bend
BEAUTY

THE ULTIMATE GUIDE TO SKIN HEALTH & LONGEVITY

Section 1

How Diet, Lifestyle, and the Environment Impact Your Skin

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NOTICE TO READER

This book is not intended to provide medical advice or to take the place of medical advice and treatment from your personal physician. Readers are advised to consult their doctors or qualified health professionals regarding specific health questions. Neither the publisher nor the author takes responsibility for the possible health consequences of any person reading or following the information in this book. All readers, especially those taking prescription or over-the-counter medications, should consult their physicians before beginning any nutrition or supplement program.

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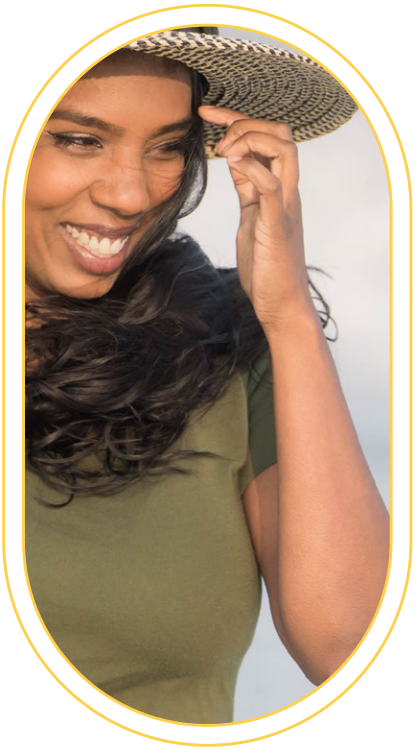
About this eBook Series

This series is divided into three separate sections to make it easier to enjoy.



Section 1

How Diet, Lifestyle, and the Environment Impact Your Skin.

Focuses on skin health and longevity, and what influences both.

Section 2

More than Skin Deep: The Latest Science of Skin Health & Aging

Describes what your skin reveals about your health, and how it impacts your health.

Section 3

The Top Foods and Nutraceuticals to Benefit Skin Health & Longevity

Presents the clinical research supporting the benefits of our favorite foods and supplements to maintain your skin health and longevity.

Welcome

Let us focus our thoughts on your journey though Section 1. You will:

Learn about Skin Structure and Function

- Describes your skin's structure and its function as a protective chemical and physical barrier between you and the outside world as part of your body's total antioxidant defense and detoxifying systems.
- It establishes the connection between your skin health and longevity and defines skin aging.

Learn about Factors Influencing Skin Health

Describes what factors influence your skin health including:

Your specific Skin Climate® that is partly governed by your unique genetic make-up

- Environmental factors including your diet and lifestyle
- Your level of exposure to:
  Pollution/environmental toxins
  UV radiation from sunlight
- Includes explanations of how each of those factors directly impact your skin and overall health.

You will learn that healthy skin and longevity is a lot about maintaining proper balance!

PRO TIP

While reading this series, you may encounter some unfamiliar terms. Relax, take your time, and use the **Glossary of Terms** at the end to help you understand the meaning of any such words you may encounter along your journey.

There is also a **List of Abbreviations** to remind you of what various acronyms stand for if you need it. In addition, there is a **Conclusion** provided at the end of each **Section**, where simply explained summaries of what you just read are provided. Stopping at those locations will allow you to refresh and gather your thoughts before proceeding to your next destination.

And fear not, even if you don't understand all the details discussed (i.e., the WAY that things function or physiological changes that take place), you will still learn a lot about which foods and supplements can enhance various aspects of skin health and those that can contribute to your longevity.

The knowledge you gain will be well worth your effort. Your life could depend on it.

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1.0

Introduction

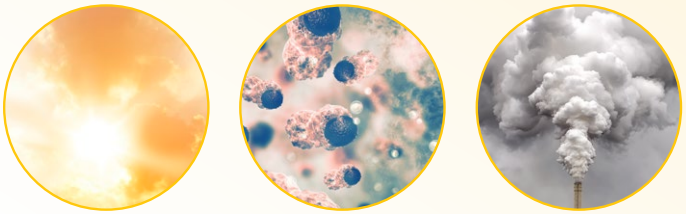
Beautiful skin is about how you look and feel. It's the nourishing of body and mind, which radiates with confidence to the world around you.

Your skin's appeal is attributed to its texture, colour, smoothness, and characteristics such as elasticity, firmness, moisture content, and sweat and sebum production[1].

Your skin is also your largest organ. Necessary to your survival, it provides a chemical and physical barrier that protects you from harm including pathogens, sunlight, pollution, temperature changes and dehydration[1]. It can detect heat, cold, pressure, touch, and pain, which allows you to interact with your environment without injury and enables you to derive pleasure. It also synthesizes vitamin D and enables topical drug delivery. But its most understated roll is as a **secondary detoxifying organ** that is part of your body's **total antioxidant defense** and **detoxifying systems**. Through these

means, your skin helps to inactivate reactive substances that can cause cell and tissue damage. These substances arise from exposure to[2]:

- **Sunlight**
- **Internally produced waste substances**
- **Externally derived toxins**



Your skin helps to inactivate and excrete these toxic substances, that otherwise would build up within your body, and could contribute to various age-related diseases[2-6].

Maintaining healthy skin, is therefore not just about looking your best and feeling good about that, it is more about keeping you healthy, and most importantly, keeping you healthy longer!

Like any other organ, your skin needs to be healthy to function correctly. That health, and ageing of your skin, depends on many internal and external factors. Since your skin is in constant contact with the external environment, it is subject to more insults than most of your other organs. Hence, your skin is where the first visible signs of ageing occur [7].

External factors, such as excessive sun exposure, extreme climatic conditions, air, and water borne pollution, and stress can promote skin ageing and the incidence of skin problems. But the rate of skin ageing also depends on genetic factors (i.e., what you inherit from your parents and grandparents), exercise, adequate rest, and in particular diet. An imbalance towards the negative factors contributes to skin photo-ageing and inflammation and can significantly affect immune function and ultimately your health [1].

Macro- and micro-nutrient status is well accepted to be important for skin health and appearance [1, 7, 8]. These nutrients, as well as other beneficial bioactive substances, can come from various:

- **Whole foods** including vegetables, berries, mushrooms, nuts, and seafood.
- **Supplements** including specific vitamins, minerals, bioactive peptides, polysaccharides, polyphenols, carotenoids, and polyunsaturated fatty acids.

Their regular intake may protect against sun damage and signs of skin ageing based on various human clinical trials. In addition, selected supplement use is a promising strategy to relieve certain skin disorders, and prevent, delay, or minimize premature skin ageing [1].

This eBook leads you on a scientific journey to discover the connection between healthy skin and longevity. First, you will learn what influences your skin health. Then you will find out what your skin reveals about your health and how your skin impacts your health, as we travel through the Gut-Skin Axis, the Liver-Skin Axis, and the Brain-Skin Axis. Along the way, you will learn about all the research and human clinical studies highlighting the benefits of our favorite foods and supplements to maintain your skin health and longevity.

PRO TIP

GOOD TO KNOW:

Your liver is your primary and your skin is your secondary detoxifying organ.

CLEARLY DEFINED:

Macronutrients are proteins, carbohydrates, and fats.

Micronutrients are vitamins and minerals.

2.0

Skin Health & Longevity

Changes in the appearance of skin are often the first visible signs of ageing and this can have implications for our emotional and mental wellbeing [7].

Visible signs of skin ageing include wrinkles, sagging, and pigmentation that can affect your facial shape, texture, and color [9]. Skin sagging, and wrinkles especially, influence how we see other people, and can also make us afraid of social exclusion if we have them [10]. In fact, a study of 1713 mostly Caucasian American women, over 50 years old, found their ageing self-image and society's response to their ageing, caused them great mental suffering.

More than 50% of them felt a change in the way people, and society in general, responded towards them, at the same time that their sagging skin and wrinkles began [11]. This point is extremely important because it shows how much women link the start of their emotional pain related to ageing, with the appearance of wrinkles and sagging; two main clinical signs of skin ageing [10].

Well, what exactly is skin ageing? Before we can understand that we need to understand what constitutes *healthy skin*.

Healthy and youthful skin is perceived as soft, smooth, even colored, and moist; or at least not dry. Rough, dry skin develops when water is lost from its surface and is not adequately replenished from within its lower layers. This is called trans epidermal water loss (TEWL). So, skin health is measured based on its TEWL, roughness, and colour, where more intense redness indicates greater inflammation. In addition, structural properties such as elasticity, firmness and fatigue tell how well the skin can stand up to everyday abuse. For example, skin that has good elasticity can stretch when required and bounce quickly back to its original shape without sustaining injury or wear. This quality along with firmness and strength enable healthy skin to function properly. Unfortunately, it is these qualities that deteriorate with age, which is evident through development of wrinkles, sagging and thinning.

2.1 Skin Structure

Your skin is composed of three layers *(Fig. 1)*:

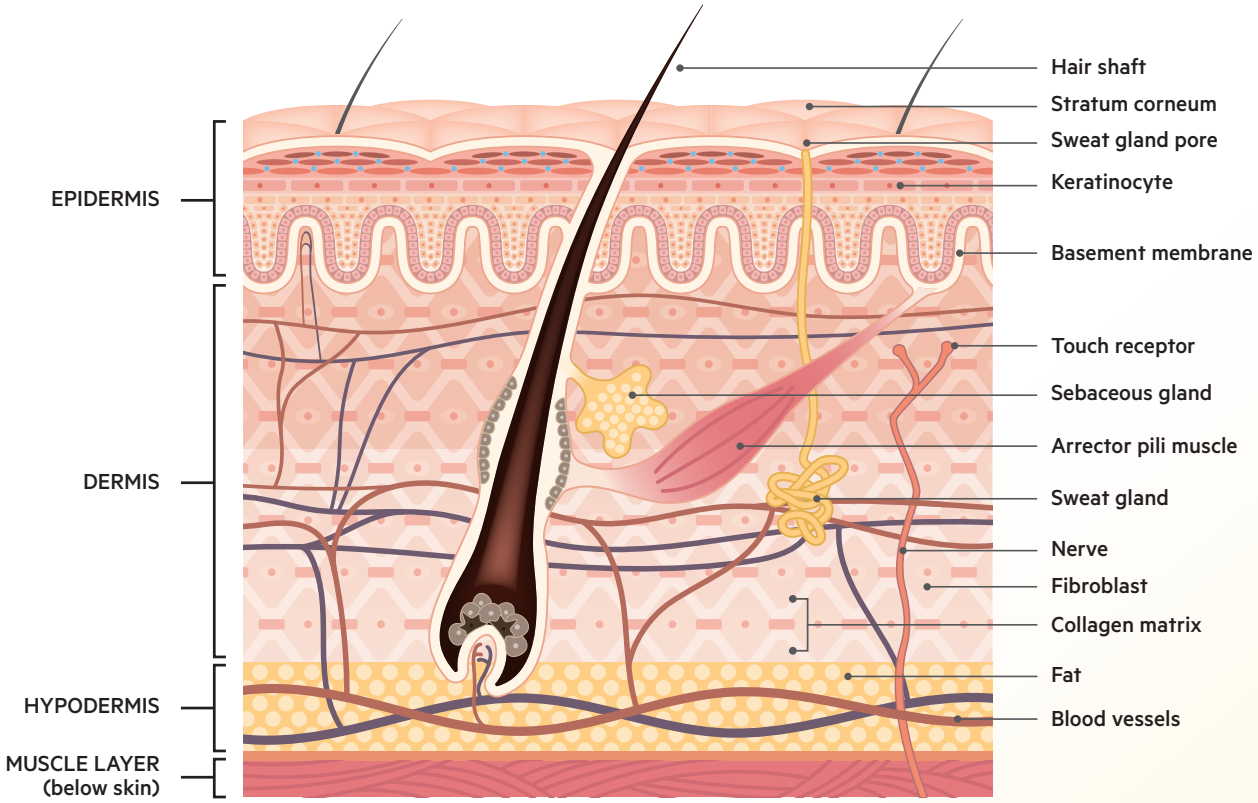
- The **epidermis** is the outer barrier layer made up of cells, mostly keratinocytes
- The **dermis** is the inner layer that provides strength, elasticity, and nutritional support for the epidermis.
- The **hypodermis** is the lower fatty layer that stores nutrients for energy production and insulates the body from temperature changes and physical trauma. It connects the skin to the muscles and bones below [12].

Interspersed throughout the top two skin layers, are hair follicles and sweat and sebaceous glands. Between the top two layers is a specialized basement membrane that attaches the epidermis to the dermis [7]. It contains stem cells that have self-renewing capacity that can persist throughout life and are critical for proper epidermal regeneration [12].

The epidermal keratinocytes are arranged in layers which form as they divide and specialize to perform their unique function, while moving away from the basement membrane and towards the skin's surface [7]. While doing so, they undergo a process called keratinization, where they produce and secrete specialized proteins and lipids/fats, while losing their organelles (Think about it like you losing your organs, like your liver, kidneys, etc.). Consequently, the uppermost skin layer that interacts with the outside world is composed of flattened metabolically 'dead' cells. These cells are stuck together with lipids that form a water-impermeable barrier known as the stratum corneum [7].

Your epidermal homeostasis (balance/stability) relies on finely tuned processes. For example, when stem cells divide and multiple, they need to "make a choice", between remaining as stem cells or specializing to become

Figure 1: Skin Structure



keratinocytes. When things go wrong in such processes, it can cause skin ageing and/or tumor formation [12].

The dermal layer has fewer cells than the epidermis. However, it has many blood and lymphatic vessels, and nerves, and consists primarily of extracellular matrix [7], which is the mixture of substances that are secreted by skin cells and that fill spaces between them.

Fibroblasts are the main cells within the dermis. They are involved in various processes including growth of healthy skin, wound healing, skin ageing, and cancer development and growth [12]. They produce and maintain the extracellular matrix components including substances such as ceramides, hyaluronic acid, and proteins called collagen and elastin. Elastin is also synthesized by keratinocytes [13]. These protein fibers are held together by bonds within and between strands, to form a dense network throughout the dermis, which provides structural support for the epidermis [14].

All the extracellular matrix components are critical to maintain skin integrity and architecture [15]. For example, dermal elastic fiber changes cause loss of flexibility and tensile strength, damaging collagen changes induce skin stiffness [16], and loss of hyaluronic acid leads to dry skin [14] that is less able to maintain its shape [10]. Since elastin plus collagen fibers contribute to skin elasticity [17], damage to or loss of either or both, impairs skin's contractile properties [18], making it prone to sagging and wrinkles. All these changes are associated with ageing [15].

2.2 Skin Function

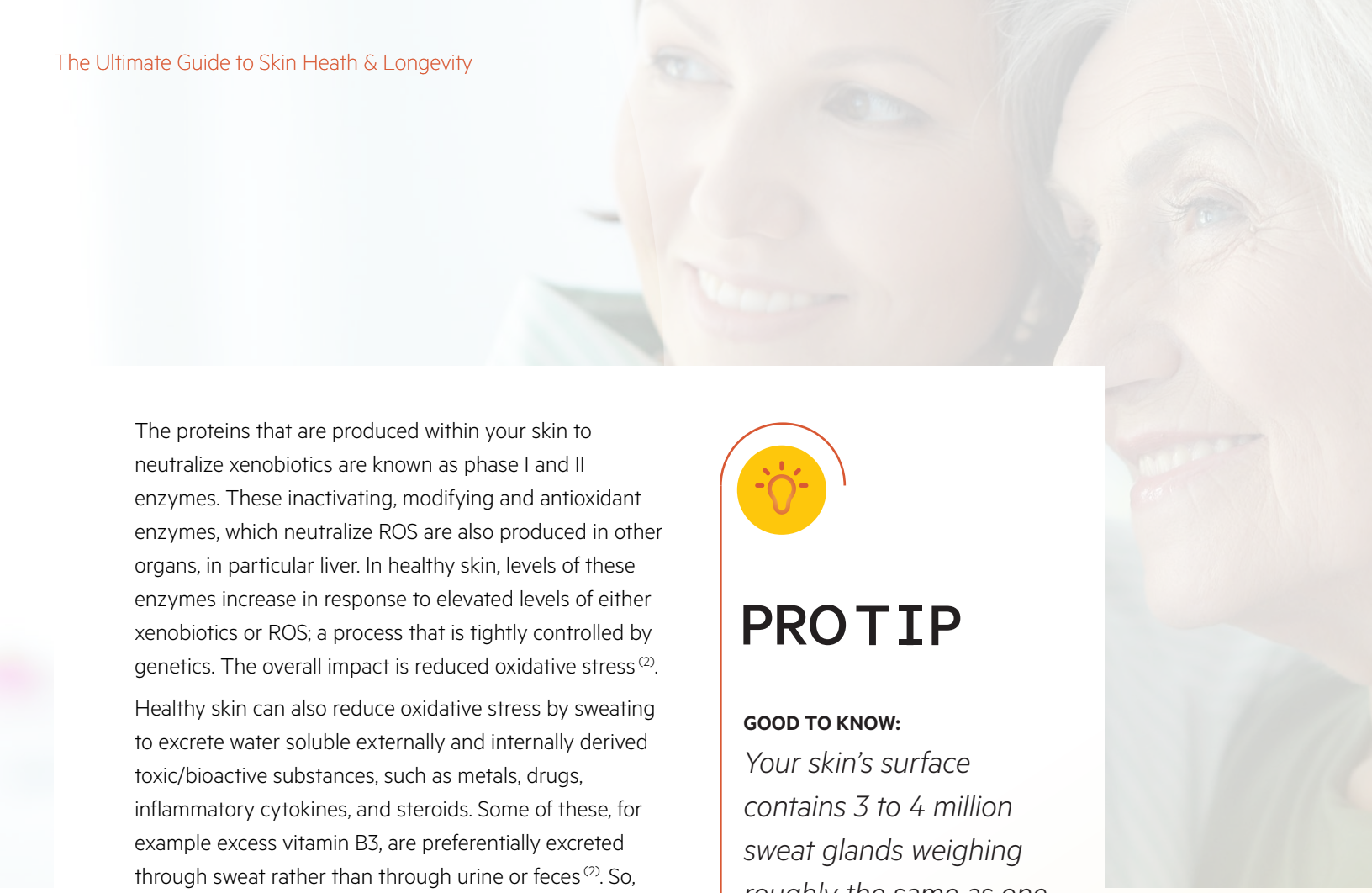
Your skin's primary function is to create a chemical and physical barrier between you and the outside world.

Physical Barrier: The epidermal stratum corneum creates a water-impermeable barrier [14]. The effectiveness of that barrier depends on its properties including the amount of sebum produced, hydration, TEWL, and skin surface pH [19]. The dermal scaffolding created by its network of collagen and elastin fibers, along with the help of hyaluronic acid [14], entraps fluids, which helps maintain skin moisture and permits exchange of ions, nutrients, metabolites and waste products with surrounding cells and tissues [17].

Both collagen and elastin are susceptible to degradation by protein digesting enzymes [20] that play an important role in tissue remodeling associated with various normal or disease processes such as forming new tissues, angiogenesis (forming new blood vessels), tissue repair and wound healing. However, they can also contribute to skin ageing by digesting collagen and elastin, which destabilizes the extracellular matrix, leading to fragile and loose skin. The protein digesting enzyme production is precisely controlled by genetics to maintain extracellular matrix homeostasis. However, many stresses, including ultraviolet (UV) irradiation from sunlight, can modify their gene expression, which may impact skin function/health and appearance [15].

Chemical Barrier: The above-mentioned changes to the physical barrier that impact its function are visibly apparent. However, while those are taking place, invisible changes are also occurring that negatively impact the chemical barrier function. These changes affect the skin's total antioxidant defense and detoxifying systems, and that interferes in its role as a secondary detoxifying organ. In that capacity, your skin helps [2]:

- **Scavenge and inactivate reactive oxygen species (ROS).** These are highly reactive and unstable molecules that can cause severe damage to surrounding molecules and ultimately cells and tissues. They include, but are not limited to, free radicals. For example, they also include things like lipid peroxides, that are not free radicals.
- **Inactivate and neutralize xenobiotics.** These are externally derived chemicals including heavy metals, drugs, environmental pollutants, cosmetics, and dietary components such as food additives and synthetic supplements. If these toxins build up within your body, they are one of the major sources of ROS [2] and may contribute to developing various age-related diseases [2-6].
- **Facilitate toxin excretion through sweat and sebaceous glands.**
  - Externally derived inactivated xenobiotics can be excreted through sweat.
  - Internally produced bioactive waste substances such as hormones, and excess lipids and cholesterol, can be excreted through sebaceous glands [2].



The proteins that are produced within your skin to neutralize xenobiotics are known as phase I and II enzymes. These inactivating, modifying and antioxidant enzymes, which neutralize ROS are also produced in other organs, in particular liver. In healthy skin, levels of these enzymes increase in response to elevated levels of either xenobiotics or ROS; a process that is tightly controlled by genetics. The overall impact is reduced oxidative stress [2].

Healthy skin can also reduce oxidative stress by sweating to excrete water soluble externally and internally derived toxic/bioactive substances, such as metals, drugs, inflammatory cytokines, and steroids. Some of these, for example excess vitamin B3, are preferentially excreted through sweat rather than through urine or feces [2]. So, your skin's ability to sweat is important to help remove toxins from your body!

Finally, healthy skin helps eliminate excess lipids from your blood stream. These fats-soluble substances, that do not dissolve readily in water, include triglycerides, fatty acids, cholesterol, squalene, and wax esters. Studies show these substances are secreted in sebum after eating a fatty meal. This highlights skin's minor role in helping to maintain triglyceride and cholesterol homeostasis [2]; two risk factors associated with metabolic syndrome [21]. Metabolic syndrome is a group of health problems that occur together, increasing your risk of heart disease, stroke, and type 2 diabetes. They include increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal blood cholesterol or triglyceride levels.

PRO TIP

GOOD TO KNOW:

Your skin's surface contains 3 to 4 million sweat glands weighing roughly the same as one kidney, that can perspire roughly 10 liters of toxin removing fluid daily [2].

2.3 The Link between Skin Health and Longevity

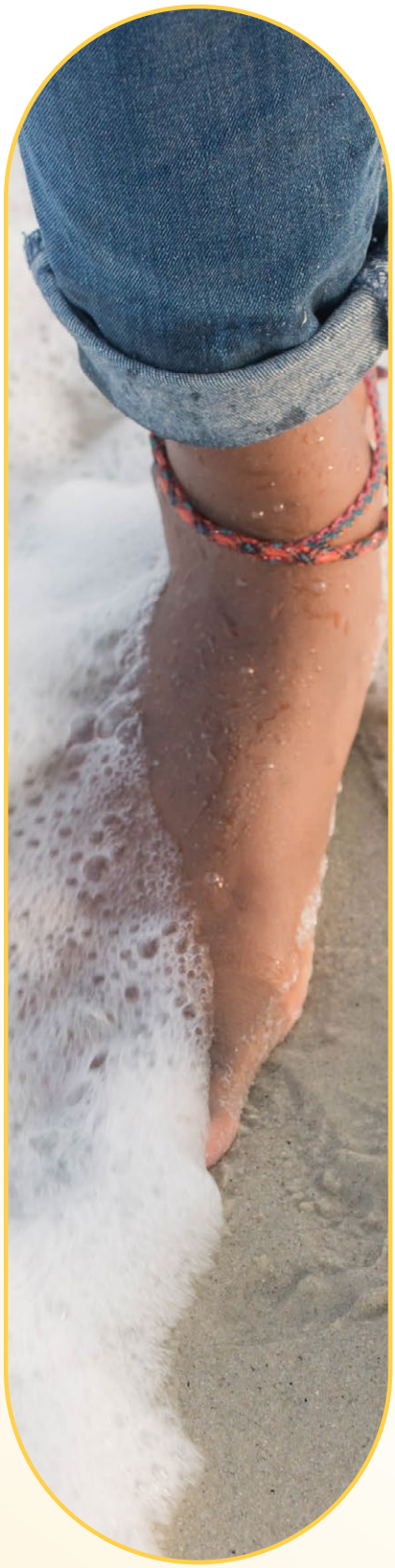
Metabolic syndrome and its associated health problems often accompany skin disorders. For example, Acanthosis nigricans, a condition that causes skin discoloration in body folds and creases, frequently develops in people with metabolic syndrome, insulin resistance, obesity, and type 2 diabetes [2]. But even more intriguing, **fewer skin wrinkles are often associated with lower blood pressure, a lower risk of heart disease and stroke, and longer life expectancy** [22]**!**

That fact solidifies the idea that an individual's skin appearance, and by association its function, reflects how well their entire body is ageing.

This connection was seen in a group of 261 women regardless of their chronological age, smoking status, degree of skin photodamage, or body mass index (BMI) [22]. Earlier studies found that the age a person looks in their photo, regardless of their real chronological age, can be used to predict their death, physical and cognitive abilities, and telomere length [23]. These findings suggest that perceived age and skin wrinkling, especially in sun protected areas, might indicate biological age and health status [24] which could impact longevity.

Longevity, that is, how long you live, is influenced by your genetics, environment, and lifestyle. People who live long lives share lifestyle similarities — many are nonsmokers, are not obese, cope well with stress, and most are women. Because of their healthy habits, they are less likely to develop age-related chronic diseases, such as high blood pressure, heart disease, cancer, and diabetes, than their same-age peers, regardless of their sex. In addition, longer life spans tend to run in families, which suggests that shared genetics, lifestyle, or both play an important role in determining one's longevity [25].

The link between youthful looking skin and better health and longevity, brings a whole new meaning to skincare. Protecting your beauty becomes all about giving your skin what it needs to be healthy and to function optimally, which can slow or turn back your clock, so you survive longer. Your skincare becomes part of creating a beautiful life!



2.4 Skin Ageing

The Problem: During ageing, skin gradually loses its structural and functional characteristics, and becomes more fragile and vulnerable to damage, which may contribute to age-related diseases and death. It loses sweat and sebaceous glands[26], collagen and elastin fibers, and hyaluronic acid, and the epidermis and dermis become thin. Combined, this can cause sagging, wrinkles, cellulite [13] and uneven pigmentation or blotches and age spot [14].

Such damage is accelerated by factors discussed in Part 3.0 What Influences Skin Health? In addition, the ability to replenish lost or damaged collagen decreases by about 1.5% annually after 21 years of age, partly because the fibroblasts make smaller amounts [27]. Changes after menopause are even more striking, including a 30% skin collagen loss in the first 5 years and a 0.6% annual loss of elastin. In addition, collagen biosynthesis remains low and is insufficient to repair or even replace lost collagen [28]. Simultaneously, the production [29] and activity [30] of enzymes that break down collagen and elastin increase, which further contributes to skin tone loss.

Skin ageing negatively affects its permeability, angiogenesis, lipid and sweat production, immune function, vitamin D synthesis, wound healing, body temperature regulation, fluid balance, electrolyte and protein homeostasis, waste removal, sensory perception which creates vulnerability to external stimuli, and its ability to protect other organs against harmful environmental factors [31]. It can also lead to development of benign and malignant diseases (skin cancer) [32].

Intrinsic ageing is genetically determined and is unavoidable. It involves irreversible degenerative changes with age [32] including atrophy, fibroblast and collagen loss, and blood vessel thinning. However, extrinsic ageing can be modified. It primarily results from exposure to sunlight and other environmental factors [29], poor sleep and nutrition, and stress [32, 33], which leads to increased production of protein degrading enzymes [29], collagen and elastin degradation, loss of hyaluronic acid, further reduced fibroblast numbers [28], and increased inflammation and apoptosis/cell death [29].

The Solution: Prevention is the best and most effective way to fight extrinsic skin ageing [33]. That process can be slowed by modifying the contributing factors mentioned above. For example, by ensuring adequate nutrition to optimize skin resiliency, which ultimately impacts skin health, appearance, and longevity.

3.0

What Influences Skin Health?

Your Skin Climate®, or underlying condition, impacts how your skin functions.

In the same way that overall climatic conditions impact our weather, your Skin Climate® impacts how your skin functions. Think about it like this. A tropical climate is typically hot and humid, while a polar climate is cold and dry. In the same way, an inflammatory Skin Climate® has low levels of antioxidants and internal antioxidant enzymes, while a normal/healthy Skin Climate® has ample levels of these important protective agents.

Your Skin Climate®, or underlying condition, impacts how your skin functions.

For example, a Skin Climate® with adequate antioxidants and internal antioxidant enzymes might reduce your chances of getting a sunburn, in the same way that using rain gear protects you during a tropical rainstorm. On the other hand, a Skin Climate® that does not have enough antioxidants and internal antioxidant enzymes cannot protect you from the sun's ray, in the same way as accidentally leaving your rain gear on the bus cannot protect you from the rain when you are trekking through the rain forest!

3.1 Skin Climate®

Your Skin Climate® impacts how your skin functions by influencing homeostasis, tissue breakdown, repair and thus, the ageing process. Since your body is what nourishes your skin, what you put inside it has a bearing on your Skin Climate®, in addition to your overall health.

In essence, what is happening on the inside, drastically affects what you see on the surface[33]. Your beauty comes from within!

Skin Climate® is affected by various dietary and lifestyle habits as well as environmental factors, and this can impact your health. In fact, your resulting skin health can tell a lot about what ails you. According to the American Academy of Dermatology, skin changes, including rashes, growths, discoloration, and texture differences, can indicate serious health problems[34]. For example, gastrointestinal disorders are often accompanied by visual skin changes, and many skin abnormalities are associated with liver damage. Similarly, troublesome skin problems occur in various psychiatric disorders..

In essence, your skin condition reflects what is happening inside your body, including your inflammatory status. Many common skin conditions, including accelerated skin ageing, stem from inflammation[32]. In addition, deteriorating skin properties can indicate chronic systemic inflammation, that is, inflammation throughout your entire body[19]. This type of low-grade, long-term, inflammation is often termed “Inflammaging” because it is also often associated with age-related changes in body tissues. It occurs as we age, in the absence of infection, and is a highly significant risk factor for both sickness and death in ageing people[35].

Types of Inflammation

Acute inflammation is a beneficial, temporary immune response following injury or infection, that helps repair tissue. However, it can be impaired during aging, leading to further infection and poor wound healing.

Chronic inflammation has many features of acute inflammation but is typically low grade, persistent and leads to tissue damage over time. Mechanisms may include any or all the following[35]:

- Persistent production of reactive substance by immune cells which eventually damages tissues
- Increased production of inflammation producing molecules (cytokines) by damaged nonimmune cells
- Reduced cell signaling/communication necessary to start protein synthesis needed for tissue repair

Chronic inflammation is associated with many diseases that commonly occur with age including [35].

- Cardiovascular disease (CVD) which encompasses both heart disease and stroke
- Arthritis
- Type II Diabetes
- Neurodegenerative diseases such as Alzheimer's disease (AD)

Many aspects of ageing involve inflammatory processes that lead to long term tissue damage. In fact, body levels of inflammatory markers can be used to predict a person's degree of disability and the risk of dying in elderly people. These substances can be measured within blood or urine and are tell-tale of one's condition [36]. Effectively, chronic inflammation can shorten your life. It can damage body tissues and organs, which contributes to disease and ultimately reduces your longevity.

Topical vs. Oral Delivery

While topical products can play a role in skin health, the stratum corneum is specifically designed to prevent passage of many substances from the body's exterior to the inside. Therefore, most topically applied nutrients cannot easily penetrate it to reach:

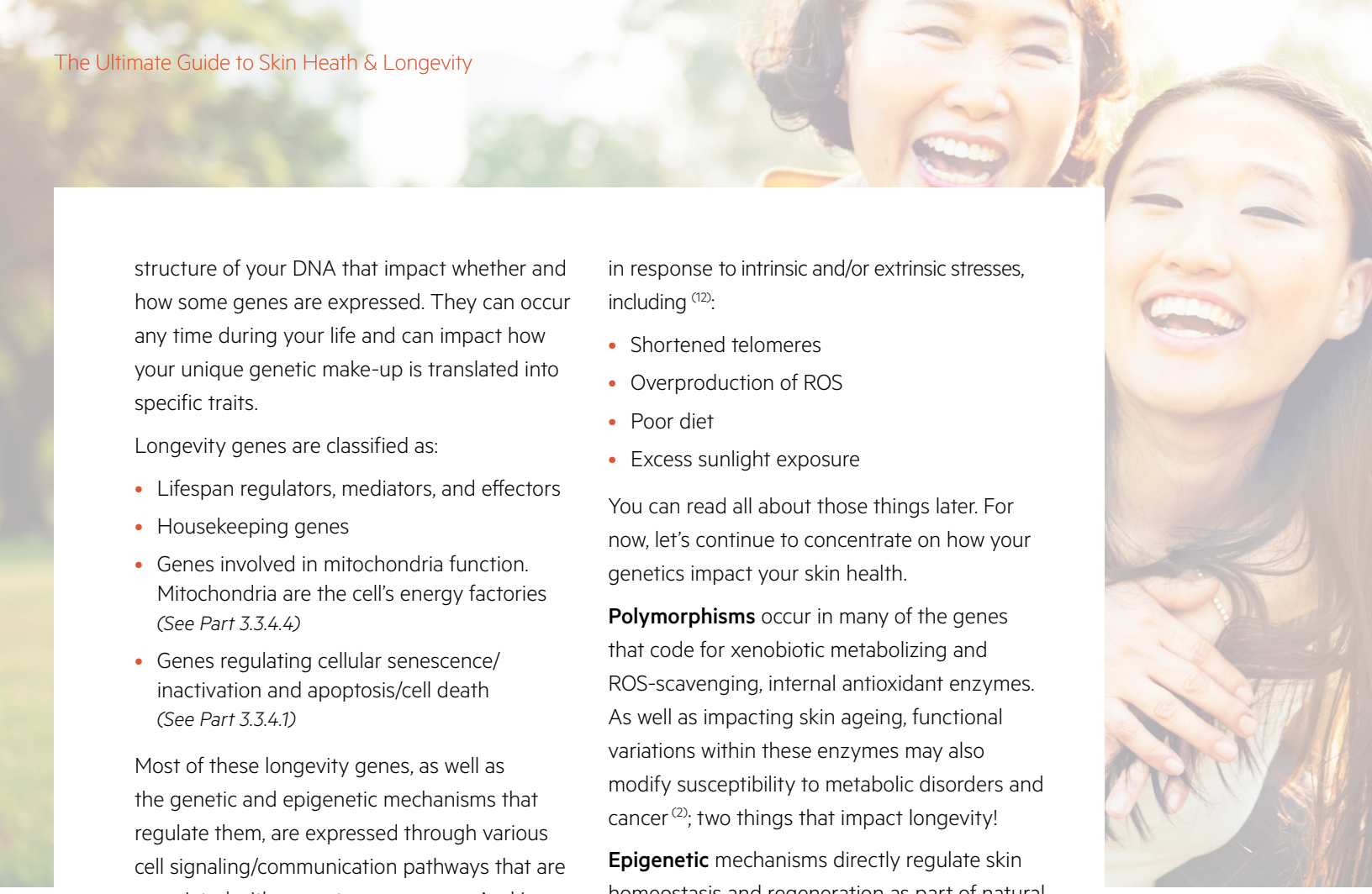
- The basement membrane where newly developing keratinocytes are growing to form the epidermis
- The dermis [7] which contains the blood vessels needed to circulate nutrients and to remove waste products.

Therefore, both skin layers are best supported by delivering nutrients to the dermis through the bloodstream.

3.2 Genetic Make-Up

During ageing, vital regenerative and reproductive functions slowly decline. As a result, you lose your ability to maintain homeostasis and become more susceptible to stress, diseases, and injuries [37]. Your genetics (i.e., traits that you inherit from your parents) can impact how you respond to many outside influences. For example, variations in the genes you inherit that control caffeine metabolism impact how you respond to it. Some of us get jittery after one cup of coffee, while others feel no effects. Such genetic variations or **polymorphisms** can have health and longevity implications. In the case of caffeine, a study has shown that people who metabolize caffeine slowly are at greater risk for heart attack than fast metabolizers [38]. But other genetic variants in some individuals can make them more susceptible to toxins, and these can have even more drastic ramifications for skin and overall health [39].

We now know that certain genes control ageing and longevity. These longevity genes increase lifespan when naturally overexpressed because of unique **polymorphisms**, or when modified through **epigenetics**. Epigenetic changes are alterations in the physical



structure of your DNA that impact whether and how some genes are expressed. They can occur any time during your life and can impact how your unique genetic make-up is translated into specific traits.

Longevity genes are classified as:

- Lifespan regulators, mediators, and effectors
- Housekeeping genes
- Genes involved in mitochondria function. Mitochondria are the cell's energy factories *(See Part 3.3.4.4)*
- Genes regulating cellular senescence/ inactivation and apoptosis/cell death *(See Part 3.3.4.1)*

Most of these longevity genes, as well as the genetic and epigenetic mechanisms that regulate them, are expressed through various cell signaling/communication pathways that are associated with your stress response. And in general, **mutations that make some of them less efficient, and regulators which suppress your response to mild stress, tend to provide life-extending benefits** [37].

In relation to your skin, it undergoes continuous renewal throughout your life partly depending on how well your skin stem cells can perform, which depends on their genetic functionality. Various pathways regulate the expression of genes involved in their homeostasis, proliferation (division and multiplication), specialization, and ageing, and this impacts their ability to effectively replace epidermal cells that are constantly lost from your skin surface. However, your skin's regenerative potential decreases as you age, partly due to the accumulation of keratinocytes and dermal fibroblasts that have undergone senescence in response to intrinsic and/or extrinsic stresses, including [12]:

- Shortened telomeres
- Overproduction of ROS
- Poor diet
- Excess sunlight exposure

You can read all about those things later. For now, let's continue to concentrate on how your genetics impact your skin health.

Polymorphisms occur in many of the genes that code for xenobiotic metabolizing and ROS-scavenging, internal antioxidant enzymes. As well as impacting skin ageing, functional variations within these enzymes may also modify susceptibility to metabolic disorders and cancer [2]; two things that impact longevity!

Epigenetic mechanisms directly regulate skin homeostasis and regeneration as part of natural ageing, but they also impact cell senescence and the damaging ageing processes [12]. For example, during ageing, the activities of some enzymes decline, including those that add methyl groups to your DNA, and Sirtuin 1 (SIRT1) which removes other functional groups, while other enzyme activities increase. These changes over time alter the genetic landscape, which modifies gene expression and leads to ageing.

The important thing to note about epigenetic changes is that even though they accumulate with age, some are reversible. Therefore, epigenetics can be used to reprogram cell fate to reduce signs of ageing [12] and effectively turn back the clock!

3.3 Environmental Factors

Your skin is more susceptible than your other organs to damaging environmental factors. For example, it is highly prone to drying by indoor heating and parched winter air. Add wind to that, and water evaporates causing even faster TEWL. This weakens and dehydrates the skin barrier, making it appear dull, flaky, and wrinkled.

Heat from the sun can pass through to the dermis and triggers production of enzymes that break down collagen and elastin. Chronic exposure induces inflammation, damages the dermal extracellular matrix, and promotes angiogenesis (i.e., blood vessel growth – like spider veins). These things promote skin ageing [40]. It can also lead to immune cell recruitment associated with non-melanoma skin cancer [41].

Long, hot baths with harsh soap are problematic too [40]. Dry skin in older people gets worse following hot baths and use of alkaline soaps [42]. Anyone taking long, and hot baths can have skin pH changes and irritation due to skin barrier disruption, which can worsen some conditions [43].

Air temperature changes may impact inactivation and excretion of toxic substances and excess nutrients. Low ambient temperatures constrict blood vessels which reduces skin blood flow and hampers delivery of triglycerides, cholesterol and some other excess nutrients destined for secretion within sebum. Lower skin temperature could also dampen the activity of some xenobiotic inactivation enzymes that typically prefer about 37 °C to function optimally. This could reduce toxin elimination [2].

On the other hand, heat exposure increases body temperature which triggers skin blood vessel dilation and sweating. Blood flow to the skin can increase from about 1 cup per minute at room temperature to 8 liters per minute at higher temperatures. Such increased surface blood flow could increase [2]:

- Delivery of toxins to the skin surface
- Elimination of water-soluble toxic substances in sweat
- Elimination of lipid soluble substances within sebum

All these changes could reduce the body's toxin load and improve its oxidative state [2]. This may be one reason why saunas are valued purification or cleansing tools for environmentally induced illnesses.

Sauna therapy benefits have been reported in people with hypertension, congestive heart failure, chronic obstructive pulmonary disease, chronic fatigue, chronic pain, and addictions [44]. Sauna bathing also dramatically decreases a blood marker of systemic inflammation [45], which could partly account for its risk lowering effects on dementia and AD; both conditions where oxidative stress and inflammation are major contributors [46]. Therefore, optimizing environmental factors to enhance skin health can also have longevity enhancing effects.

3.3.1 Diet/Food

Diet plays a role in overall skin health as well as development of several common skin diseases [47]. But which dietary approach is the best to maintain healthy skin and longevity?

The Mediterranean diet is well recognized to prevent age related diseases such as stroke, cognitive decline, and Alzheimer disease [48]. It is rich in:

- Omega-3 long-chain polyunsaturated fatty acids (LC-PUFAs) from fish
- Polyphenols from fruits, vegetables, cereals, coffee, tea, cacao, and wine
- Probiotics
- Vitamins

Similarly, a whole-food, plant-based diet helps prevent, and sometimes reverses some age associated chronic diseases. More recently, its role in preventing and reversing skin ageing has also been reported [32].

A whole-food, plant-based diet includes plant foods in their whole, unprocessed form, such as vegetables, fruits, beans, lentils, nuts, seeds, whole grains, and small amounts of healthy fats, but does not include processed foods, sweets, or animal products, such as red meat, poultry, fish, dairy, or eggs. This diet, rich in antioxidants, can help reduce circulating toxins that contribute to skin's cellular ageing and can lengthen telomeres, which are a marker for cellular ageing [32].

3.3.1.1 Advanced glycation end-product

One well-studied group of toxins that contribute to systemic inflammation and cell ageing are advanced glycation end-product (AGEs). They are created by the non-enzymatic binding of sugars to free amino groups within proteins. It is the same reaction that causes delicious caramelization when you sauté meat [49]!

AGEs formed within skin can cause rapid stiffening of extracellular matrix components including collagen and elastin. (Think about how meat shrivels and hardens when it is added to a hot pan.) This can prevent proper bonding between collagen fibers, hamper collagen and elastin repair, and delay tissue healing, which lowers skin's tensile strength [32].

Body levels of AGEs increase about 3.7 % annually from both internally produced and dietary sources [32]. As we age, this leads to cell damage and death. Oxidative stress-induced AGE formation is associated with chronic/acute inflammation, ageing, and a variety of age-related chronic diseases including, neurodegenerative disorders, atherosclerosis, vascular complications of diabetes mellitus [4], ocular diseases, cancer, and kidney disease [50].

Internal AGE formation is accelerated by external factors, including:

- Exposure to UV irradiation
- Cigarette smoking
- Poor diet.

On the other hand, a large Japanese study with 10,946 volunteers [51] found various lifestyle habits were each independently associated with

PRO TIP

Dry-brushing skin may also help remove toxins by increasing blood circulation in the skin and physically removes toxins from its surface by exfoliation.

lower AGE generation including:

- Eating breakfast
- Abstaining from sugary foods
- Not smoking
- Increased physical activity
- Adequate sleep
- Low mental stress levels

AGEs are particularly abundant in animal-derived foods and those exposed to long cooking times and high temperatures [32]. Recently the Spanish Society of Community Nutrition and Harvard University [49], recommended the following to reduce AGEs, as well as advanced lipoxidation end products (ALEs):

- Prepare foods by steaming and poaching
- Eat a varied diet rich in fresh vegetables and fruits but low in sugar and processed grains
- Add supplements containing bioactive compounds to achieve sustainable nutrition and health.

3.3.1.2 Sugar

Sugar is needed to make AGEs, so it is not surprising that higher carbohydrate intake is associated with skin ageing. Sugars cause oxidative stress by creating ROS when metabolized by the mitochondria to make energy/ATP.

Studies show that higher sugar intake is associated with accelerated skin ageing, and people with higher blood sugar levels develop dermal connective tissue fragmentation [52]. In addition, AGEs are increased by hyperglycemic diets, and not surprisingly diabetics often develop itchy skin [40]. Conversely, improved insulin sensitivity when following a low-glycemic diet improves acne [47].

Since diabetes is one of the most common age-related conditions, it is a good experimental model in which to study skin ageing. One study looked at the association between sugar metabolism and perceived age using facial photographs from 602 people who were divided into diabetic and nondiabetic groups based on their blood sugar level. It showed that higher blood sugar levels significantly correlated with an increase in perceived age regardless of whether they were diabetic [53]. That means, no matter how healthy you are, if you eat a lot of sugar, you might look older!

PRO TIP

Higher blood sugar levels are linked to looking older! So if you want to reduce premature skin aging, aim to control your blood sugar levels [53]. One way is to avoid eating refined sugars.

3.3.1.3 Polyunsaturated fatty acids

Omega-3 and omega-6 long-chain polyunsaturated fatty acids (LC-PUFAs) derived from dietary fat impact your skin and whole-body structure and function. They can modify cell membrane composition, gene expression, metabolism, and communication [54], and play an important role in regulating your inflammatory response. The latter can impact your Skin Climate®, to either promote or reduce inflammation.

Most of your dietary fats contain the parent essential fatty acids (EFAs):

- Linoleic acid (LA): an omega-6
- Alpha-linolenic acid (ALA): an omega-3

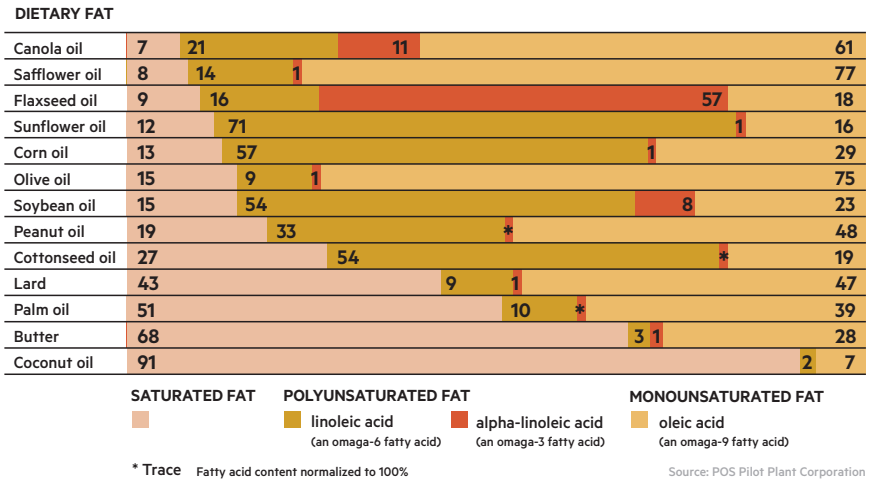
These are called essential because your body cannot make them, and so you must eat them. They are metabolized (processed within your body) to various LC-PUFAs that can each impact inflammation in their own specific ways. These include gamma-linolenic acid (GLA) and arachidonic acid (AA) made from LA, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) made from ALA.

The EFAs and LC-PUFAs are also found in many foods. Flaxseed and walnuts are rich in ALA, but only a small portion of the ALA you eat, ends up as either EPA or DHA within your body [55, 56]. However, EPA and DHA, are abundant in fatty fish, and are present in lesser amounts in other fish and seafood including algae, meat, and eggs. LA is abundant in many nuts, fatty seeds [57] and their vegetable oils including soybean, sunflower, and corn oils. AA is found in poultry, animal organs and meat, eggs, and to a lesser extent

in fish and other seafood [57]. GLA is relatively rare in common foods but is abundant in borage oil and evening primrose oil.

Although, historical media posts abound with statements like "Dietary omega-6s or LA or AA cause inflammation", that is an oversimplification of the scientific facts. Clinical studies in healthy adults show that increased intake of either LA or AA does not significantly increase the body levels of many inflammatory markers. In addition, these studies even suggest that LA and AA may reduce inflammation in some circumstances. Considering these two observations, **the problem is NOT necessarily that we eat too much LA or AA. Instead, it is that we eat too little omega-3 EPA and/or DHA.** Thus, rather than omega-6 fatty acids causing inflammation themselves, they instead interfere with the anti-inflammatory and inflammation-resolving effects of the omega-3 fatty acids [58]. In essence, it is an unbalanced omega-6/omega-3 ratio in favor of omega-6 PUFAs that is proinflammatory.

Figure 3: Fatty Acid Content of Various Dietary Oils



PRO TIP

The RATIO of dietary omega-6 to omega-3 fatty acids helps control inflammation.

Fatty acid experts generally recommend that a healthy, inflammation controlling diet should have a 1:1 ratio of omega-6 to omega-3 fatty acids [59]. which is a far cry from the more than 15:1 ratio within our typical Western diet [60]. To achieve this, you should:

- Avoid eating large amounts of LA-rich vegetable oils such as sunflower, corn, cottonseed and soybean oils and choose oils with higher ALA content relative to LA, like flax oil and walnut oil
- If you eat animal products, choose ones that are high in omega-3s such as fish, omega-3 eggs, and grass feed beef which has a higher omega-3 content than meat from grain fed animals [61, 62].
- Take an omega-3 LC-PUFA rich fish oil supplement. If you are vegan, or prefer not to eat fish products, take a DHA/EPA supplement derived from algae oil.

Increasing your Omega-3 LC-PUFAs intake can reduce skin inflammation that can cause damage and destruction of collagen and elastin, which contributes to wrinkle formation. In addition, eating more omega-3 LC-PUFAs may help you live longer. A study of elderly nursing home residents found that higher blood DHA levels were significantly associated with improved longevity. Since blood LC-PUFA levels mainly depend on one's eating habits, this essentially means that eating more DHA could make you live longer [64].

However, it is important to know that omega-3 LC-PUFAs are lipids that are highly susceptible to oxidation due to their chemical structure which includes multiple double bonds. These bonds are prone to oxidative instability. This puts an extra demand on your skin's antioxidant system to maintain the required antioxidant capacity needed for photoprotection [65]. Therefore,

ensuring adequate antioxidant intake is important to maintain your antioxidant status.

This is particularly important to prevent the formation of ALEs.

PRO TIP

Most North Americans eats less than the recommended intake of omega-3 LC-PUFAs [63].

These are formed when oxidized lipids, including fatty acids, attach to proteins through non-enzymatic reactions. This is like how sugars attach to proteins to form AGEs [66]. In skin, ALEs can prevent elastin repair [4].

Like AGEs, ALEs may contribute to the development of various oxidative based [66], and often age-related diseases [4]. However, consuming **antioxidants** may have the potential to prevent AGE and ALE formation in the body [66].

The next part of your journey will tell you more about those substances!

3.3.1.4 Antioxidant content

Antioxidant nutrients are present in many foods, especially vegetables and fruits, so a rich and varied diet including these foods usually meets our antioxidant requirements. Plant foods contain roughly 64 times more antioxidants than animal products, and owing to their plant pigment content, green vegetables contain the highest amounts of antioxidants of any vegetables, while berries contain the highest amounts of antioxidants of any fruit. In general, the more intense the color of the vegetables or fruits, the more antioxidants are present [32, 33].

Regular intake of antioxidant-rich foods can prevent tissue damaging effects of ROS [32]. However, when excessive oxidative stress is present, dietary antioxidant intake may be insufficient [33].

Antioxidants include:

- Nutrients that work by directly preventing free radical damage. These include vitamin C, vitamin E, plant polyphenols, carotenoids, and glutathione.
- Nutrients that are required for optimum performance of internal antioxidant enzymes include minerals such as selenium, iron, copper, zinc, and manganese.

Antioxidant intake is relevant at any age, but especially during aging because, as we age, our appetites decrease so we typically eat less, and we absorb less of what we do eat [40]. These differences in micronutrient intake can impact skin health as shown in the following studies:

- In 2753 healthy older adults, higher fruit intake was associated with fewer wrinkles while more red meat and snacking was associated with more facial wrinkles in women, but not men [68].
- In 177 Greek-born elderly subjects living in Australia, those eating more vegetables, olive oil, fish and legumes, and less butter, margarine, milk products and sugar had fewer precancerous skin lesions [69].

Not surprisingly, regular fruit and vegetable intake is associated with reduced risks of cancer, CVD, stroke, Alzheimer disease, cataracts, and some functional declines associated with ageing [70].

3.3.1.5 Calorie restriction

Calorie restriction tricks your body into thinking that you are starving. It responds by telling your mitochondria to use fatty acids to make energy/ATP rather than sugar, because pound for pound, more energy can be made from

PRO TIP

OXYGEN

A blessing and a curse. On the one hand, oxygen is essential to air breathing organisms like us because our mitochondria need it to make our energy. On the other hand, oxygen is harmful because it can continuously make ROS that contribute to our aging [67].

fat than sugar. A side effect to that metabolic change, is lower ROS production in the mitochondria and increased production of your internal antioxidant enzymes. That has the potential to reduce your oxidative stress and may have a positive impact on your skin and chronological aging!

While routinely eating too many calories especially from carbohydrates/sugar can negatively impact health and longevity [71], caloric restriction can extend both healthspan (the length of time you remain healthy) and lifespan (how long you live) [72]. In fact, of all the health-preserving and longevity-promoting interventions tested so far, calorie restriction without malnutrition, seems the most robust [72] to delay the start and progression of age-related metabolic disease and to extend life [33, 73]. In addition, other less restrictive forms of intermittent fasting, including time restricted feeding [74] and alternate day fasting [72], can activate similar longevity preserving pathways like caloric restriction [74].

Calorie restriction reduces metabolic rate, energy expenditure, and core-body temperature, while reducing oxidative stress-induced cellular damage and inflammation, improving immune status, and increasing stress resistance [73].

Human clinical studies suggest this metabolic slowing occurs through thyroid hormone reduction and improved cardiovascular health [72, 75, 76]. Specifically, it can lower body fat, improve blood triglyceride and cholesterol levels and blood sugar control [73], improve general health including mood, sex drive, vigor, relationships, and sleep quality [77], and enhance immune function [72] and xenobiotic detoxification [78]. It can also delay age-onset type 2 diabetes, CVDs and cognitive loss [76, 78], and lower cancer incidence [73].

All the beneficial changes attributed to calorie restriction happen because of metabolism reprogramming that shifts the body from storing fat, to instead using it to create energy/ATP. This occurs primarily through the stress sensing MAPK pathway which provokes appropriate genes to modify their activity. This metabolic shift also enhances detoxification, the inflammatory and immune response, as well as cell proliferation, specialization, development, and apoptosis to preserve life. In experimental models, EPA supplementation can instruct the MAPK pathway to enhance immunity and cell protection [78], and DHA can induce antioxidant effects in healthy men through similar means [79].

Various other nutrient/stress sensing substances or pathways can mimic calorie restriction and may promote longevity, including SIRT1 [73, 80]. However, the exact mechanisms are yet to be fully discovered, understood, and explained in humans [73].

In skin, calorie restriction affects its structure and function, and can rescue both age-related and photo-induced skin changes through anti-inflammatory, anti-oxidative, stem cell maintenance, and metabolic processes [26]. However, its direct effects on skin ageing have so far not been evaluated. Nevertheless, some food and supplement components such as resveratrol, that mimic calorie restriction by impacting the same pathways, are effective against skin ageing. Such use of calorie restriction or calorie restriction mimetics has great potential to rejuvenate and maintain healthy skin, as well as improve age-related skin disorders [26].

More research is needed to determine if restricting your calorie intake can improve your skin health. But there is a growing body of evidence to suggest it may improve longevity.

3.3.1.6 Electrolyte balance

Electrolytes are inorganic salts that are present both inside and outside the cell. They include potassium, sodium, magnesium, calcium, chloride, phosphate, sulfate, and hydrogen carbonate. You obtain these nutrients from the food you eat, and the water you drink, but they are easily lost from your body primarily through excretion in urine and sweat.

Electrolytes carry an electric charge that affects the bioelectrical status of the cell, and that attracts water. Blood vessels supply these electrolytes to your skin. On a whole-body level, they maintain hydration, muscle and gland function, homeostasis, and waste disposal. At the cellular level, they regulate pH levels, help conduct electricity that impacts nerve transmission and muscle action and enable well-regulated exchange of nutrients and waste products within cells and between cells.

PRO TIP

Everyone should consult a health care practitioner before attempting calorie restriction or intermittent fasting to rule out potential adverse effects due to critical or hidden medical conditions [72].

In skin, electrolytes help to retain water within its layers, which contributes to its moisture and barrier function.

Ageing reduces our ability to excrete either concentrated or dilute urine, ammonium, sodium, and potassium. Even so, under normal conditions older people can still maintain water and electrolyte balance. However, this may be jeopardized by illness, certain medications, or stress. In addition, unexpected electrolyte abnormalities may occur without obvious kidney disease, simply from structural and functional kidney changes associated with ageing. This is called “senescent kidney” [81].

Data showing whether ageing skin also contributes to full body electrolyte imbalance is scarce, as is any showing whether healthy skin may help the kidneys to preserve whole body electrolyte homeostasis. In any event, ensuring a balanced electrolyte intake will help maintain skin hydration and barrier repair, and this alone helps to maintain skin health and longevity.

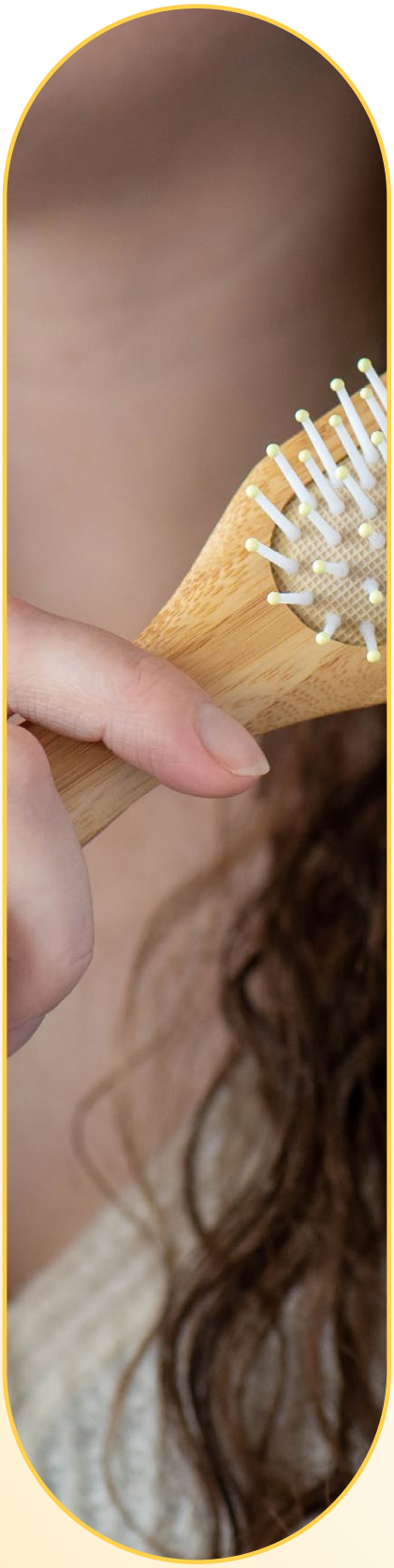
3.3.1.7 Microcirculation enhancers

Capillaries are the tiny blood vessels that connect small arteries and small veins. They enable the exchange of water, oxygen, carbon dioxide, nutrients and waste substances between blood and surrounding tissues and single cells. As we age, the number of capillaries within a given area of tissue decreases because of declining levels of angiogenic growth factor (AGF) [82].

AGF stimulates angiogenesis to support tissue growth, and so maintains healthy skin and wound

PRO TIP

As our population continues to age, there is a growing increase in the prevalence of chronic kidney disease and associated diabetes and hypertension.



repair. It also helps maintain an effective blood supply to other body areas, so it is no stretch to imagine that waning microcirculation during ageing could contribute to other common features among the aged including [82, 83]:

How well your skin microcirculation is functioning can predict your overall health status!

- Cold intolerance
- Muscle weakness
- Transient memory lapses

Microcirculation dysfunction contributes to the development and progression of cardiometabolic and renal disease and is associated with increased cardiovascular related death. It starts with oxidative stress, followed by inflammation within the internal lining of the blood vessels [87].

Proper functioning of microcirculation within the skin is such a good predictor of how it is functioning in other parts of the body, that it can be used to predict long-term outcomes and adverse cardiovascular events [88]. This shows how intricately linked skin health is with overall health and longevity.

Capillaries within aged skin do not expand or contract well in response to warm or cold stimuli, respectively [88]. This can significantly impact skin maintenance and repair, as well as whole body toxin elimination. Therefore, foods and supplements that enhance microcirculation may provide both skin enhancing and life preserving effects.

3.3.1.8 Detoxifying foods

Many foods and supplements enhance xenobiotic detoxification; a process that occurs in liver as well as within individual cells throughout your body, including your skin. It takes place through metabolic pathways involving various enzymes that change the chemical structure of xenobiotics (i.e., compounds foreign to your normal biochemistry, such as any drug or toxin). It is divided into

PRO TIP

CLEARLY DEFINED:

Angiogenesis is the sprouting or splitting of new blood vessels from those that are already present. It is "good" in the context of normal and healthy tissue growth and repair, but it is "bad" in relation to cancer where is enables cancer growth and spreading/metastasis. Cancer cells stimulate angiogenesis when they become deprived of oxygen by excreting growth factors such as AGF. Angiogenesis also plays a role in many age-related diseases. However, many foods and supplements can enhance healthy angiogenesis [84-86].

three phases with the first two mainly taking place in liver and skin cells [89, 90]:

- **Phase I** involves creating a more water-soluble/dissolvable form of the toxin [91]. The modified toxin has a form of oxygen that reacts better with enzymes in the phase II reaction below. That is a good thing, because it makes it easier for the Phase II enzymes to eliminate the toxin. The downside is: **These modified toxins are ROS and are the MAIN REASON why toxins increase YOUR ROS BIOLOAD!**

derived from fatty acids and steroid hormones. They attach reduced glutathione onto these lipophilic compounds so they can be excreted through bile or subsequently undergo other changes to form mercapturic acids [90]. In fact, the amount of mercapturic acid in your urine can be used to estimate your level of exposure to air pollutants [92]. It can also be used to assess how well foods like broccoli sprouts or supplements that include sulforaphane are enhancing your xenobiotics detoxification [93].

Overall, as we age, Phase I metabolism decreases, which means that toxins hang around longer.

- **Phase II** involves internal antioxidant enzymes that modify the toxin to make it more water-soluble so it will mix well with blood or bile. These enzymes attach various substances to it, such as glutathione.
- **Phase III** involves further changes to help transporter proteins to recognize the modified toxin and pump it out of the cell. The modified toxin is then carried either by:
  - Blood to the kidneys or sweat glands for disposal.
  - Bile to the gallbladder where it is pumped into the small intestine for disposal.

In essence, this process converts lipophilic compounds into hydrophilic products that are more readily excreted.

Many factors can affect xenobiotic metabolism including age, gender, drug-drug interactions, diabetes, pregnancy, liver or kidney disease, inflammation, and genetics [89]. In addition, xenobiotic metabolism by microorganisms that reside within us can produce end products that impact our health.

Certain internal antioxidant enzymes are especially important to reduce oxidative stress caused by harmful inflammatory substances

Phase I and II metabolism requires the presence of glutathione, which is found in many body tissues [95]. It is also in foods including spinach, avocados, asparagus, and okra [96]. However, dietary glutathione is poorly absorbed and so eating foods that help the body to make glutathione is important. These include sulfur-rich dietary proteins, such as beef, fish, and poultry. But some human studies show that eating sulfur-rich vegetables may also reduce oxidative stress by increasing glutathione levels [97-99]. These include cruciferous vegetables like broccoli, Brussels sprouts, cauliflower, kale, watercress, and mustard greens [97-99]

PRO TIP

CLEARLY DEFINED:

Lipophilic means fat loving = dissolves in fat

Hydrophilic means water loving = dissolves in water

CLEARLY DEFINED:

Xenobiotic metabolism

Comes from the Greek word:

- **Xenos** means stranger
- **Biotic** means related to living beings

These pathways exist in various forms in all living species and originated in our ancient evolutionary ancestors

and Allium vegetables, including garlic, shallots, and onions [100].

Foods rich in vitamin C may also help preserve existing glutathione levels by attacking free radicals first, thereby sparing glutathione, but studies proving this have so far only tested vitamin C supplements. They also found that vitamin C helps significantly increase active glutathione levels [101, 102]. This highlights the important antioxidant role that Vitamin C plays in neutralizing free radicals and ultimately in xenobiotic detoxification.

Other things that impact glutathione metabolism in various ways include:

- Overall antioxidant status of your diet
- Selenium [103]
- Silymarin [104, 105]
- Turmeric [106]
- Sleep
- Exercise
- Alcohol

Glutathione deficiency is associated with various chronic, age-related diseases and mitochondrial dysfunction [95]. In addition, the impact of body's toxin load on skin health and appearance is well documented. This highlights the integral role that detoxifying foods can play in both skin health and longevity.

PRO TIP

GOOD TO KNOW:

Some people are affected by toxins more than others owing to their unique genetic make-up (i.e., polymorphisms in their detoxification enzymes like GST). This can make them more susceptible to many health issues including increased miscarriages risk, birth defects, heavy metal and chemical contaminant toxicity, asthma, and age-related and/or neurodegenerative diseases, including multiple sclerosis, AD, and cancer [39, 94].

3.3.2 Lifestyle

3.3.2.1 Exercise

Exercise may enhance skin health and longevity by reducing inflammation [107] and internal production of ROS [108], while simultaneously enhancing internal antioxidant [40] and detoxification defenses [2]. However, exercise is a double-edged sword, where a balanced approach is the best. That is partly because too much creates oxidative stress while not enough overtime can contribute to metabolic syndrome [2].

Studies show that strenuous exercise in professional athletes can increase their oxidative stress [40], while in healthy untrained young adults, the degree and type of oxidative stress that develops depends on exercise intensity and duration [109]. On the other hand, studies show that exercise can increase antioxidant defenses through glutathione assisted detoxification, and that combining cardio and circuit weight training increases glutathione more than practicing either alone [110].

Specific to skin, moderate exercise can improve dermal circulation, reduce AGEs [40] and induce sweating which helps to eliminate toxins [2]. All would be expected to improve skin function and reduce skin ageing. But to date, no clinical study has shown a clear relationship between [40]:

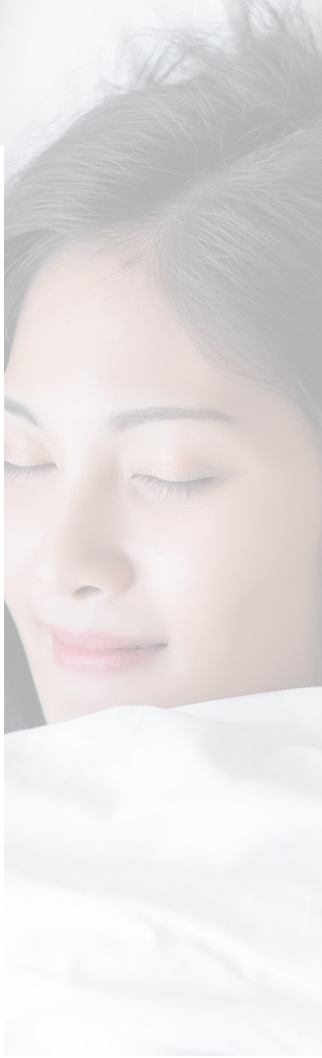
- Physical inactivity and skin ageing
- Intense physical activity and skin ageing

One of the best benefits of exercise is reduced inflammation. Studies show it can reduce inflammatory markers in older adults. In fact, a long-term exercise routine can actually re-program your metabolism to make fewer inflammatory metabolites on a routine basis through epigenetic changes. Such genetic changes coupled with less inflammation were measured in one study of older adults who exercised regularly and another study involving a 6-month walking regimen. However, intense training that exceeds an individual's physical abilities can have the opposite effect [107]. So again, balance is everything!

So, what impact does all this have on longevity?

Endurance exercise can also activate the MAPK pathway in skeletal muscle [108]. That tells the mitochondria to use fatty acids instead of sugar to make energy, and that produces fewer harmful ROS, which ultimately reduces oxidative stress that can harm body tissues.

Routine moderate exercise is key to reducing inflammation that could benefit both skin health and longevity.



A study including 1,683,693 global volunteers, found that going from physically inactive to achieving the recommended 150 minutes of moderate-intensity aerobic activity per week, lowered their risk of dying from CVD by 23%, CVD incidence by 17%, and type 2 diabetes by 26% over the next 13 years [111]. In healthy adults, such moderate aerobic exercise extends life span and likely health span by 2-6 years [112].

Overall, exercise improves blood sugar regulation and cognitive function, and resistance exercise increases or maintains muscle mass [112]. Maintaining skeletal muscle mass during ageing is important because muscle loss increases health problems in older adults [113]. On top of that, muscle mass and strength are intricately linked to bone mass. All three increase during late adolescence and early adulthood but start to decline noticeably from about age fifty. **And their decline impacts how old you look!**

Clinical studies show that muscle and bone communicate with one another through various factors [114] that can improve bone health [115]. That is important because, bone mineral density in your face decreases with age, the same way as it does in bones throughout your body. This change may contribute to your face appearing older [116]. **So, exercising, in addition to making you live longer, may make your face look younger too!**

Maintaining muscle mass also partly depends on your protein intake. The Recommended Dietary Allowance (RDA) of protein for a healthy adult with minimal physical activity is 0.8 g protein per kg body weight per day. But to promote muscle protein accumulation and physical strength, dietary intakes of 1.0, 1.3, or 1.6 g of protein per kg body weight per day is recommended for people undergoing minimal, moderate, or intense physical activity, respectively [117]. In addition, research suggests that protein supplementation can enhance muscle mass and strength gains achieved through resistance training and can even preserve existing muscle mass when practicing calorie restriction [118]. Therefore, ensuring adequate protein intake will help you both build new muscle and preserve your existing muscle.

3.3.2.2 Sleep

Too little good quality sleep causes oxidative stress that produces inflammation, which contributes to skin ageing and reduced longevity.

Studies show detoxifying enzymes are significantly lower and oxidative stress is higher in people with insomnia compared to those getting enough rest [119], and even occasional sleep loss negatively affects facial appearance [120]. For example, when women were photographed after normal sleep hours and after sleeping for a shorter period, observers who rated their appearance in both photographs said the sleep deprived versions had hanging eyelids, swollen eyes with darker circles and the corners of their mouths drooped [121]. But what happens if you rarely get enough sleep?

Well, poor sleep quality and quantity, which is defined as 5 hours or less, is associated with increased skin ageing and decreased skin barrier function. On the other hand, after exposure to UV light, good sleepers have significantly better "sunburn" recovery, and

PRO TIP

EVERYTHING IS CONNECTED:

Human studies show that intermittent fasting at specific times stimulates gut microbiota fluctuations that trigger subsequent body changes, which in turn restore a healthier circadian clock resembling that of our ancient ancestors [127, 128].

subjectively think they look better than their poor sleeping counterparts [122]. Also, people with obstructive sleep apnea are perceived to appear more alert, more youthful, and more attractive after successful treatment for their condition, and their facial surface volume and color improves (i.e., becomes less red) [123].

Poor sleep may trigger inflammation that could produce skin ageing effects. It certainly did in 608 patients with the inflammatory skin condition, rosacea, where a strong association between sleep quality and rosacea severity was measured [124].

In addition, poor sleep quality is also associated with elevated systemic inflammation in healthy older adults. For example, in 232 sixty- to seventy-year-olds in the Australian Research Council Longevity Intervention study, those who had difficulty getting to sleep had higher blood levels of various inflammatory markers [125].

Good quality sleep is critical for regenerative cell growth. Poor quality sleep leads to cell dysfunction due to circadian rhythm alterations that impact the production of the hormone, melatonin. Such alterations in sleep patterns

Getting your "beauty sleep" takes on a whole new meaning now, doesn't it?

over time can increase risk for cardiovascular disorders, and malignancy, in particular breast cancer [126].

3.3.2.3 Stress

Stress can arise from many sources such as poor diet and exercise habits, but the stress I am talking about here is psychological stress. It is your mind's reaction to extreme circumstances. You feel it, and those feelings are expressed through your emotional response. But perhaps what you don't realize, is that your whole body also reacts to those extreme circumstances. Prolonged psychological stress can alter homeostasis, stimulate ROS production leading to chronic inflammation, which contributes to immune dysfunction that can impact your skin health and longevity.

Just like exercise, psychological stress can have both good and bad effects. Small amounts or short periods of stress, like the excitement you feel when planning a vacation or a night out-on-the-town, can be beneficial, and even healthy, and can enhance your immune function. On the other hand, chronic stress in the absence of an immune challenge, like prolonged mourning of a loved one or financial insecurity, has the opposite effect [107].

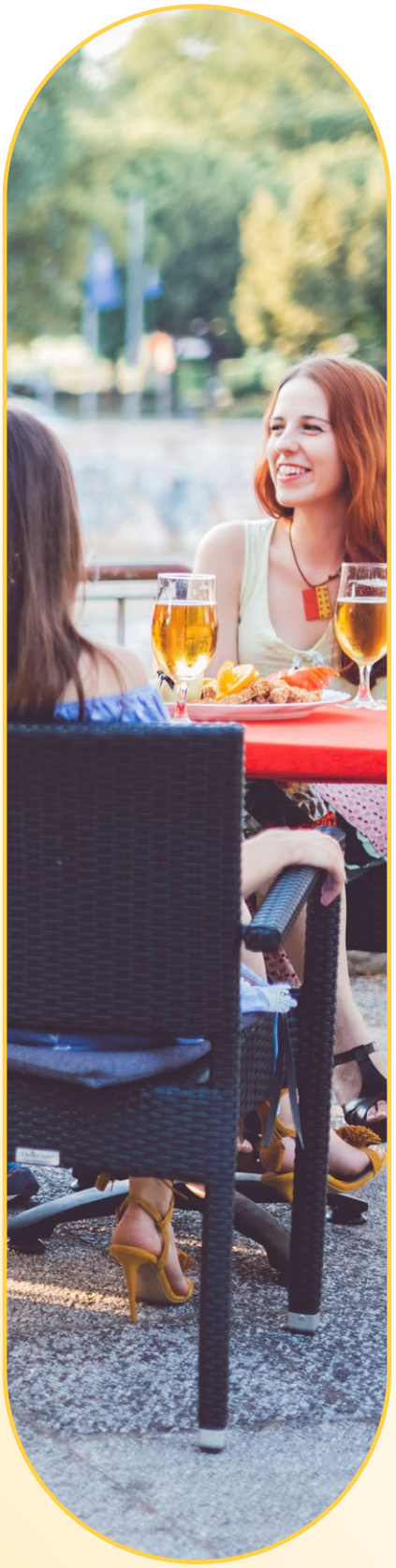
In skin, chronic psychological stress alters its barrier homeostasis, and increases ROS generation, inflammation, and production of enzymes that break down collagen and elastin, which contributes to skin ageing [40]. In fact, a study examining the impact of financial stress on perceived age found people who were highly stressed, looked older to other people than their actual age [129].

Chronic psychological stress stimulates the production of stress hormones [107], whose job is to warn you of a threat, so that you can respond to save yourself. However, when stress is chronic, for example when someone is depressed, their body ignores these constant warning signs [107], a bit like the way that an abused person becomes tolerant of their abuser. This tolerance to continuous stress hormone exposure, stimulates overproduction of inflammatory substances. Inflammation surges forth through various mechanisms including gene expression and increased ROS production. DNA gets damaged [130] and immune cells become activated. But these immune cells also become

Your mental well-being is key to reducing chronic diseases and promoting longevity [131].

less sensitive to the warning signs [107]. Together, this leads to immune suppression and systemic inflammation/ inflammaging [130]. Both effects can impact skin health and longevity.

Chronic stress can seriously damage your immune system, make you more prone to sickness and infections, and can impact how metabolic diseases develop. For example, stress-related depression activates some biochemical



pathways that lead to "accelerated ageing" characteristics, and development of age-related diseases, including metabolic disorders and dementia. Related research shows that psychological well-being is key to reducing chronic diseases and promoting longevity [131].

3.3.2.4 Alcohol consumption

Nutritional deficiencies can develop when alcohol replaces normal food in the diet, resulting in fewer calories, protein, and micronutrient intake. In addition, the digestive tract and liver do not digest and process food the way they should, which hampers proper nutrient absorption [132]. Therefore, it is no surprise that many adverse health effects are associated with chronic and excessive alcohol intake.

Some of these damaging health effects are likely attributed to oxidative stress. For example, research shows that lung glutathione levels decrease by 80–90% in alcohol abusers [133], most likely due to oxidative stress [134]. Thus, limiting your alcohol intake may help you maintain healthy glutathione levels, both within your lungs and in other body tissues. Such improvements in internal antioxidant capacity may beneficially impact both skin health and longevity.

Skin changes associated with alcohol abuse are well document [132] and are an early warning sign of this practice. It causes dry, fragile skin that loses elasticity. It also produces, rashes, itching, flushing, hyperpigmentation, spider veins, and in late stages, yellowing associated with jaundice. Associated vascular changes include benign skin growths, dilated veins, and reddish palms, while related skin diseases include psoriasis, sun sensitivity leading to painful, blistering skin lesions [135], squamous cell carcinoma, basal cell carcinoma, and melanoma [132].

Not surprisingly, alcohol abuse is also linked to liver cirrhosis, brain damage and pancreatitis, and increased risk of oral, liver, pancreatic and breast cancer [132, 135]. All these conditions have a direct negative impact on longevity.

3.3.2.5 Smoking

Smoking increases the quantity of toxic substances in your body that need to be inactivated and eliminated. At the same time, it reduces the circulating concentrations of many antioxidant vitamins including vitamin C and various carotenoids [136]. Therefore, it places huge stress on your internal antioxidant system, which ultimately negatively impacts both your skin healthy and longevity.

Cigarette smoking causes premature facial wrinkling [137- 140], and their severity increases with both the number of packs per day and the years you smoke [141]. But it is not just tobacco cigarette smoking that is bad for your skin. Water pipes containing non-tobacco-based preparations reduce nicotine exposure, but they

may also expose you to equal or even higher amounts of other toxic compounds – things like heavy metals, cancerous nitrosamines, polycyclic aromatic hydrocarbons (PAHs), mercapturic acid metabolites and radioactive isotopes. And if you smoke tobacco in a water pipe, you typically do so for longer than if you were to have a cigarette, which can expose you to almost double the nicotine dose [142].

Smoking decreases microcirculation, which damages connective tissue components important to its integrity [143]. It also triggers inflammation. Indeed, there is a connection between the severity of facial wrinkles in smokers and development of chronic

What does your skin reveal about your health?

obstructive pulmonary disorder (COPD), which is a chronic lung disease that involves systemic inflammation. That connection is so significant, that facial wrinkling in smokers can be used as a biomarker/indicator of their susceptibility to COPD [19].

I do not have to tell you that tobacco smoking causes all sorts of cancers, and that cancer reduces longevity. But I will anyway. During 2010–2014, approximately 3.3 million new tobacco-associated cancers were reported in the United States [144] and although in Canada there is a trend towards less smoking, it is still a main risk factor for many cancers [145,146]. Not surprising, diseases associated with cigarette smoking also occur with water pipe smoking. Water pipe smoking causes eczema on the hands, psoriasis on the lips, squamous cell carcinoma in the mouth, COPD, CVDs, and cancer; and infants of women who smoke water pipes often die [142]. That is pretty indicative of its impact on longevity.

3.3.3 Pollution/environmental toxins.

Your skin fights a tough battle! As a detoxifying organ, it is your front line of defense against environmental insults, and yet it is also damaged by that very enemy. Toxins like chemicals, pesticides, solvents, and plastic-related compounds are present in the air we breathe, the water we drink and bathe in, foods we eat and personal products we use every day. Even many skincare ingredients may have estrogen-mimicking chemicals that must be metabolized and eliminated by your liver.

Oxidative damage from atmospheric pollution can cause significant skin damage. In a study of 400 Caucasian women aged 70-80 years, greater exposure to air pollution in traffic produced more pigment spots on their forehead and cheeks, an indication of skin ageing [147]. Air pollutants are photosensitizers that generate ROS when exposed to UVA radiation from sunlight. This in turn causes oxidative and genetic damage in skin that leads to photodamage and cancer formation [148].

Even staying inside can't protect you from fossil fuel derived air pollution effects in high-risk areas. For example, in Taizhou, China, where pollution levels were measured in 30 households, higher levels were positively associated with signs of skin ageing including forehead pigment spots and upper lip wrinkles [149].

Exposure to air pollutants also causes systemic inflammation that increases your risk of getting sick and dying of respiratory, cardiovascular, metabolic, neurological, carcinogenic, and autoimmune diseases [107].

It is a snow balling cascade of events starting with ROS generation leading to mitochondrial dysfunction and a consequent drop in energy production. At the same time, epigenetic changes can take place that damage DNA and telomerase activity, which contributes to premature aging. Then inflammatory pathways are activated, which stimulate the immune response, your defense against damaging invaders. Despite these attempts by the body to resolve the inflammation, tissues become excessively infiltrated

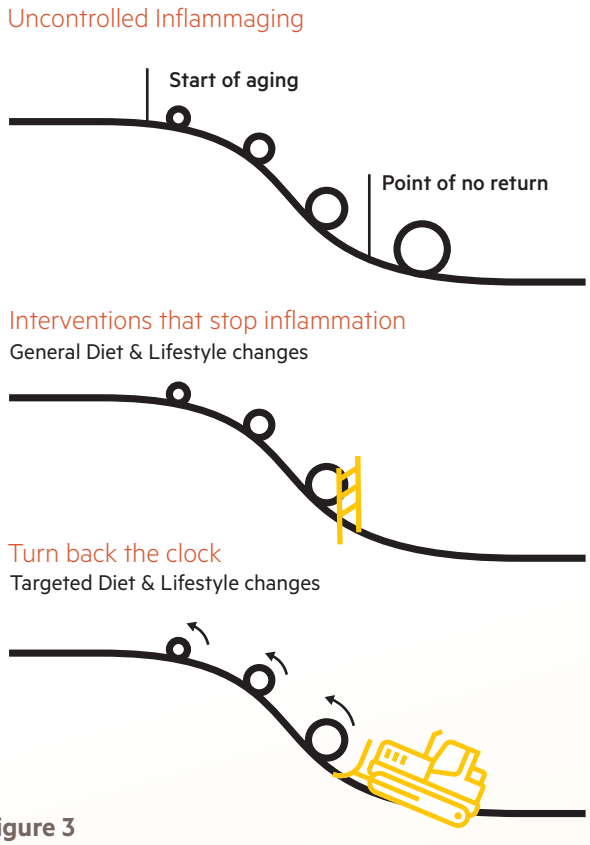


Figure 3

with certain lymphocytes called Tregs. Tregs are associated with autoimmune disorders. At the same time, nuclear factor erythroid 2 pathway (Nrf2) is inactivated. Nrf2 is the master antioxidant regulator that normally prevents oxidative stress and resolves inflammation. Without Nrf2's activity, the inflammaging snowball continues to roll on, contributing to development of age-related diseases – like CVD and cancer.

Overall cancer burden is increased by exposures to food and airborne carcinogens. For example, aflatoxin contaminated food likely contributes to liver cancer risk. In addition, environmental carcinogens such as PAHs, play a significant role in human cancer development through both food and airborne exposures [150]. Obviously reducing exposure to these food, water and air born toxins would help to reduce cancer risk. However, in many cases, exposure is unavoidable because we:

- May unknowingly ingest aflatoxins and other mycotoxins in contaminated food
- Can be exposed to secondhand cigarette smoke
- Live in megacities where creating clean air requires significant economic investments [92] and even global co-operation.

In these circumstances, detoxifying foods and supplements become attractive ways of reducing body burden with a goal to improve skin health and longevity.

3.3.4 UV Radiation

When your skin is exposed to sunlight, its UV radiation causes a dramatic increase in the production of ROS. The sudden increase in ROS causes oxidative stress. The subsequent damaging effects of oxidative stress occur through many mechanisms that involve changes in protein and lipid structures, inflammation initiation, immune system suppression, DNA damage, and activation of signaling pathways that affect gene expression, cell proliferation, and apoptosis. All these fluctuations away from homeostasis contribute to cancer initiation. Therefore, regulating ROS levels is critical to maintain normal skin homeostasis [151] and health. That is a lot to take in from one paragraph, so let me break it down.

Cells produce various kinds of ROS when exposed to factors that contribute to their formation include UV light, X-rays and gamma-rays, air pollutants, tobacco smoke, heavy metals, and some drugs [4]. Internal factors include, inflammation induced by trauma or autoimmune disorders, genetic defects, age-associated mitochondrial dysfunction, and even cancer [152].

ROS are formed constantly during normal life where oxygen is needed to make energy, especially in mitochondria [39]. Many such ROS generating processes are essential to life, and therefore ROS are not necesarily "bad".

During homeostasis (i.e., unstressed conditions), cells normally contain low ROS levels due to the protective activities of their internal antioxidant system that consists of:

- **Internal antioxidant enzymes**
- **Non-enzyme components** including:
  – Vitamins A, vitamin C, and glutathione being the most important
  – Others include vitamin E, flavonoids, carotenoids., and metal ions of iron, copper, zinc, and manganese.

These antioxidants can scavenge and inactivate ROS and in doing so, protect your cells from harmful oxidative stress [4].

The primary non-enzymatic antioxidant in your skin is vitamin E. After acting as an antioxidant, its oxidized form is regenerated by vitamin C, which is considered as skin's secondary antioxidant. Vitamin C is then replenished from either vitamin A or other diet derived antioxidants. Overall, this cascade of events helps to reduce oxidative stress [32].

Oxidative stress is defined as a persistent imbalance between ROS generation and the ability of a biological system to neutralize them [4]. This can be attributed to:

- Inadequate antioxidant intake
- Increased generation or decreased clearance of ROS due to various stressors
- Unique genetic variations that impact internal antioxidant enzyme production or activity [39].

Oxidative stress allows ROS to directly damage cellular components including lipids, proteins, and DNA, and to disrupt membrane structures. This can include molecular damage and/or communication disruptions within and between cells. It also produces highly reactive lipid peroxides which can react with proteins to form ALEs and induces reactions between proteins and sugars which form AGEs.

3.3.4.1 Impact on Skin Structure and Function

ROS produced in skin by UV radiation exposure causes a sequence of events that directly damages DNA, fatty acids, carbohydrates, and proteins, including collagen and elastin [13], and suppresses the immune response [153]. They can also affect signaling molecules, such as the stress sensor MAPK, activate enzymes that produce inflammatory substances from polyunsaturated fatty acids [154], and stimulate

PRO TIP

CLEARLY DEFINED:

Free Radicals are unstable atoms. Atoms consist of positive and neutral charged particles surrounded by layers containing negatively charged electrons. Electrons like to exist in pairs. Atoms with paired electrons are stable; that is, they have no desire to interact with other atoms. Atoms with one or more unpaired electrons, are highly reactive and unstable free radicals. They can be formed as necessary intermediates in many normal biochemical reactions, but when generated in excess can damage macromolecules. There are many types of radicals, but those of most concern in biological systems are derived from oxygen and known collectively as reactive oxygen species (ROS).

Antioxidants are molecules that donate electrons to free radicals to make them stable.

production of melanin, the enzyme that makes skin pigment [155].

Although skin is naturally equipped with enzyme and non-enzyme antioxidants described above, their effectiveness can be limited by nutrient status and age. If they do not neutralize existing excessive ROS, the resulting oxidative stress causes indiscriminate damage to a wide range of biomolecules [156] including collagen and elastin and the cellular machinery involved in their production. Such oxidative stress stimulates epidermal keratinocytes and dermal fibroblasts to produce inflammatory substances. These in turn, instruct the cells to make enzymes that break down collagen and elastin, which leads to extracellular matrix digestion [15], which further increases intracellular ROS levels [156].

Repetitive skin exposure to ultraviolet B (UVB) radiation primarily produces wrinkles. Ultraviolet A (UVA) predominantly contributes to sagging skin called solar elastosis, which is one of the main markers of skin photo-ageing. It creates disorganized and non-functional elastic fiber deposits [13] and decreases hyaluronic acid levels [157]. Over time, repeated UV exposure eventually causes so much damage to skin cells, in particular their mitochondria, that they can no longer function normally.

They then undergo either:

- **Cellular senescence** which is irreversible growth arrest (i.e., the cell stops dividing, forever). That can happen in response to various cell stressors including oxidative stress, DNA damage, telomere erosion, and oncogenic activation.
- **Apoptosis** which is programmed cell death. It happens when cells become damaged beyond repair and is one method the body uses to get rid of abnormal cells.

Both are protective mechanisms to prevent cancer development. However, both processes can also be hampered, which leads to carcinogenesis.

3.3.4.2 Impact on Photo-ageing

As you chronologically age, ROS production and accumulation increases, while the capacity of your internal antioxidant defenses decrease, leading to progressive cell damage [158]. This causes natural skin deterioration by oxidizing and degrading skin proteins and triggers inflammation [156].

Photo-ageing is additional skin damage attributed to repeated sunlight exposure. This has both immediate and delayed adverse effects including sunburn/ inflammation that can progress to photosensitivity, immunosuppression and eventually to cancer formation [159].

Combating this destructive process that contributes to both skin ageing and deteriorating health can include:

- **Increasing your intake of antioxidant rich foods and supplements**
- **Increasing your internal antioxidant defense mechanisms** through Nrf2, which activates many antioxidant, anti-inflammatory, and detoxifying enzymes. Through these means, Nrf2 supports the structural and functional integrity of your mitochondria [152].

3.3.4.3 Impact on Carcinogenesis

Sunburn and excess sun exposure can cause premature skin ageing, immune system damage, cataracts, and non-melanoma and melanoma skin cancers [160]. Skin cancer occurs in three distinct stages: initiation, promotion, and progression.

- **Initiation** is irreversible and is caused by DNA damage upon exposure to a carcinogen such as a ROS derived from chemicals or UV radiation.
- **Promotion** is a long-lasting reversible phase where initiated cells multiple to form benign tumors upon repeated exposure to promoting agents.
- **Progression** involves transformation of benign tumors into invasive and malignant tumors that can spread to other body areas [161].

Both UVA and UVB are called complete carcinogens because they can initiate, promote, and progress cancer formation. UVA is weaker than UVB as an initiating agent but is a potent promoting agent [161]. It is the most important source of oxidative stress in human skin [162].

3.3.4.4 Impact on Mitochondria

One of the most toxic effects of free radicals and ROS is damage to cellular membranes. That damage starts with oxidation of membrane polyunsaturated fatty acids. This can cause many negative effects including:

- Increased membrane rigidity
- Decreased activity of membrane-bound enzymes
- Altered activity of membrane receptors
- Altered membrane permeability

However, free radicals and ROS can also directly attack membrane proteins and produce lipid-lipid, lipid-protein and protein-protein bonds that cause further membrane damage.

Mitochondria are particularly prone to this membrane damage. These organelles are the cell's powerhouses where energy/ATP is made [152]. During this process they produce ROS, but at the same time they are extremely vulnerable to their attack [163]. This vulnerability is amplified in the ageing process.

During ageing, mitochondria become dysfunctional due to:

- Age-related increases in tissue ROS generation [4]
- Accumulation of mitochondria DNA mutations/damage [163]
- Impaired oxidative phosphorylation (i.e., inability to make ATP) [163]
- Insufficient production of internal antioxidant enzymes [163]

This causes further overproduction of ROS [164].

Your body can react to this mitochondrial damage in various ways:

- It can increase production of internal antioxidant enzymes through Nrf2 activation, provided the necessary nutrients or activators are present to stimulate that response [4].

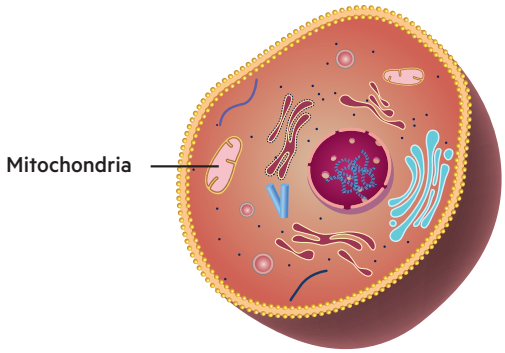


Figure 4: Mitchondria – a cell organelle that breaks down food and releases energy.

- It can selectively repair or eliminate defective mitochondria. This process is called mitophagy and is a specialized form of autophagy. This can save the cell from undergoing apoptosis/programmed cell death, under certain conditions.

Unchecked oxidative damage to mitochondria in cells throughout the body can contribute to overall ageing [5, 164] in the same way that oxidative damage in skin cell mitochondria accelerates skin ageing [32]. Mitochondrial damage and dysfunction are believed to be involved in age-related neurodegenerative diseases such as AD, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis [165].

Since mitochondria play a crucial role in the ageing process [5], a targeted approach to preventing their harm by ROS may contribute to healthy skin and longevity. That strategy could include [33]:

- A well-regulated lifestyle
- With caloric restriction
- Body care to remove toxins
- Appropriate exercise
- Under low stress conditions
- While eating a balanced nutritional diet
- Including antioxidant rich foods

And perhaps enjoying (see Section 3):

- Our Favorite 12 Foods to Maintain Skin Health
- Our Favorite 12 Supplements to Maintain Skin Health

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Conclusion

What did you learn in Section 1?

Your skin performs many functions that are important to your overall health. It provides a protective chemical and physical barrier between you and the outside world, helps you interact with your environment, makes vitamin D and is part of your body's total antioxidant defense and detoxifying systems. Many factors impact how well your skin can do its job including:

- Your specific Skin Climate® that is partly governed by your unique genetic make-up
- Environmental factors including your diet and lifestyle
- Your level of exposure to:
  – Pollution/environmental toxins
  – UV radiation from sunlight

Most of the factors that negatively impact your skin's function, either contribute to the amount of toxins within your body or prevent you from eliminating them through your internal detoxifying systems. These factors not only contribute to signs of skin aging including thinning, discoloration, wrinkles, and dryness; they also adversely impact how the rest of your body functions. Over time, they either contribute to the start or to continued progression of metabolic syndrome, and age-related diseases including CVD, arthritis, type 2 diabetes, AD, and cancer. All these conditions decrease your longevity.

Your body seeks to maintain homeostasis (balance/stability). Mild, short-lived forms of stress can improve skin health and longevity by stimulating your antioxidant enzyme production, detoxification, and healthy cell survival mechanisms. Some examples of mild stressors include:

- Calorie restriction
- Moderate exercise
- Pleasing and exciting life events

However, excess, and long-term stress by various factors can have the opposite effect. Your body works best when a proper balance is maintained. Additional examples where balance is particularly important include:

- Omega-3/6 fatty acid intake
- Electrolyte and fluid intake
- Gut microbiome composition

Maintaining your healthy skin and longevity is a lot about maintaining proper balance!

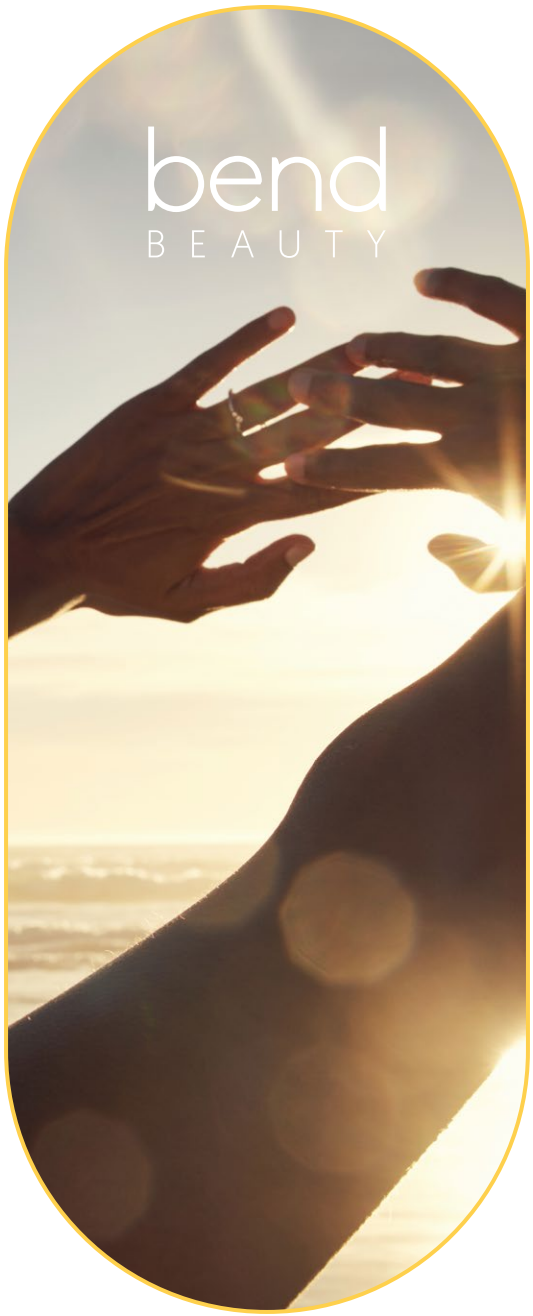
When balance is disturbed by too many negative factors, you can take steps to restore it by choosing appropriate foods and supplements. In the next sections we detail:

- Our Favorite 12 Foods to Maintain Skin Health
- Our Favorite 12 Supplements to Maintain Skin Health

In Section 2:

You will find out:

1. How skin health is connected to health in other areas of your body
2. What your skin condition can tell you about how other parts of your body are functioning
3. How the health of other body systems can impact skin health
4. How skin health can impact the health of other body systems



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Glossary of Terms

Angiogenesis
The process of making new blood vessels from pre-existing vessels.

Apoptosis
A form of programmed cell death that occurs under normal physiological as well as pathological/disease conditions and involves specific changes in shape and biochemical features.

Cytoprotective
A term used to describe anything that provides protection to cells against harmful agents.

Epigenetic
Nongenetic influences on gene expression

Homeostasis
The constant state of steady internal, physical, and chemical conditions maintained within living organisms that enables optimal functioning and includes many metabolic variables being kept within limits.

Mitochondria
Known as the powerplants within cells, are organelles/"organs" with cells, that create energy from nutrients through a process called cellular respiration.

Nrf2
Is a protein that help regulate a work of antioxidant proteins that can help protect against oxidative damage. This oxidative damage can be triggered by injury and inflammation and involves the production of free radicals. The Nrf2A pathway is a major mechanism in the cellular defense against oxidative stress which controls the expression of genes whose protein products are involved in the detoxication and elimination of ROS.

Polymorphisms
Variants within DNA sequences of genes that potentially alter the functionality of proteins synthesized based on the resulting modified genetic code.

Senescence
When a cell ages and permanently stops dividing but does not die. During this phase, the cell is essentially in 'suspended animation' because it is resistant to growth-promoting stimuli, typically in response to DNA damage.

List of Abbreviations

AD = Alzheimer's disease

AGFs = Angiogenic growth factors

ATP= Adenosine triphosphate

AA = Arachidonic acid

AGEs = Advanced glycation end-products

ALA = Alpha-linolenic acid

ALEs = Advanced lipoxidation end products

BMI = Body mass index

COPD = Chronic obstructive pulmonary disorder

CVD = Cardiovascular disease

DHA = Docosahexaenoic acid

DNA = Deoxyribonucleic acid

EFAs = Essential fatty acids

EPA = Eicosapentaenoic acid

GLA = Gamma-linolenic acid

LC-PUFAs = Long chain polyunsaturated fatty acids

LA = Linoleic acid

Nrf2 = Nuclear factor erythroid 2 pathway

PAHs = Polycyclic aromatic hydrocarbons

RDA = Recommended Dietary Allowance

ROS = Reactive oxygen species

TEWL = Trans epidermal water

UV = Ultraviolet radiation

UVA = Ultraviolet A

UVB = Ultraviolet B

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