InsideOut is formulated to support and enhance all the layers of the skin, hair and nails, and the supporting structures. The result is healthier, stronger, more vibrant skin; hair and nails that can better resist damage due to wear and tear, regardless of the cause.

By providing ingredients that are essential for the body’s natural synthesis and maintenance of the skin, hair and nails, and supporting layers, InsideOut helps heal and protect all three from all manners of stress and trauma, including sun exposure and aging.
InsideOut is the one stop solution for healthy and vibrant skin, hair and nails.

InsideOut will:

1. Increase the health and strength of the dermis, epidermis and supporting structures, resulting in healthier, younger looking skin.

2. Decrease wrinkles, help clear up any skin problems, and increase healing while at the same time decreasing side effects from environmental stresses, including exposure to the sun, and cosmetic procedures and surgery.

3. Improve dry skin by boosting the health and strength of the layers of the skin so that it naturally keeps moisture locked in.

4. Give added protection to the skin from damaging rays of the sun and increase healing of photo damages skin.

5. Decrease the formation and increase the healing of stretch marks, regardless of the cause.

6. Decreases inflammation, scarring and fibrosis secondary to skin damage.

7. Help firm up sagging skin in the face, neck and body.

8. Help deal with areas of skin that have too much or too little pigment.

9. Increase scalp and hair health and strength resulting in faster hair growth, increased hair follicle health and activity, a fuller head of hair, and decreased damage from hair coloring, curlers, perms, blow dryers, etc.

10. Increase nail strength and thickness, get rid of white spots, protect nails from the damage of using artificial nails.

11. Optimize the functioning and protective effects of the oil and sweat glands, thus helping to prevent dry, damaged skin and hair.

12. Benefit the whole body and improve your health and energy.
Your Skin, Hair and Nails

Although we don’t usually think of it that way, your skin is the largest organ in the body and includes the skin and accessory structures such as hair, nails and glands. And it does much more than just present our outward appearance to the world. Its two main layers the epidermis (outer layer) and dermis (inner layer), have protective, cardiovascular, neurological and immune functions that are important for our survival.

So while the look and feel of skin is something that preoccupies many of us, it’s the function of the skin that is paramount to our health and well-being. And in turn strong healthy skin gives us that young, vibrant, healthy look that we’re all after.

The skin and its appendages, including hair and nails, all have the same basic nutritional requirements and are affected by the nutritional state of the body. However, there are some differences depending on how you treat them.

For example your skin may be stressed more depending on how much you have done to it. All the various procedures such as dermabrasion, injections, defoliating agents, plastic surgery, and many others all stress the skin, and in the long run, increase scarring, decrease elasticity, and make it less able to withstand normal wear and tear.

Hair can be stressed out by various common treatments such as perms, dying your hair, excessive use of hair spray and gels, excessive washing, etc. And nails by the use of nail polish and remover, false nails, excessive manicures, etc.

In all of these cases the skin, and subsequently your hair and nails, needs help to deal with the various insults in order to stay healthy and vibrant.

InsideOut was formulated to help you cope with all of the above stressors, as well as aging and normal wear and tear. After using InsideOut for a month (it takes that long to see the effects as the repair and the strong new growth make themselves seen and felt) you’ll see the difference that consistent use of InsideOut will make to your skin, hair and nails.

Your Skin Reflects What’s Inside

Having healthy skin is not just about the skin itself, it’s also about total body health. All the things that you do to decrease damage to your whole body and minimize the effects of aging, will also benefit your skin.

What you see, your skin, hair and nails, are a reflection of what’s going on in your body. That’s because, like the rest of your body, all three derive nutrition, vitality and health from the body’s metabolic processes, which in turn are partially dependent on the nutrients you take in.

It’s from the inside that the outside is kept healthy and vital. Just like the rest of your body, your skin, hair and nails are affected by the way you live and what nutrients you provide. In
fact if you have inner health, your outside won’t be as affected by environmental or internal stress and abuse.

So if your skin is showing signs of premature aging – sagging, wrinkling, dryness, and roughness – then chances are your body is showing them as well.

And even in cases where the skin has aged more than the rest of the body (in most cases due to excessive long term sun exposure) it’s more important to deal with the damage systemically, from the Inside Out so that the living layers can heal, rather than cosmetically covering it over, from the Outside In.

**Beautiful Skin from the Inside Out**

The much-advertised daily scrub and then an application of the latest miracle skin cream will do little to keep your skin healthy and young looking. In fact it’s little more than window dressing, and so are the various treatments touted for their cleansing and rejuvenating qualities.

The fact is that treating the surface of the skin with moisturizing lotions, removing layers of dead skin cells and opening blocked pores is only a small part of keeping your skin healthy and beautiful.

The problem with all the various skin treatments available today is that they’re dealing with the appearance of the surface of your skin, which is made up of several thin layers of dead cells, and making up less than 5 percent of the total skin.

Because this layer is built to be relatively impermeable (that’s how it protects us) and is composed of dense but dead inert material, using all those creams, lotions and scrubs is nothing more than you would be doing by applying a wax coat to your car. It may look good for a while, but if the paint is bad and the body has rust spots, that wax of coat won’t do much for the looks of the car or for protecting it against rusting out.

Likewise, most skin preparations just affect the dead layer of skin and provide a superficial effect that lasts only as long as the dead skin remains in place. They do nothing past the epidermal layer and do not nourish the living dermal layer of skin.

In fact not only do they do very little to nourish and heal skin, some of these treatments, because they irritate and inflame the skin, and eventually result in thin, weak and scarred skin, are destructive in the long run.

The same applies to your hair and nails. As we’ve already mentioned many of the treatments result in damage to both even though they’re meant to make them “look” better. In the end the cumulative damage can be substantial unless you make an effort to stem it.
You can take two approaches when dealing with skin problems and anti-aging. One is the superficial approach using skin care products, plastic surgery, Botox® and anything else that tries to make you look younger without really doing anything about what caused the problems in the first place.

The second is to take a systemic approach in which you deal with the underlying reasons behind the changes in your skin and body.

The superficial approach is endemic in our society, fostered by massive companies that use aggressive marketing and pervasive ads to make you believe that they have the answer to making you look younger and more beautiful.

However, except for those that medically need it, the superficial approach is mostly smoke and mirrors. Sure it may feed your ego and that in itself may make you feel better for a while. However, although it may initially look good, it doesn't really do anything to make the skin stronger and healthier both in the short and especially in the long term.

You can sand, peel, inject, laser, apply, suction, cut and paste, and all the rest but what you're actually doing is setting yourself up for more and more of the same. That's because regardless of what they tell you, none of it lasts. In fact almost all of the treatments increase aging by stressing out the skin so that it tries harder to heal itself and in the long run just ages faster. It just doesn't look that way to most people because you're constantly covering it up one way or another so that the real damage doesn't show as much, at least not at first.

The classic, but mistaken pitch that you get from the salesmen of these products (and there are plenty of them since there's so much money in it) is that by irritating the skin in some way, either by sanding, peeling, using lasers, injecting, or whatever, the basic response is that the tissues will increase collagen production.

Sure the body will respond by producing more collagen but it also responds by increasing scarring and in fact deteriorating the integrity and plasticity of the collagen in the long run, more than it would have done naturally. The end result is older skin that is thinner, more scarred, less elastic and more vulnerable to further damage.

And it's not just the long-term effects that result in increased damage to the skin, the complications of many of these procedures in the short term are also played down. For example skin resurfacing procedures with the carbon dioxide (CO₂) laser, chemical peels,
and dermabrasion have significant complication profiles including the loss of skin elasticity.\textsuperscript{1,2,3,4,5,6,7,8,9,10,11,12,13}

As do the use of various “fillers” such as the resorbable heterologous fillers (bovine collagen, acid hyaluronique), autologous fillers (lipofilling, dermis-fat graft), biodegradable fillers (New-Fill), and permanent fillers (silicone, Artecoll, Evolution, Aquamid, DermaLive, DermaDeep, Bioplastique, Paraffin).\textsuperscript{14}

Also cosmetic surgery, from Botox® injections to Liposuction, can result in significant complications and even death.\textsuperscript{15,16,17,18,19,20,21,22,23,24,25}

**The Injury/Healing Dichotomy**

Most cosmetic procedures involving the skin operate on the principle that if you injure the skin it will repair itself and in the process actually improve the way it looks. But in the end it’s like robbing Peter to pay Paul.

To understand why all you have to do is think about how the body responds to injury. First it tries to heal the injured tissue but then scarring and catabolic processes take over, especially if the inflammatory stimulus is chronic.

The chronic inflammatory response induced by the repeated use of many “abrasive” cosmetics and processes is actually counterproductive in the long run rather than being helpful. In fact one of the more credible theories of aging is based on an increased inflammatory response leading to degenerative changes in the tissues of the body.

Some feel that many of the conditions that afflict us as we age, including the superficial signs of aging, are associated with inflammatory responses. Various levels of chronic inflammation are associated with all the classic diseases of old age, including cardiovascular disease, diabetes, Alzheimer's and frailty.

So the idea of increasing inflammation on a chronic basis to decrease the long-term effects of aging is ridiculous at best.

On the other hand the use of topical emollients, creams containing antioxidants, seaweed, herbs, collagen ingredients, and other compounds to decrease aging, while having some merit, isn't much better. The point is that compounds applied topically have limited abilities to reduce skin aging. In fact, it's unlikely that any of these products provide more than a short term improved look and feel but with still the same old tired skin underneath.

The best way to rebuild the skin's integrity and defenses, and decrease the effects of aging is to treat it from the inside out rather than from the outside in.
Packaging the Product

The natural cosmetic and cosmeceutical industry would have you believe that applying their lotions, creams and sprays will fight off the ravages of time and the environment and rejuvenate your skin. For them it's all about getting you to believe that their products will make you younger and more beautiful. Whether it's true or not is secondary.

Part of that belief in their products lies in their beautifully crafted packaging. It's getting to the point that the packaging is one of the most important decisions made when launching a new skin product.

Most of the companies work hard to make a package that's appealing to those looking to appear more beautiful and youthful. They know that a beautiful package can do wonders for their sales. As such, more work often goes into the packaging than to the product itself. Just have a look at the visually-alluring, injection molded, beautifully crafted packages for some of the more expensive lines of anti-aging skin-care products.

And then there's the names of these products. Powerful and imaginative names that promise much more than the products can deliver.

With InsideOut, while the label is professionally done and attractive, it's not about the packaging. It's about what's inside.

First of all the ingredients in InsideOut are of the highest quality with no contaminants or impurities. What's on the label is what's inside.

Secondly tablets are used instead of capsules since you can get 4 times the ingredients in each compressed tablet than you can in capsules containing loose powder. As well, the tablets are engineered to break up instantly in the special environment that exists in the gastrointestinal tract. As such, the tablets disintegrate fully and are 100% absorbed.

And lastly its the ingredients in InsideOut that work together synergistically to rejuvenate and beautify your skin, hair and nails, and improve your health.

So with InsideOut it's definitely not about the packaging, not about covering things over, not about placebo effects - it's about results.
The Before and After Pictures

And then of course there are the before and after pictures that show through pictures-don’t-lie technology, just how effective a product or procedure really is.

The question you have to ask in all of these pictures is BEFORE AND AFTER WHAT? In most of these pictures the before pictures have been embellished to make them look as bad as possible, and the after pictures have been manipulated to make them look as good as possible.

Basically the before and after pictures are designed to literally pull the wool over you eyes. They’re a scam and a sham and proof that PICTURES LIE. That’s why I don’t make extensive use of them in the marketing of InsideOut.

Also it’s difficult to show in a picture just how much healthier and stronger skin is and looks after using InsideOut since these kinds of changes are difficult to show in the very limited format of a 2 dimensional picture.

In the end, all the hype, pictures and testimonials won’t give you the proof you need. In fact, there’s no better proof than success, and you’ll see this for yourself when you use InsideOut.

However………..

We have had such amazing success in some of our people who have been using InsideOut religiously for up to several months that I want to share one of our success before and after pictures with you.

The after picture was shot after this woman had used InsideOut consistently for 6 months.
What's the Answer?

So if cosmetics, surgery, spas, and all the other beauty and anti-aging products and treatments aren't the real answer, what is?

Simple.

What you need to do is to decrease damage to tissues in the body, and provide effective ingredients and ways for your body to repair itself. This is done by decreasing inflammation and oxidant damage to the body as a whole rather than just making an anti-aging statement.

You can't provide intensive protection against free radicals that damage cellular structures, and you can't decrease inflammation in the body, by using creams and lotions. It just doesn't work that way. You have to work from the inside out rather than piling nutrients on dead layers of skin.

An important part of the solution to dealing with damaged skin and stemming the effects of aging is using the right nutritional ingredients, including structural components, antioxidants, natural anti-inflammatory and immune system stimulators.

And That's What InsideOut Is All About.

Free radical damage and chronic inflammation are widely held to be responsible for the deterioration in our bodies as we age. InsideOut contains potent antioxidant and anti-inflammatory properties that effectively decrease the ongoing damage caused by stress and aging, and contains the stimulus, nutrients and building blocks for repairing damaged tissues.

The bottom line is that emphasis on youthful skin should be on a systemic or inside level rather than on a topical or outside one.

The foundation for youthful skin comes from having a healthy and strong body that is able to better withstand the destructive influences of our environment and aging. Once that's in place, the creams and lotions and other non-destructive therapies can be used as window dressing.

Using InsideOut to Counter the Problems and Side Effects of Cosmetic Procedures

InsideOut should be part of every cosmetic and plastic surgery procedure. In fact it may well represent one of the more important tools for the cosmetic practitioners and plastic surgeons (many of whom incorporate skin care into their practice and should incorporate InsideOut) for improving healing time and the outcome, and decreasing the incidence and severity of adverse effects.

So if you do decide to have some of the minimally invasive procedures done such as Botox® injections and laser treatments or the more invasive cosmetic procedures such as
having fat injected into problem areas, or even more extensive plastic surgery, then you should be taking InsideOut before during and after in order to counter some of the short term and long term adverse effects from these procedures.

Not only will InsideOut make your skin healthier and decrease short and long term adverse effects of these procedures, it will also increase healing and thus decrease downtime, the post procedure time when swelling, redness and discomfort can make you self conscious and compromise your lifestyle.

**That’s Not All**

But that’s not all. InsideOut will also rejuvenate you at the same time, giving you more energy and bounce than you’ve had for years.

**What’s not in InsideOut**

And it’s not just what’s in InsideOut that’s important, it’s what’s not in it as well. In looking at the possible list of ingredients, I eliminated those that I felt were useless or even counter productive.

For example you won’t see thymus extracts or glandular material in the list of ingredients. Thymus extracts are usually ground whole thymus glands of young calves that are dried or strained.

There are several reasons why I don’t include thymus extract in InsideOut. One is that the bovine tissue (cows calves) used for the extracts could harbor viruses or prions such as those that cause mad cow disease.

Another is that it’s unlikely that very much of the peptides present in thymus extracts would make it intact past the harsh environment of the gastrointestinal system.

And a third reason is that the use of thymus preparations, if indeed any of the peptides made it into your system, would decrease your ability to naturally produce these peptides.

It’s likely that the successful use of exogenous thymic peptides shuts down your own production of these peptides. And that’s a bad thing as it takes time for your body to ramp up the thymus machinery once you discontinue the thymic peptides.

That doesn’t happen with InsideOut since it acts by increasing the formation of your natural thymic peptides by using ingredients such as arginine and zinc that ramp up your thymic peptide producing machinery, rather than shutting it down. So if you go off InsideOut you’re still in business, even if your levels go back down to what they were before using InsideOut.
The Layers of the Skin

The skin is the largest organ in the body and is more complex than it appears on the surface.

In fact the skin usually reflects what’s going on inside of us. Changes in skin texture, moisture, elasticity and pliability, and the appearance of conditions such as acne, eczema or psoriasis, all point to underlying imbalances in the workings of the body.

The skin is composed of the outer epidermis and the underlying dermis. The surface of the epidermis is all that we see and its main function is to serve as a thin shield of compressed keratin containing cells that protect us from environmental assaults such as light, heat, infections, etc.

The dermis is composed of connective tissue containing collagen and elastic fibers, hair follicles, oil glands, the ducts of sweat glands and a small amount of fatty tissue. It’s these collagen and elastic fibers that support our skin and endow it with its elastic qualities - the ability to stretch and then return to shape in good order.

Hair is composed of cornified threads of cells that develop from the epidermis. Like hair, nails develop from the epidermis. The healthier and stronger the epidermis, the stronger and healthier the hair and nails.

Oil glands secrete sebum, a substance that keeps the skin soft and pliable and prevents excessive moisture evaporation from the skin's surface. Sweat glands, obviously, secrete sweat, the major temperature-regulation mechanism of the body. Sweat also plays a role in eliminating wastes. To have healthy looking and functioning skin, it’s important that these glands work optimally.
Inflammation and Skin Integrity

Both photo-aged and aged skin show the results of chronic inflammation. It's felt that damaged and aging skin is the result of cumulative damage to the collagen and cellular structure that keeps the health and integrity of skin intact.

The cumulative damage to skin is a result of two processes, a baseline aging process that goes on in all of us regardless of environmental influences, accentuated by various diseases and conditions, and the accumulation of damage by environmental processes such as sun exposure, smoking, trauma, psychological factors, air pollution, etc.

Both of these processes result in a cumulative and chronic inflammatory reaction that takes its toll on skin, the degree of the reaction or damage to skin being dependant on genetics, diseases present, and the severity of the environmental stressors.

In the end, however, it all boils down to common inflammatory processes. All factors lead to increasing severity of the inflammatory response, whether it be the aging or disease processes, oxidative effect from free radicals, sun damage, etc., which in turn lead to increasingly damaged skin. The damage eventually manifesting itself as sagging, wrinkled, old looking skin.

InsideOut is formulated to decrease inflammation in all the ways that it's inappropriately increased in the body, whether by free radicals, sun damage, disease, lipid peroxidation, aging or trauma. Regardless of how it’s produced, InsideOut has a way to reduce it and in so doing decrease damage to skin and allow any damage that’s present to heal itself. Inside Out, rather than just by applying a band-aid approach.

It's important to realize that when all the potions, lotions and creams have been applied to the surface of the skin, collagen, elastic fibers and extracellular matrix still need to be repaired and correctly formed and nourished to provide the structural support the skin needs. Collagen nutrition is one of the mainstays of good skin health.

Collagen First

Collagen and elastic fibers feature as important components of the dermal layer. If these components are not in optimal condition, the skin loses its supporting matrix.

This is most commonly seen as a process of aging. The collagen and elastic fibers stiffen and break, resulting in loss of firmness, elasticity and moisture-retaining properties. The skin begins to sag and develop wrinkles. Aging also brings with it a decrease in the size of the oil glands, which leads to skin dryness and flaking and an overall reduced capacity of the skin to heal.

Collagen is formed from three amino acids: glycine, hydroxylysine and hydroxyproline. We cannot ingest hydroxylysine or hydroxyproline. However, we can ingest their immediate precursors. Lysine and proline can convert to hydroxylysine and hydroxyproline, but only
in the presence of vitamin C. Without vitamin C, this conversion cannot occur and collagen formation will suffer. This conversion also relies on the presence of zinc, another nutrient vital for good skin health. Shark cartilage, a rich source of the collagen-building blocks lysine, proline and glycine.

All of these ingredients, and many others as we'll discuss in detail below, are present in InsideOut.

**Free radical damage**

The importance of antioxidant protection in skin health is widely undervalued. Antioxidants serve to protect cells from free radical damage. Free radicals induce inflammation, destroy cells and hasten the ageing process.

The most immediate and visible signs of ageing are reflected in our skin. Antioxidants can do a lot to preserve the skin’s function and longevity. As a result, they play a crucial role in maintaining the health of the skin and its supporting structures, as well as most other tissues and organs in our bodies.

**Protection Against Photoaging**

Photoaging describes damage to the skin caused by exposure to sunlight including wrinkles, mottling and pigmentation of the skin, and skin roughness. While these changes are usually associated with aging, photoaging makes people look older than they really are.

Solar radiation stresses human skin, mainly by increasing free radical formation, and is associated with short and long term effects including sunburn, premature skin aging, and skin cancer. It affects both layers of the skin. It makes the top layer of skin, or epidermis appear rough and dull and thin in places, and also more prone to age spots and skin cancers.

In the dermis, sun exposure causes damage to the elastic fibers and a slow down in both collagen production and effective repair. The result is that the skin loses elasticity, visible wrinkles and sagging appear, and skin appears much older than it actually is.

The usual methods of using sunscreens, staying in the shade and covering exposed skin are still among the best methods for protecting skin. Additionally, research now indicates that several nutrients and antioxidants can aid in protecting skin from damaging UV rays, healing damaged skin and may contribute to lowering the risk of developing age spots and skin cancer.
Photoprotective Ingredients in InsideOut

InsideOut contains all of the ingredients that have been found to be protective from both the immediate effects of the sun, and the long term photoaging effects.

Antioxidants

It’s been shown that antioxidant levels decrease with age\textsuperscript{29,30} and that oral antioxidants can counteract some of the adverse effects of the sun on the skin.\textsuperscript{31,32,33,34,35}

In clinical trials, a number of antioxidants, including carotenoids, vitamins E and C, N-acetylcysteine (NAC), and many others contained in green tea, rosemary extract, and pine bark extract have been found to be capable of scavenging free radicals generated during photooxidative stress caused by sunlight.

For example one study looked at the photoprotective potential of the dietary antioxidants vitamin C, vitamin E, lycopene, beta-carotene, and the rosemary polyphenol, carnosic acid.\textsuperscript{36} The authors concluded that all of the substances showed photoprotective potential to varying degrees.

As well many antioxidants have additional effects. For example, besides being an antioxidant, Vitamin C is essential for collagen formation. In the body, beta-carotene is converted into vitamin A, which is essential for proper development of the skin. Research shows that vitamin C, beta-carotene, quercetin and members of the catechin family can protect against skin damage caused by UV rays. Also some antioxidants can have a beneficial effect on hyperpigmentation of the skin.\textsuperscript{37}

Furthermore, antioxidants are more effective when more than one is present at the same time. For example, when beta-carotene is combined with vitamin E (another antioxidant), skin protection is enhanced. Other studies show that antioxidant protection increases as the diversity and quantity of antioxidants increases in the diet.

Green Tea

Green tea contains natural antioxidant polyphenolic compounds known as epicatechins. Researchers have shown that green tea polyphenols -- taken orally or applied topically -- exert photoprotective effects that inhibit ultraviolet radiation-induced skin tumors (tumorigenesis).

Studies have also shown that green tea extract possesses anti-inflammatory activity, protecting against ultraviolet (UV) light-induced skin inflammation (erythema) and photooxidative stress.\textsuperscript{38,39} The major polyphenolic chemopreventive constituent in green tea responsible for these biochemical or pharmacological effects is (-)-epigallocatechin-3-gallate (EGCG).

When researchers tested green tea extracts in animal models they found that these polyphenolic compounds afforded protection against chemical carcinogenesis and
photocarcinogenesis in mouse skin. In similar experimental studies with human skin, green tea polyphenols again demonstrated anti-inflammatory and anticarcinogenic properties.40

Vitamin C and E

In one study, a group of 40 healthy volunteers were given vitamin E or vitamin C or both. The researchers found that the combination of C and E together protected the skin and suppressed the sunburn reaction.41

In another study the authors concluded that the combination of vitamins C and E could be exploited for the prevention of solar radiation-induced skin cancer in an antioxidant intervention study.42 These and other studies suggest that vitamin E has a synergistic effect with ascorbic acid, due to vitamin C’s ability to recycle vitamin E.43

Carotenoids

Studies have shown the protective effects of oral carotenoids on skin exposed to UV radiation.44 One study found that sunburn was suppressed significantly with a combination of carotenoids (such as beta-carotene) and vitamin E. The researchers concluded that the antioxidants provided protection against erythema in humans and were effective in diminishing sensitivity to ultraviolet light.45

Selenium

There is evidence to show that selenium can inhibit sun damage and skin cancer and thus may be useful as a photoprotectant.46,47

One of the reasons for selenium’s effects is that the sensitivity of human dermal fibroblasts to UVA radiation has been linked to a decrease in intracellular glutathione levels. The results of one study found that that compounds capable of inducing glutathione synthesis can act with selenium to protect cells against UVA damage.48

Another study found that a combination of vitamins E and C, carotenoids, selenium and proanthocyanidins (such as pycnogenol) offered photoprotection to UV irradiated skin.49 In this study the authors postulated that since endogenous antioxidants are decreased in skin and blood during UV exposure a combination containing both lipid and water-soluble compounds including: carotenoids (beta-carotene and lycopene), vitamins C and E, selenium and proanthocyanidins, might be useful. They found that this combination slowed down the time of the development and grade of UVB-induced erythema and concluded that protection of the skin against irradiation can be achieved by the use of exogenous antioxidants.

Zinc

Zinc, the important trace mineral for DNA protection against oxidative stress, has been shown to decrease UVA1-induced early and delayed apoptosis in human fibroblasts.50,51 Zinc supplementation protects against UVA-induced DNA damage in human skin fibroblasts.52
A combination of selenium and zinc has also been found to have protective effects against UV-A damage.\textsuperscript{52}

**Omega 3 Fatty Acids**

Fish oil, which is rich in omega-3 polyunsaturated fatty acid, has been shown to have photoprotection effect. In clinical trial, there was decreased UVB-induced sunburn cell formation and inflammation after 3 months of fish oil ingestion. Furthermore, ingestion of fish oil was shown to reduce UVA provocation response.\textsuperscript{53}

A recent study looked at the potential for oral agents for incidence of skin cancers and photo-ageing and concluded that the **omega 3 fatty acids** have the potential to reduce the ultraviolet induced release of cytokines and thus protect skin from ultraviolet exposure.\textsuperscript{54} More specifically a recent study found that **EPA** offered some protection against ultraviolet induced skin damage and may reduce skin cancer in humans.\textsuperscript{55}

**Creatine Monohydrate**

A recent study found that topical creatine has beneficial effects on skin damage because of its ability to recharge the energy mechanisms in these cells that deal with the protection and repair of skin damaged by free radicals.\textsuperscript{56} For more information see the section on creatine below.

**Conclusion**

When you go out into the sun, take along sunscreen, protective clothing, and InsideOut for added protection against the damaging rays of the sun.
Stretch Marks and InsideOut

Stretch marks are tears in skin that turn into scars. They happen for various reasons, including certain diseases and the use of some medications. However, the most common reason is when skin is overstretched due to weight gain. This happens when you gain weight faster than the skin can accommodate.

Although the skin is usually fairly elastic, overstretching it as a result of tissue growing faster than the skin layers can stretch results in small tears in the underlying layers of the skin. These tears or stretch marks, like any other trauma to the skin, heal with the formation of scar tissue.

An early sign of stretch marks developing is when an area of skin becomes flattened and thin with a pink color. They then develop into reddish or purplish lines that may appear indented and have a different texture from the surrounding skin. Although they vary in size, they’re usually around three or four inches long and up to half an inch wide.

As they heal, stretch marks usually turn lighter and become much less noticeable. However they don’t go away and are visible as glossy skin that appears streaked in silver or white with some degree of depression and wrinkling.

Who Gets Them and Where

Men and women can get stretch marks on several areas of their bodies, including the abdominal area, thighs, hips, chest/breasts, upper arms or lower back.

While anyone can get stretch marks, some are more susceptible to them than others. That’s because the susceptibility to stretch marks depends on genetic and environmental factors so that every person and situation is unique. Differences in skin strength and elasticity and ability of the skin to grow causing some people to be more susceptible to stretch marks than others.

In general, however, stretch marks, while more common in women than in men, and in adults, can happen to anyone at any time, with some factors increasing the incidence.

For example, people who are overweight often have stretch marks. So do women who have gone through one or more pregnancies.

Power athletes and bodybuilders are prone to getting stretch marks, mostly around the upper arms, shoulders and chest tie ins, not because of rapid body weight and body fat gain, but because of rapid gains in muscle that these sports can produce.
the use of anabolic steroids and even corticosteroids may make them more prone to stretch marks.

What Can You Do About Them?

While not harmful to your health, stretch marks can make you overly conscious of the way you look and can have a psychological impact, in some cases they can even be socially debilitating.

There are two different and complimentary approaches to dealing with stretch marks. One is prevention the other treatment. Cosmetic treatments often try to deal with both while surgical treatments usually deal with trying to get rid of them once they form.

It makes good sense to consider both sides of the equation since stretch marks are in essence scars and are extremely difficult to eradicate completely once they form. This is why prevention is so important.

But what’s the best way to deal with stretch marks?

Although there are many creams and other skin products on the market that claim to prevent and/or heal stretch marks, the truth is that most are pretty useless. That’s because they don’t penetrate deep enough to significantly affect the damaged tissues or to strengthen tissues so that they resist tearing.

The only way to effectively strengthen the skin and the supporting tissues and to increase healing is to supply your body with the means and nutrients to do both. And this is what InsideOut does.

I formulated InsideOut to increase the strength and elasticity of your skin and stimulate the production and regeneration of new skin cells and skin matrix. When you use InsideOut your skin will become stronger and its natural elasticity will be increased. This will significantly aid in the prevention of dermal ruptures that eventually result in stretch marks.

Thanks to its restorative effects InsideOut will also effectively help to fade out and diminish the impact of existing stretch marks while at the same time helping to prevent new stretch marks from forming.

InsideOut can help provide the skin with the essential elements it needs to not only help maintain its maximum elasticity, which helps to prevent stretch marks, but to recover from existing stretch mark scarring.

InsideOut helps stimulate the normal tissue regeneration process that occurs after stretch marks are formed. By strengthening and thickening the layers of the skin it helps to normalize the surface of the skin and diminish the appearance of stretch marks, both old and new.
InsideOut also helps to protect the skin from further damage by maximizing the elasticity and resiliency of the skin.

**Cosmetic and Surgical Procedures**

Because stretch marks are made up of scar tissue the only way to physically minimize them is through surgical procedures. For that you need to see a dermatologist (a physician who specializes in dealing with skin problems) or a plastic surgeon.

These doctors may use one of many types of treatments - from actual surgery to techniques such as microdermabrasion and laser treatment - that reduce the appearance of stretch marks. 69 70 72 73 74 75

But even here the use of InsideOut will better prepare the skin for the procedures, improve the results, decrease healing time and help eliminated any side effects.

InsideOut is beneficial to anyone with who is trying to prevent the occurrence of stretch marks, or repair the damage caused by existing stretch marks, regardless of the cause. And because it strengthens and helps heal the skin, it’s also beneficial for anyone who’s thinking of having cosmetic or surgical procedures done to get rid of the stretch marks.
The Bottom Line

*InsideOut* is formulated to support collagen, the extracellular matrix and all the cells involved in the production of healthy skin and in the healing of damaged skin. It will support and enhance all the layers of not only the skin but also its supporting structures.

By providing ingredients that are essential for the body’s natural synthesis and maintenance of the skin and supporting layers, it aids in protection against the effects of stress, trauma, sun exposure, and aging, and aids in the healing of damaged skin.

The result is a healthier, stronger skin that can resist damage due to wear and tear, the sun and aging.

Many natural ingredients and remedies have been used over the centuries that have not only alleviated symptoms of tissue stress, but also shown to help rebuild tissue and restore these tissues. Many of these natural substances aid in recuperation, help heal damaged skin and help strengthen skin and musculoskeletal support tissues.

All these substances, as well as various vitamins, minerals, antioxidants, amino acids, and others, if used in a proper and timely fashion, have a positive effect on the immune system, and both preventing and treating skin damage from wear and tear, regardless of the cause.

*InsideOut* is a comprehensive, multifaceted, synergistic nutritional supplement that can heal and rejuvenate your skin the only way that is really meaningful, from the Inside Out.
Ingredients in InsideOut.

BioCell Collagen II™

Water and large molecules fill the spaces in-between the cells and collagen fibers. One of the major components of the ground substance are the proteoglycans and structural glycoproteins, which trap water molecules and lend strength, rigidity and resiliency to the extracellular matrix in the skin and dermal layers.

Proteoglycans are large molecules formed by many linear chains of polysaccharide units called glycosaminoglycans (GAGs). GAG chains radiate out from a protein core like bristles of a bottlebrush. Sulfation and the complexes of the GAGs determine their biological activity. These complexes, which may contain hundreds of attached proteoglycan aggregates, constitute a significant role in cartilage tissue.

Proteoglycans act as a molecular sieve moderating the movement of cells, and nutritive and inflammatory substances. They are also responsible for attracting and maintaining water balance within the tissue. The high density of negative charges of these molecules attracts and binds water molecules. Because they attract and hold water, they form a ‘sponge’ that, when compressed, absorbs force and distributes it equally, thereby decreasing degeneration secondary to various stresses and trauma.

BioCell Collagen II™ provides low molecular weight compounds, which are readily and easily absorbed into the bloodstream. The components of BC II including chondroitin sulfate, hyaluronic acid (HA), and glucosamine sulfate can support proteoglycans and glycosaminoglycans (GAG’s) involved in collagen production and increasing collagen synthesis.

The low molecular weight compounds present in Biocell Collagen II™ are more biologically available and more effective than the higher weight compounds present in many other preparations.

The amino acid profile of BioCell Collagen II™ is rich in the primary amino acids, such as arginine, proline and glycine that make up the type II collagen molecule and as such is conducive to collagen formation and repair.

Hyaluronic Acid

BioCell Collagen II™ naturally contains ultra high concentrations (min. 10%) of low molecular weight hyaluronic acid, which is vital for the health of soft connective tissue.
where it is a major component of the extracellular matrix, and is present in synovial joint fluid, cartilage, the eye, and in skin tissue both dermis and epidermis.

Hyaluronic acid is unique among the GAGs in that it does not contain any sulfate and is not found covalently attached to proteins as a proteoglycan. It is, however, a component of non-covalently formed complexes with proteoglycans in the ECM. Hyaluronic acid polymers are very large (with molecular weights of 100,000 - 10,000,000) and can displace a large volume of water. This property makes them excellent for strengthening skin tissue and for giving it increased resistance to wear and tear.

Hyaluronan (HA), a nonsulfated glycosaminoglycan composed of repeating disaccharide units of N-acetylgulcosamine and glucuronic acid, is one of the major extracellular matrix components in both the epidermal and dermal layers of the skin. HA is well known to hold water, maintain the extracellular space, and facilitate the transport of ion solutes and nutrients.

Interestingly enough, BioCell Collagen II actively inhibits hyaluronidase, an enzyme that breaks down hyaluronic acid this increasing HA levels in tissue.

**Glucosamine**

Glucosamine sulfate is one of the basic substrates for synthesis of these important macromolecules in connective tissue. The synthesis of glucosamine from glucose and glutamine is the rate-limiting step in GAG production.

Since the ability to convert glucose to glucosamine declines with age and with increasing trauma to the body, whatever the source, because of a reduction in the amount of the enzyme glucosamine synthetase, providing glucosamine allows the body to bypass that rate limiting step and produce the collagen it needs as it needs it.

Studies have shown that oral supplements containing glucosamine, as well as amino acids, minerals and antioxidants (all of which are in InsideOut) can improve the appearance of visible wrinkles and fine lines.

**Chondroitin**

Chondroitin sulfate is a very large molecule, composed of repeated units of glucosamine sulfate. Like glucosamine, chondroitin sulfate attracts water. It is mainly known because it is a major component of cartilage. However, it’s also been found that it has significant effects on skin.

In a recent study oral chondroitin was found to have dramatic effects on skin. In this study the use of oral chondroitin was found to increase in the hydration and softening of the skin and to reduce swelling, redness, flaking, and itching of psoriasis with a clearance of psoriasis in one patient.
There is some controversy about the absorption of chondroitin sulfate and thus its usefulness. Recent studies, however, have confirmed its absorption and oral bioavailability.\textsuperscript{79,80}

**Methyl sulfonyl methane (MSM)**

MSM stands for Methylsulfonylmethane, a stable odorless metabolite of DMSO. MSM, a natural form of organic sulfur found in low concentrations in our bodies. Along with glucosamine sulfate, it is a basic substrate for the synthesis of connective tissue. Many claims have been made for MSM, including relief from arthritis, muscle pain, joint pain and inflammation, beneficial effects on the immune system, and scar tissue reduction, and there are a few studies that support these claims.\textsuperscript{81,82}

A recent paper looked at the possibility that MSM may exert some effect on inflammation and arthritis secondary to increases in serum sulfate.\textsuperscript{83} These effects would also exert some benefits on skin.

**Creatine**

A recent study found that topical creatine has beneficial effects on skin damage because of its ability to recharge the energy mechanisms in these cells that deal with the protection and repair of skin damaged by free radicals.\textsuperscript{84} As such, used topically, creatine may be useful not only to counter the damaging effects of sun on the skin but also for the prevention and treatment of aging human skin.

But while topical creatine may be useful, taking it orally may be even more beneficial. That's because aging, at least in part, is likely due to changes in mitochondrial function that are an important cause, as well as a consequence of aging.\textsuperscript{85}

Much of that is due to the dysfunctional effect of decreased mitochondrial function on ATP (the ultimate energy source for the body) synthesis. As well, mitochondrial dysfunction can increase the formation of free reactive oxygen species (ROS) and thus inflict further damage on cellular structure and function, which in turn increases the aging process.

Despite the important function of creatine as an essential energy precursor, the endogenous synthesis of creatine in humans is not sufficient to provide us with all the creatine our bodies need to function optimally.

The body needs about 2 grams of creatine a day to account for the amount of creatine that is metabolized to creatinine irreversibly. The creatinine is then excreted in the body. Part of this turnover can be replaced through exogenous sources of creatine in foods, especially meat and fish, and of course by supplementing with creatine monohydrate or creatine phosphate (the two most common forms available in supplements with the monohydrate
being by far the most widely available). The remainder is derived via endogenous synthesis from the precursors arginine, glycine and methionine.

And we need more creatine if we’re under stress, physical or psychological and also as we age. For example cells in the skin show signs of a declining creatine level, likely because of stress and changes in our skin as we age, including decreases in the blood supply.

But it seems, according to this study, that for the skin (and this applies for every other cell and tissue in the body), that creatine has beneficial effects on skin damage by its ability to recharge these cells energetically, and thus protect them against free radical-induced cell damage.

This study looked at the effects of a topical creatine application, with the conclusion that the use of creatine in cosmetic and dermatological formulations would be useful for prophylaxis and treatment of aging human skin.

In my view, however, oral creatine may be even more useful for the skin, working from the inside out, and of course for the rest of the body. A recent study, for example, found that creatine protects from mutations of mitochondrial DNA, the same mutations that play a role in neurodegeneration, normal aging, premature aging of the skin (photoaging), and tumors.86

Also the use of oral creatine has been shown to increases cellular hydration, thus potentially making it useful for increasing epidermal hydration and therefore for damaged/dry/cracked skin. The combination of magnesium and creatine (both in InsideOut) has also been shown to have an increased effect on cellular hydration.87

**Alpha Lipoic Acid**

Alpha lipoic acid (ALA) is a hot topic these days among many skin care conscious people. And for good reason since it’s been shown to have several properties that impact on skin health and repair.

ALA is a natural substance that has potent antioxidant and anti-inflammatory properties that can recycle other antioxidants such as vitamin C, vitamin E and glutathione. It also is important for optimizing energy metabolism and thus provides an important impetus for youthful skin repair functions.95

It has been shown to inhibit cross-linking among proteins, a process that contributes to the aging process in the body and especially in collagen-heavy tissues such as skin. Alpha-lipoic acid activates a collagen-regulating factor known as AP-1 that turns on enzymes that digest glycation-damaged collagen and thus make the skin more supple and youthful looking.

It also improves vascular function in skin and helps the repair process in damaged tissues.96,97
As well, it helps neutralize and remove various toxic metals, including mercury, from the body.

All of these properties allow ALA to exert beneficial effects on skin, hair and nails. And while ALA is mostly contained in topical skin creams and lotions, it’s much more effective when taken orally, as in InsideOut, especially since the formulation also contains other supportive and healing ingredients that have additive and synergistic effects.

Amino Acids

Amino acids contribute to skin health and repair in many ways. For example, proline and glycine are essential for collagen production. Both are in the BioCell Collagen II™, and extra glycine and proline are also added to InsideOut. Proline is the precursor to hydroxyproline, an essential ingredient in collagen production and thus in skin health and repair.

Methionine, an essential sulfur bearing amino acid is necessary for collagen and protein and tissue formation. It has been shown to stabilize and protect skin and also has shown to be useful in the treatment of damaged skin.

Arginine aids in the release of growth hormone, a powerful hormone that aids in collagen tissue repair. As well, arginine increases nitric oxide formation, which causes vasodilatation and improves circulation promoting the healing of damaged tissues. It has also been shown to act as a mild analgesic and relieve pain. A report in The Lancet (Vol. 352, July 25, 1998) suggests that it may help promote soft tissue repair.

Arginine enhances the immune system, specifically by stimulating the thymus gland and the manufacture of T cells. This increase in T cell activity can be effective in fighting bacteria, viruses, cancer tumor cells, AIDS, chronic fatigue, and other immune system related health challenges.

Taurine is a sulfur-containing amino acid, the second most abundant amino acid, and the most abundant free amino acid found in muscle and skin. It has cytoprotective properties and aids in the protection and healing of skin and musculoskeletal tissues. Taurine also increases cellular hydration and is therefore useful for increasing the water content of dry skin.

For example, taurine is considered a potent antioxidant and cytoprotective agent that may be useful for combating the adverse effects of physical and psychological stress, and aging.108,109

Histidine may also play a role in skin health by decreasing inflammation.
Serine is needed in the formation of the phospholipids of cell membranes and contributes to "membrane fluidity." It is good for the skin and has even been used as a natural moisturizer in skin creams.

Methylcobalamin (Vitamin B12), Pyridoxine (Vitamin B6), Thiamine (Vitamin B2), Folic Acid, and Methyl donors Betaine (Trimethylglycine), and Choline

Methyl donors are important for the methylation reaction, which adds a methyl group (one carbon atom and three hydrogen atoms), on proteins, enzymes, chemicals, DNA, and amino acids like homocysteine. Methylation is important for maintaining many functions in the body including genetic expression, neurological, musculoskeletal and skin function.

InsideOut contains a number of ingredients involved in methylation, including vitamin B12 (as methylcobalamin – the biologically active form of B12 that has an added methyl group – the synthetic B12, cyanocobalamin, a much cheaper form of B12 with a cyanide molecule, has to be metabolized to methylcobalamin in the body), folic acid, B6, betaine, dimethylglycine and choline.

These ingredients optimize macronutrient metabolism and help maximize muscle mass and decrease body fat, often acting synergistically to achieve their effects. As well, they decrease serum levels of homocysteine, cholesterol and C-Reactive proteins, markers and mediators of heart disease and inflammation in the body.

The health effects of all three of these B vitamins, the prevalence of deficiency and effects of supplementation of all three, especially in the elderly, have been extensively documented.

These studies have shown that several of the medical parameters, such as homocysteine, cholesterol and C-reactive protein, markers of heart disease and inflammation in the body, are decreased by the use of these vitamins, and by the use of some of the other ingredients in InsideOut, including betaine (trimethylglycine – three methyl groups attached to the amino acid glycine) and choline.

Antioxidants

Both solar radiation and aging are felt to increase ROS generation, which in turn damages the collagen in skin and leads to wrinkles and all the other changes we see in aging skin. As well, it’s been shown that antioxidant levels decrease with age.

Now we know that we can counteract the effects of free radicals in the body through our internal antioxidant system. In fact we have complex mechanisms in place that can easily handle baseline oxidant stress. However, it’s also well known that under stress, whether it
be exposure to the sun, intense exercise, or the ravages of time, our internal antioxidant systems are often not enough.

This is where natural antioxidants in our diet, and as nutritional supplements, can be useful to boost our internal system to more effectively deal with oxidant and other free radical stresses as well as detrimental metabolic and cellular mechanisms.

The vitamins A (especially in its B carotene form), C and E are perhaps the best known of the antioxidants. Lesser-known compounds such as lycopene, selenium, quercetin and alpha lipoic acid are also potent antioxidants and extremely useful.

For example, lipoic acid can prevent some skin collagen abnormalities.

While many compounds, such as alpha lipoic acid are useful if taken internally, they are not effective when used on the surface of the skin.

A variety of antioxidants work best to protect and strengthen collagen and the cell membranes, guarding against the damages of free radical activity.

Antioxidants form a front line defense against cell damage caused by free radicals, which are involved in epidermal and dermal damage and inflammation and even in the aging process. The use of antioxidants can reduce free radical damage that occurs under normal living conditions. They can also attenuate the stress induced damage to injured tissues caused by an increase in free radicals, thus accelerating the healing process.

Antioxidants, such as vitamins C and E, selenium, green tea, pine bark extract (pycnogenol), rosemary extract, reduced glutathione and N-acetyl-cysteine (NAC), all present in InsideOut, can play an important role in reducing inflammation and fatigue, decreasing tissue damage, and in both preventing and treating damaged skin.

Green tea for example, has been found to have beneficial effects on the healing of skin, the reduction of the harmful effects of photoaging and other skin damaging conditions, and in the prevention certain skin cancers. A recent review has proposed various mechanisms for the chemopreventive, natural healing, and anti-aging effects of green tea on human skin.

Pycnogenols (proanthocyanidins), a group of bioflavonoids, have several properties that have beneficial effects on skin, including vascular wall strengthening properties and free radical scavenging activity. They also stimulate the synthesis of collagen and connective ground substance tissue.

Although bioflavonoids are widespread in nature, the powerful proanthocyanidin compound is most abundant and available from the bark of the maritime pine and grape seeds.

The term pycnogenol refers specifically to the maritime pine extract that is used in InsideOut. Pycnogenol contains a minimum of 85% pycnogenols by weight.
Rosemary extract contains potent antioxidant compounds such as carnosol, carnosic acid, rosmarinic acid and ursolic acid. Several studies have shown rosemary extract provides antioxidant action as well as helping preserve skin health and texture.\textsuperscript{117,118,119,120}

A recent study published on line and to be published later on this year, looked at the effects of a serine and vitamin B\textsubscript{6} antioxidant (both in InsideOut) on prevention of chronic skin photoaging.\textsuperscript{121} The authors found that the antioxidant had significant protective effects against skin damage induced by chronic UVB irradiation.

As well, oxidative damage has been shown to contribute to the pathogenesis of damaged skin, whatever the cause. And the use of antioxidants, such as NAC,\textsuperscript{122} shown to have therapeutic value for reducing endothelial dysfunction, inflammation, scarring and erosion of collagen.

**Dimethylaminoethanol (DMAE)**

In the past it’s been difficult to firm up sagging skin by way of nutrition and non surgical cosmetic treatments. That is one of the main reasons why surgical facelifts are so popular. However, as we’ve already seen InsideOut contains several ingredients that can affect collagen and elastic fibers in the skin and help improve the look of sagging skin. DMAE is another ingredient that can firm up facial tissues.

DMAE is related to the B vitamin choline and is used in the body to make the neurotransmitter acetylcholine. Although the role of acetylcholine as a neurotransmitter is well known, recent evidence also shows that acetylcholine regulates basic cellular processes such as growth and repair.

A recent study found that DMAE has significant effects on skin. In this study the topical use of DMAE was found to decrease forehead lines and fine wrinkles around the eyes, and improve lip shape and fullness and the overall appearance of aging skin.\textsuperscript{123} The authors of the study concluded that “the benefits of DMAE in dermatology include a potential anti-inflammatory effect and a documented increase in skin firmness with possible improvement in underlying facial muscle tone.”

**Boswellia Serrata Extract**

The gum resin of Boswellia serrata, also called salai guggal, has been used as an herbal treatment for inflammatory conditions for centuries in Ayurvedic medicine. Boswellia inhibits pro-inflammatory mediators, such as leukotrienes, and reduces degradation of glycosaminoglycans in connective tissues.

Clinical studies including humans with inflammatory conditions and administered Boswellia reported improvements after 7 days. The extracts also were well tolerated by patients.
Trypsin, Bromelain and Papain,

Oral agents containing various natural enzymes, including bromelain, trypsin, and papain, have been used in Europe to treat injuries and arthritis. Such enzyme combinations may reduce inflammation and skin damage. Several studies in animals have shown beneficial effects from the use of these enzymes.

Papain, which derives from papayas, bromelain, from pineapples, and trypsin, present in humans, are effective proteolytic enzymes and are useful in the oral treatment of injuries and arthritis. These proteolytic (protein-digesting) enzymes aid in modulating inflammation several ways. They aid increase absorption of other substances and help to degrade inflammatory debris in the body. Repair to skin and other tissues commences at a faster rate while inflammation is contained.

Carnosine

Carnosine, a dipeptide made up of the amino acids alanine and histidine (histidyl-alanine) was added to InsideOut because of its many beneficial effects. It has been shown to have significant antioxidant and anti-inflammatory properties, increase healing, enhance the immune system, and provide anti-aging effects.

It also inhibits glycation, a destructive protein/sugar reaction that occurs in the body and which contributes to aging through a number of mechanisms including the breakdown of connective tissue, a loss of elasticity, and a decrease in cellular hydration. Carnosine, along with alpha lipoic acid, provides protection against glycation and premature aging.

Cayenne Pepper

Capsaicin, the primary active ingredient in cayenne, is involved in pain mediation and has anti-inflammatory properties. As well, it has beneficial effects on circulation and protective effect on the lining of the stomach. It is used traditionally for the treatment of various skin disorders, including shingles and psoriasis.

Flavonoids – Rutin and Quercetin

Flavonoids are plant pigments that provide the yellow and orange color in citrus fruits. One of the main function of bioflavonoids is to increase capillary strength, reduce permeability, and regulate absorption.

They also assist vitamin C in keeping connective tissues healthy. Quercetin is consistently the most active of the flavonoids and is indicated for all inflammatory conditions and is especially useful for the skin. Studies have shown that quercetin helps in preventing excessive scarring.
Rutin and Quercetin have been shown in recent studies to have significant anti-inflammatory activity in cases of both acute and chronic inflammation.\(^{134}\)

A recent review article concluded that there is evidence to suggest that flavonoids may be beneficial to connective tissue for several reasons, which include the limiting of inflammation and associated tissue degradation, the improvement of local circulation, as well as the promoting of a strong collagen matrix.\(^{135}\) These compounds also have significant antioxidant properties.

**Ginger**

Ginger (Zingiber officinale) is described in Ayurvedic medicine to be useful in inflammation and rheumatism. Sources suggest that one of the mechanisms by which ginger shows its therapeutic effects could be related to inhibition of prostaglandin and leukotriene biosynthesis, thereby working as a dual inhibitor of eicosanoid biosynthesis.\(^{136}\) The bioactive constituents (the main one being [6]-gingerol) have been shown to inhibit the enzymes that facilitate production of several pro-inflammatory factors. Besides its anti-inflammatory effects, ginger has been shown to be a powerful antioxidant.\(^{137}\)

**Ginkgo Biloba**

Ginkgo biloba herb is extracted from the Gingko biloba tree and has many useful effects including increasing blood flow to various tissues including skin and the brain, and works against free radicals.

Ginkgo biloba has been shown to improve blood circulation to the skin, brain, hands, feet and legs.\(^{138}\) It’s also a potent antioxidant and has significant anti-inflammatory effects on skin.\(^{139}\)

Terpines in Gingko biloba appear to block Platelet Activating Factor. PAF is a chemical messenger that causes inflammation and problems with blood vessels. It’s also a potent antioxidant and as such helps protect tissues from oxidative damage.

A recent study also found that Ginkgo is effective for arresting pigment loss in the skin.\(^{140}\) It’s also felt that a combination of **B12** and **folic acid** will also help treat loss of pigment, or vitiligo.\(^{141}\)

Another recent study found that Ginkgo has protective and therapeutic effects against sunburn after UVB irradiation.\(^{142}\)

**Green Tea Extract**

Green tea extract, besides being rich in antioxidants, also has significant effects on inflammation.
Crude polyphenols from the extract have been shown to inhibit inflammation and carcinogenesis (formation of cancers) when fed to laboratory animals.

A recent study looked at the effects of green tea on found that the use of oral green tea contributed to the beneficial effect on the elastic fibers in the skin.143

A recent review looking at the effects of green tea on the skin concluded that green tea constituents have significant healing, antioxidant, anticancer, antiaging, and anti-inflammation effects on human skin.144

**Omega-3 and Omega 6 Oils – GLA, DHA and EPA -**

Synthesis of collagen involves a cascade of biochemical modifications of the original building blocks. Many enzymes, cofactors and growth promoters influence these modifications, which are crucial to the structure and function of mature collagen and other tissues so important to integrity of skin and connective tissue.

Dietary fatty acids are precursors for hormones and determine the composition of our cell membranes, influencing the production of pro- and anti-inflammatory substances. Omega-3 fatty acids, found in fish oils (mainly **EPA** and **DHA**) and flaxseed oil, have been shown to reduce oxidant stress145 (oxidative stress or free radical damage is a factor of importance in the development of inflammatory events) and suppress the production of pro-inflammatory compounds in the body146 and therefore influence inflammation in the skin, connective and musculoskeletal system.147

A recent study looked at the potential for oral agents for incidence of skin cancers and photo-ageing and concluded that the omega 3 fatty acids have the potential to reduce the ultraviolet induced release of cytokines and thus protect skin from ultraviolet exposure.148 More specifically a recent study found that EPA offered some protection against ultraviolet induced skin damage and may reduce skin cancer in humans.149

**Gamma linolenic acid (GLA)** has also shown anti-inflammatory properties and is useful for treating some skin conditions.150,151

**S-Adenosyl-L-methionine (SAMe) – Increasing Endogenous Production**

Methyl donors are important for the methylation reaction, which adds a methyl group (one carbon atom and three hydrogen atoms), on proteins, enzymes, chemicals, DNA, and amino acids like homocysteine. Methylation is important for maintaining many functions in the body including genetic expression, and neurological and musculoskeletal function.

Usually this methylation process occurs through a compound called S-adenosyl-L-methionine (SAMe). However, SAMe, because of it’s volatility and incompatibility, can’t be
incorporated into a multi-ingredient formula such as InsideOut so the alternative is to include ingredients that have been shown to increase endogenous production and at the same time reduce the increased levels of homocysteine that can follow.

SAMe, is synthesized from the amino acid methionine and its level in the body is increased by dietary methyl donors such as folic acid, B12 (especially the methylcobalamin that is used as the preferred form of B12 in InsideOut rather than the synthetic cyanocobalamin, the usual form of B12 found in most other supplements), B6 and betaine (trimethyl glycine). These nutrients are also needed to reduce homocysteine levels and decrease cardiovascular disease.

Various clinical trials and animal studies suggest that SAMe may be effective, among other things, in reducing inflammation.\textsuperscript{152} It’s also felt to have significant direct and indirect (by increasing glutathione synthesis) antioxidant effects.\textsuperscript{153}

**Shark Cartilage**

Shark cartilage has been shown to have some analgesic and anti-inflammatory effects.\textsuperscript{154,155} As well, shark cartilage has been shown to inhibit angiogenesis and stimulating immune function.

**Silicon**

Silicon is considered an essential trace element and is required for the formation of skin, ligaments, tendons, cartilage and bone.\textsuperscript{156} This is thought to be due to its role in the enzyme prolyhydroxylase, which is responsible for the formation of collagen in bone and elastin, cartilage and other connective tissues.

**Stinging Nettle Extract**

Nettle extracts have long been used as an adjunct treatment for arthritis in Europe and is now beginning to gain popularity in the United States. Cell studies using extracts of nettle leaf have demonstrated a variety of active substances that inhibit prostaglandin production and cytokine secretion.

Tumor necrosis factor-alpha (TNF-\(\alpha\)) and nuclear factor are factors associated with chronic inflammatory conditions. These factors as well as another cytokines called interleukin-1B (IL-1B) have been identified as factors that aid the destruction of collagen and related tissues. Nettle leaf significantly reduces the concentration of these factors, thus improving inflammatory conditions as seen evidenced in human clinical trials.\textsuperscript{157}
Turmeric

Curcumine, the active component of turmeric, is documented to have anti-inflammatory and antioxidative benefits.\textsuperscript{158} As an antioxidant, curcumine reduces the activity of certain enzymes, inhibiting all branches of the arachidonic acid cascade, and thus reducing inflammation.

Of all the spices and herbal preparations it seems that only the spice turmeric has any significant anti-inflammatory effects. This was the conclusion of a study of a variety of Ayurvedic and herbal preparations, which was presented recently at the 9th Asia Pacific League of Associations for Rheumatology Congress.

In this study, a variety of herbal and Ayurvedic preparations were tested in rats. The rats were fed oral doses of the varied herbal and Ayurvedic recipes. Only turmeric showed anti-inflammatory effects when tested on irritated paws of the rats.

As well, turmeric has also been shown to have protective effects against chemical damage to human skin and connective tissue.\textsuperscript{159}

Vitamins and Minerals

Vitamins and minerals are useful for skin care in general and in particular for the prevention and treatment of damaged and aging skin.\textsuperscript{160,161,162,163,164,165,166}

Recovery and repair of tissues require a host of vitamins and minerals that participate in synthesis of new cells and tissue. For example, certain vitamins and minerals are required to facilitate the formation of endogenous anti-inflammatory compounds, including Vitamin B\textsubscript{6}, Vitamin E, Vitamin C, niacin, zinc, selenium, taurine and magnesium (all present in InsideOut). Many vitamins and minerals also serve as antioxidants and help protect cells against the oxidative damage produced by inflammation.

Vitamin C, levels of which are decreased with aging,\textsuperscript{167} is necessary for collagen synthesis and is a strong antioxidant. Vitamin C is involved in the enzymatic hydroxylation of proline to form 4-hydroxyproline, an amino acid that is an integral part of collagen and elastin.

As well as being an antioxidant, vitamin E, has been demonstrated to reduce pain and inflammation.

Vitamins C and E have synergistic effects when used together.\textsuperscript{168,169}

Both of these vitamins are important in treatment of inflammation, as shown in studies, possibly by reducing oxidative stress induced by TNF-\textalpha. As well, both are involved in healing\textsuperscript{170} and in decreasing damage to the skin, including damage from ultraviolet rays\textsuperscript{171} and from toxic substances.\textsuperscript{172}
**Taurine** may also prove useful in combination with both vitamin C and E, as it has been shown to increase vitamin C levels in various tissues.\(^{173}\)

Several clinical studies have shown the anti-inflammatory effects of **niacinamid**e. **Pantothenate** (pantothenic acid, vitamin B5) has been shown in several studies to influence wound healing and collagen synthesis.

Ample amounts of **vitamin B12** are also included in InsideOut, at levels 10 times the amount found in most other products. As well, the B12 is in the form of **methylcobalamin**, the metabolically active form of B12, which is better absorbed and used by the body compared with the synthetic cyanocobalamin, the less expensive form of B12 usually used in nutritional supplements.

**Methylcobalamin**, as well as other methyl group donors such as **folic acid, betaine, methionine**, with the aid of **vitamin B6**, have multiple functions in the body including increasing the formation of SAMe (see above) and the conversion of homocysteine (high levels are a risk factor for cardiovascular disease) to the essential amino acid methionine.

Methyl donors are important for the methylation reaction, which adds a methyl group (one carbon atom and three hydrogen atoms), on proteins, enzymes, chemicals, DNA, and amino acids like homocysteine. Methylation is important for maintaining many functions in the body including genetic expression, and neurological and musculoskeletal function.

These ingredients decrease serum levels of homocysteine, cholesterol and C-Reactive proteins, markers and mediators of heart disease and inflammation in the body.\(^{174,175}\) Reducing homocysteine levels also improves cellular antioxidant systems.\(^{176}\)

Many minerals are required for normal cell function and several serve as cofactors in the many enzymatic processes involved in synthesis of connective tissue macromolecules. **Calcium** and **phosphorus** (in the form of phosphates), and **vitamin D** to regulate both, are important for skin as well as the health of supporting tissues.\(^{177,178,179}\) Vitamin D is also useful on its own for skin rejuvenation and for the treatment of certain skin conditions.\(^{180,181}\)

**Boron** and **manganese** are critical cofactors for collagen and GAG synthesis and metabolism. Some pharmaceuticals are known to negatively interact with some minerals. Supplementation of these minerals should ensure adequate supply in the body.

Clinical evidence suggests that **zinc** deficiencies have a high impact on connective tissue synthesis, and that zinc can help to restore thymic function, has significant anti-inflammatory properties and functions as an important antioxidant for skin.\(^{182}\) A recent review looked at the physiologic importance of zinc to skin, the biochemical basis for these effects, and pharmacologic aspects of zinc therapeutics.\(^{183}\)

Zinc primarily acts as cofactor in many enzyme systems that regulate cell proliferation and growth and in immune integrity. Diminution of collagen synthesis and strength as well as impaired healing is seen in animal tissues with zinc deficiencies.
Copper is a co-enzyme for lysyl-oxidase, which is essential for the conversion of collagen and elastin, and subsequently for skin health and function. It also has antioxidant (it’s part of the endogenous antioxidant copper-zinc superoxide dismutase) and anti-inflammatory properties that aid in the healing of damaged skin.

The use of the above vitamins and minerals may add a protective barrier to the skin and help prevent some problems. For example, white spots on your nails (leukonychia) have not been proven to be a zinc or other nutrient deficiency, although it has been reported in cases of severe calcium deficiency.\(^{184}\) However, many people on InsideOut have noticed a sharp decrease in white spots. That may be because InsideOut covers marginal zinc and other possible nutritional deficiencies that may contribute to the formation of white spots.

**White Willow Bark**

Salicin, a glycoside present in most willow tree bark, has been a known source of pain relief since Hippocrates. Derivatives of salicylates are widely used for their analgesic and anti-inflammatory properties. Aspirin is the best known of these compounds, and salicin is its precursor. The most accepted mechanism of action proposed for the salicylates is inhibition of prostaglandin biosynthesis. Aspirin and other salicylates inhibit cyclooxygenase enzymes, which are responsible for conversion of arachidonic acid to prostaglandins, mediators of inflammation.

A recent study showed that aspirin and fish oil together had a more favorable effect on the pro-and anti-inflammatory factors than aspirin alone.\(^{185}\) Also, the natural sources of salicin have fewer side effects than aspirin.

**Yucca Leaf Extract**

Yucca contains natural steroid-like compounds that have anti-inflammatory, analgesic and antioxidant properties. These saponins also block the release of toxins from the intestines that inhibit normal formation of cartilage. Yucca has also been shown to have some anti-tumor effects.

**Other Ingredients**

**Lemon Myrtle Leaf** is used by the Aborigines of Australia for its anti-inflammatory properties.

**Thyme-Leaved Gratiola** is an herb is traditionally used in inflammation.

**Withania Somnifera** (Ashwagandha) also known as Indian Ginseng, is often used to reduce inflammation.
Summary

InsideOut doesn’t cover up skin damage and aging but intervenes at the origin of the problem and helps rebuild and strengthen skin, hair, nails and supportive tissues.

Used consistently, InsideOut improves skin health, helps prevent acute and chronic skin damage and reverses damaged skin and inflammation.

Because of its photoprotectant effects, it can be useful for decreasing the harmful effects of exposure to the sun, adding an extra dimension to widely used sun screen protection and the use of protective clothing.

It’s also useful to strengthen the skin and thus decrease the side effects of various cosmetic procedures thus decreasing the resulting pain, inflammation, scarring, and other side effects as well as decreasing down time after the procedure.

MD+ InsideOut, will safely reduce stress on skin and subcutaneous tissue, and speed up recovery without the side effects associated with many of the drugs and surgeries used today.
## InsideOut Nutrition Panel

<table>
<thead>
<tr>
<th>Supplement Facts:</th>
<th>Serving Size: 4 Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Servings Per Container: 30</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (as Beta Carotene &amp; Palmitate)</td>
<td>4,000 IU</td>
<td>80%</td>
<td>Shark Cartilage</td>
</tr>
<tr>
<td>Vitamin C (as Ascorbic Acid)</td>
<td>200 mg</td>
<td>3333%</td>
<td>Lecithin (with Phosphatidylcholine)</td>
</tr>
<tr>
<td>Vitamin D (Cholecalciferol)</td>
<td>200 IU</td>
<td>50%</td>
<td>Stinging Nettle Extract (Leaf)</td>
</tr>
<tr>
<td>Vitamin E (dl-Acetyl Tocopheryl Acetate)</td>
<td>75 IU</td>
<td>250%</td>
<td>Omega 3 Fish Oil Complex (DHA EPA)</td>
</tr>
<tr>
<td>Vitamin B1 (Thiamine Mononitrate)</td>
<td>10 mg</td>
<td>667%</td>
<td>Quercetin Dihydrate</td>
</tr>
<tr>
<td>Vitamin B3 (as Nicotinamide)</td>
<td>20 mg</td>
<td>100%</td>
<td>Rutin</td>
</tr>
<tr>
<td>Vitamin B6 (Pyridoxine HCL)</td>
<td>10 mg</td>
<td>500%</td>
<td><strong>InsideOut Proprietary Complex 2370 mg</strong></td>
</tr>
<tr>
<td>Vitamin B12 (Methylcobalamin)</td>
<td>250 mcg</td>
<td>4.167%</td>
<td>Alpha Lipoic Acid, Betaine HCL, Boron (As Amino Acid Chelate), Boswellia Serrata Extract (resin), Bromelain, Carnosine, Cayenne (fruit), Choline (as Bitartrate), Coenzyme Q10, Creatine Monohydrate, DMAE Bitartrate, Genistein, Ginger Root Extract (root), Ginkgo Biloba Extract (root), GLA (Borage Oil), Glucosamine, Glutathione, Glycine, Green Tea Extract, L-Arginine, Lemon Myrtle Leaf, L-Histidine, L-Lysine, L-Methionine, L-Proline, L-Valine, L-Trypophan, Lycopene, MSM (Methyl-Sulfonyl-Methane), N-Acetyl Cysteine, Papain USP, BioCell Collagen I/III</td>
</tr>
<tr>
<td>Collagen II</td>
<td>300 mg</td>
<td>5%</td>
<td>Pine Bark Extract (Pycnogenol), Rosemary Extract (leaf), Silymarin Extract (fruit) Taurine, Thyme-Leafed Grapeseed (whole plant), Turmeric Extract (Curcuma longa) (root)</td>
</tr>
<tr>
<td>Chondroitin Sulphate</td>
<td>100 mg</td>
<td>20%</td>
<td>White Willow Bark, Withania (root), Yucca Extract (whole plant)</td>
</tr>
<tr>
<td>Hyaluronic Acid</td>
<td>50 mg</td>
<td>8%</td>
<td></td>
</tr>
</tbody>
</table>

*Other Ingredients: Cellulose, Stearic acid, Croscarmellose sodium, Magnesium Stearate, Hypromellose, Silicon Dioxide, Titanium Dioxide.*

*Daily Value Not Established*
References


124 Oral enzyme therapy in osteoarthritis of the knee. Proteolytic enzyme are effective with few risks. MMW Fortschr Med 2001 Jun 7;143(23):44-6.
Can Aging be Prevented?
Fortunately, with a daily program that includes sun protection along with replenishing and renewing the skin with certain key agents, it is possible to quickly and dramatically improve the appearance of aging skin. Dr. Mauro Di Pasquale’s InsideOut was designed as a complete system that will work fast to reduce the appearance of environmental aging while protecting the skin from future damage. With daily use, most people will achieve younger-looking, better-feeling skin within just a few short weeks. And, with continued use, visible results can be maintained and extended.