeks	Randomized, double-blind, placebo-controlled trial	HA (M.W.: 30 K)	42 female patients with dry skin (in Japan)	Significant increase of skin moisture	Yoshida, T. <i>et al.</i> (2009) [18]
Oral consumption of HA at 37.52 mg daily for 30 days	Randomized, single-blind, placebo-controlled trial	Mixture containing HA (M.W. of HA: 2,500)	107 healthy subjects (in China)	Significant increase in skin moisture Significant increase in skin pH	Terashita, T. <i>et al.</i> (2011) [19]
Oral consumption of HA at 100 mg daily for 12 weeks	Prospective open-label trial	Mixture containing HA(M.W.: unknown)	26 healthy female subjects (Caucasian, African-American, Hispanic, and others)	Improved aging symptoms on the face	Schwartz, S. R. <i>et al.</i> (2012) [20]

2.2 ABSORPTION

In regards to HA absorption: In the oral administration test of radioactively labeled, high Molecular Weight (MW) HA (MW: 1×10^6), approximately 90% of ingested HA was absorbed and used by the body (rodent study).

It is noted that this radioactively labeled, high- and low-MW HA (MW: 1×10^6 and 1×10^5 , respectively) accumulated preferentially in skin tissues. (28,29)

2.3 MECHANISM OF ACTION

HA oligosaccharides (MW: $1-2 \times 10^3$) increases HA production in human fibroblasts by displacing endogenous HA from the receptors and promoting a stimulatory effect on further HA production (30). It's been shown that low MW HA are used as primers when high-molecular-weight ("MW") HA is synthesized in cells (31). Another study shows that High MW HA (MW: 1.1×10^6) promotes cell proliferation of human fibroblasts and increased population of collagen lattices (33).

Overall, HA seems to work in two ways. First, it stimulates an increase in the number of HA producing cells. Increased in number of cells hence increases the number of cells that suppress the skin's water loss. Second, HA also seems to increase the amount of HA synthesis in the in these cells.



It appears that both low- and high-MW HA transfers to the skin and affect the fibroblast cells to promote HA synthesis and cell proliferation. Both of which contribute to skin moisture (retention) and collagen production.

3.0 NAD⁺ SYSTEM AND NICOTINAMIDE

Nicotinamide adenine dinucleotide (NAD⁺) is a critical signaling molecule and an essential substrate for “sirtuins” - a class of enzymes that mediate several pathways involved in aging and age-related physiological changes. Nicotinamide is the precursor of Nicotinamide Adenine Dinucleotide (NAD), a key coenzyme in the production of adenosine triphosphate (ATP). ATP is our cellular energy “currency” that transports chemical energy within cells.

The availability of NAD⁺ and related metabolites declines in humans during normal aging (51-54) and may contribute to physiological aging. **Nicotinamide supplementation has been shown to increase NAD⁺ levels in humans with a number of studies evaluating the effect on increasing life-span, preventing neurological degeneration, improving cardiovascular health, mitigating cancer risk, and improving the immune system function.**

Although the verdict is still out on some of the above uses, Nicotinamide has been shown to be safe and well-tolerated in a number of human studies. The safety of high-dose nicotinamide has been reviewed by Knip and colleagues who concluded, based on 19 previous studies, that ‘nicotinamide has been used at pharmacological doses (of up to 3 g/day) in many people over many years with a low incidence of side effects and toxicity’ (55).

The effects on cardiovascular health, lifespan, and overall cancer risk are difficult to evaluate. Ultimate verdicts on these uses are still out. **However, it’s clear that Nicotinamide can reduce the incidence of skin cancer.**

A 2016 Phase III clinical trial published in New England Journal of Medicine evaluated 386 high-risk participants and found a 23% lower rate of non-melanomatous skin cancers, 20% lower rate basal cell cancers, and 30% lower rate squamous cell cancers, all compared to placebo. These findings have previously been confirmed with Phase I and II trials.

Participants taking Nicotinamide have been shown to have reduced fatigue, better energy levels and sleep, and reduced skin water loss. Many participants also note improved appearance and complexion.

As mentioned, a number of studies are currently evaluating Nicotinamide for a number of uses. We will review the preliminary conclusion of these studies below. Nicotinamide Potential Benefits:

1. May Protect the Brain

NAD⁺ plays a key role in brain health. NAD⁺ helps control the production of PGC-1-alpha, a protein that appears to help protect cells against oxidative stress and impaired mitochondrial function. Current



research suggests that both oxidative stress and impaired mitochondrial function are linked to age-related brain disorders such as Alzheimer's and Parkinson's disease (56, 57).

Although human studies are currently underway, animal studies in Alzheimer's disease showed nicotinamide to increase NAD⁺ levels and PGC-1-alpha production by up to 70% and 50%, respectively. It was also noted that treated mice performed significantly better in memory-based tasks at the end of the study (58). Further Nicotinamide treated patient with Parkinson's disease (59) had higher NAD⁺ levels and significantly improved mitochondrial function.

2. May Improve Cardiovascular Function

During aging, blood vessels in our bodies become thicker, stiffer and less flexible. Such changes can raise blood pressure levels and cause strain on the heart. In animals, raising NAD⁺ helped reverse age-related changes to arteries. In one study in humans, nicotinamide riboside raised NAD⁺ levels, helped reduce stiffness in the aorta and lowered systolic blood pressure in adults at risk of high blood pressure (60).

3. May Help with Weight Control

In an animal study, nicotinamide helped speed up the metabolism of mice. It is, however, still unclear how much of this effect and to what degree it applies to humans. (61)

4. May Lower Risk of Cancer

High NAD⁺ levels were noted to protect against DNA damage and oxidative stress. These are the changes that have been linked to cancer development (62,63).

5. May Improve Muscular Function and Energy

Raising NAD⁺ levels helped improve muscle function, strength and endurance in mice. Again, it isn't yet clear how much this translates to humans, and more studies are needed. (64,65).

4. ANTIOXIDANTS, VITAMINS, AND MINERALS

Below we address the cofactors that are needed to keep skin healthy. Collagen, HA, and Keratin require several vitamins and minerals for proper synthetic function and maintenance. Even a slight deficiency in these factors can adversely impact skin health.

Since skin undergoes turnover every 27 days, so it's particularly imperative to maintain repletion of these cofactors.

4.1 VITAMIN C



Vitamin C (ascorbic acid) is a strong antioxidant and has a crucial role in collagen synthesis. Dietary Vitamin C has been shown to help prevent and treat ultraviolet (UV)-induced photodamage, dry skin, and prevent formation of new wrinkles and pigmentation.

Vitamin C is normally found in high levels in the skin, in both the dermis and epidermis (36,37). Aging, however, causes a decline in Vitamin C content in both the epidermis and dermis (37). Excessive exposure to UV light or pollutants (e.g., cigarette smoke and ozone) may also lower Vitamin C content, primarily in the epidermis (38-40).

As an antioxidant activity of Vitamin C protects against UV-induced damage caused by free radicals (41) UV light decreases Vitamin C content of the skin, an effect that is dependent on the intensity and duration of UV exposure (38-40)

The accumulation of oxidative damage to proteins is a distinguishing feature of both photodamage and intrinsic aging. This oxidative damage can lead to changes in skin structure.

In addition to its antioxidant functions, Vitamin C regulates the synthesis of the structural protein collagen. The role of Vitamin C in the hydroxylation of collagen molecules is well characterized (42).

Hydroxylation of collagen is necessary for its extracellular stability and support of the epidermis. Vitamin C also increases the proliferation rate of fibroblasts and stimulates DNA repair in cultured fibroblasts. (43)

Two observational studies found that higher intakes of Vitamin C from the diet were associated with better skin appearance, with notable decreases in skin wrinkling (44-45). Vitamin C may have additional roles in wound healing, for example, by promoting Keratinocyte differentiation (46, 47), stimulating the formation of the epidermal barrier (46), and re-establishing the stratum corneum (48). Additionally, higher intake of dietary Vitamin C has been correlated with a decreased risk of dry skin (49)

B-VITAMINS AND MINERALS

B-Vitamins are responsible for incredibly diverse functions in human physiology, some of which involve skin physiology. There have been several small studies to suggest that they may be individually involved in skin health. However, it is fully noted that B-vitamins are integral to collagen and extracellular matrix synthesis and to the skin's structure, function, and metabolism. **The most notable vitamins that have scientific evidence are Biotin, Niacin, and B-6.**

Additionally, two important minerals are required for extracellular matrix regeneration and have shown effects in skin regeneration and wound healing. These include Zinc and Copper. They are required only in small amounts, but deficiency in either drastically reduces healing and regeneration rates. Resultantly, due to rapid skin turnover and continued synthesis, it remains important to continually maintain adequate levels of these important cofactors.



CONCLUSION

In summary, the skin is a complex organ that maintains physiological homeostasis and acts as a barrier from the outside environment.

Skin health is often a reflection of overall bodily health.

Although topical skincare products intervention can be considered, many agents are not able to cross the skin barrier and often do not support skin metabolism effectively.

Novel scientific advances, discussed herein, have suggested several agents and mechanisms of stimulating regenerative processes in the skin when taken orally. Due to the weight of science behind them, they are worth consideration for maintaining skin health and regenerating skin tissue.

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