RadiénIx™ WITH QXP™

“Skin aging is like a chronic wound that does not completely heal”.

Cosmetic Dermatology
– Zoe Draelos, MD, clinical and research dermatologist

What is the scientific mechanism of skin aging?[(a)]

Intrinsic aging (*age-related*) is mediated by the “biologic clock” that affects the skin in the same manner as it affects the internal organs, i.e., by slow, irreversible tissue degeneration. Intrinsically aged skin is thinner, more evenly pigmented, shows higher laxity, and less fold accentuation as compared to photoaged skin.

Extrinsic aging is mediated by environmental factors including exposure of skin to solar UV radiation and environmental pollutants. Photoaged skin usually shows coarseness, wrinkling, sallow discoloration and irregular pigmentation.

Intrinsic and extrinsic aging are cumulative processes that occur simultaneously, and over time result in photoaging.

Multiple studies have shown that ***activation of the matrix metalloproteninase (“MMP”)*** secretion as a result of intrinsic (*age related*) and extrinsic (*UV mediated photo-aging*) aging produces a breakdown of the dermal matrix. The overall effects of these interlinked biochemical activities is reduction of procollagen synthesis, increase of collagen degradation in the dermal extracellular matrix, and increase in irregular elastin deposition.

Why: "Is skin aging like a chronic wound that doesn't heal"?

As we age and are exposed to UV, along with many environmental factors, chronic inflammation occurs at the cellular level. It is the same inflammation catalyst that occurs in a wound. This inflammation leads to the release of a group of MMP enzymes whose role is to break down tissue.

In a typical wound (not chronic), the body repairs itself, the inflammation decreases and MMP's decrease. In a chronic wound, inflammation doesn't decrease, which creates an overabundance of MMP's, leading to a long period of wound degradation, and non-healing.

In skin, especially with age, inflammation is caused by environmental factors, which, in turn, start a chain reaction that leads to MMP production. The MMP's perform there function of eating tissue (collagen, elastin, and other connective tissue), with no preference to good or bad tissue.

The analogy of a chronic wound to skin aging is that skin aging and environmental factors cause skin to have ever increasing levels of inflammation and MMP's (same as chronic wound). You many not notice the inflammation or MMP's, but it's there and happening every day.

Thus, ***"skin aging is like a chronic wound that doesn't heal."***[(c)]

Acne scarring, by example, is caused by MMP's: "Fibroblasts and keratinocytes produce enzymes including those that determine the architecture of the extracellular matrix metalloproteinases (MMPs) and tissue inhibitors of MMPs. MMPs are extracellular matrix (ECM) degrading enzymes that interact and form a lytic cascade for ECM remodeling. As a consequence, an imbalance in the ratio of MMPs to tissue inhibitors of MMPs results in the development of atrophic or hypertrophic scars. Inadequate response results in diminished deposition of collagen factors and formation of an atrophic scar while, if the healing response is too exuberant, a raised nodule of fibrotic tissue forms hypertrophic scars" [(b)]

For your own research, we recommend:
Google search: "MMP, Collagen degradation, aging, skin damage"

Peptides and the impact of MMP's.

In addition to attacking collagen, elastin and other connective tissue in the dermis, MMP's attack protein based peptides and growth factors important for maintaining youthful, firm skin.

Thus, it doesn't matter what you use for anti-aging products. If you don't reduce the MMP level in your skin, the MMP's will do their job, which is to destroy the collagen, elastin, connective tissue and protein based peptides. QXP, Radien's active ingredient, is clinically proven to down-regulate MMP's which allows the body to repair itself and allows peptides and growth factors to survive and grow, significantly improving the dermis's ability to heal.

Radien's products include many peptides directed towards photoaging, collagen re-generation, moisturizing and other mechanisms of action. Some of the peptides are available in other

products, but without QXP and the mechanism of down regulating MMP's, peptides will be destroyed in the normal course of MMP's role.

At what age do I have higher levels of MMP's?

Numerous studies have concluded that protease activity begins at the cellular level in the dermis in the 21-to-40 age group. The MMP activity is very high in the 41-to-60 age group, resulting in a greatly reduced level of collagen.

Two studies are available on the Radien website which conclude (a) intrinsic aging may predispose to tissue breakdown disorders because of MMP-2 up-regulation in normal skin and (b) these results suggest that intrinsic cutaneous ageing is associated with reduced levels of TIMPmRNA both in normal skin. This latter study is important because MMP's can be neutralized by natural inhibitors in the body known as TIMP's (Tissue Inhibitors of MMP's). There are 4 types of TIMP's, and they are produced at the same time as MMP's (to control the MMP's). The problem with TIMP's is, as we age, the level of TIMP's decrease.

In other words, it's not just the environment and inflammation, it's the simple fact that as age increases, the MMP level increases and the primary neutralizer of MMP's (TIMP's) declines. The net effect of these two natural process's is a degradation of collagen, elastin and connective tissue, resulting in wrinkles and sagging skin.

Mr. Pilant, founder of Radien, and an expert in MMP expression in chronic wounds, realized that the same technology that down regulates MMP's for the purpose of wound healing, can also be used in Anti-Aging. More specifically, lowering MMP's in the skin will slow the destruction of collagen, thus provide a skin environment where collagen can begin to grow more plentifully and peptides (which are proteins that are also eaten by MMP's), would have a much better chance of working as directed.

Chronic Wounds and Radien's expertise on MMP's.

Greg Pilant, CEO has 30 years of experience with formulating pharmaceutical technologies. He pioneered the relationship between high levels of MMP's (matrix metalloproteases) and the chronicity of chronic wounds. Chronic wounds are generally defined as wounds that have not healed after thirty days of consistent clinical treatment. These include diabetic ulcers, burns, pressure ulcers (bedsores), and venous stasis ulcers. Approximately 80% of chronic wounds display elevated levels of proteases (including MMPs), which impede or stop the wound-healing process.

MMP's, (also known as proteases) are enzymes that act on proteins, usually by cutting up the protein molecule. In particular, they cut important extracellular matrix ("ECM") proteins such as collagen, gelatin and proteoglycans when a wound occurs. Thus, the MMPs function is to degrade these ECM proteins.

In wounds, MMPs break down the damaged ECM that occurs at the edge of an acute skin wound. This enables new ECM components (eg collagen, fibronectin, and proteoglycans) synthesized by

wound cells to integrate correctly with intact ECM components at the wound edges.

It is well established that MMPs are required at the right amount, in the right place, and in the right time frame (duration) for a wound to heal. However, when MMPs are present in a wound bed at too high a level, for too long a time, they begin to degrade proteins that are not their normal substrates, such as growth factors, receptors and ECM proteins (including collagen). Wounds in this situation are often referred to as being 'stuck' in the inflammatory phase of healing, where they can remain for months and even years.

The wound healing technology ("QXP") originally developed by Mr. Pilant, down regulates MMP's, thus the wound can begin the healing process, even if it has already become chronic. In clinical studies, the wound healing technology has shown to heal approximately 80% of chronic wounds by providing a suitable environment for the wound to heal.

Radien develops, manufactures, and markets a suite of products using its proprietary dermatological formula ("QXP") for anti-aging. Radién Ix's patent-pending formulas provide an advanced anti-aging treatment using the same wound healing technology.

Available references:

1. On the Radien website is "MMP 2 Assessment as an indicator of wounds". The study is a detailed analysis of a wound and the levels of MMP over time. The down regulator of MMP's in that article is a formulation developed by Mr. Pilant.

    a) Week 0 – Regarding the MMP-2 expression level, the analysis appeared dark red, indicating a high expression level of MMP-2.
    b) After week 2 of treatment -- "Clearly recognizable declines could be observed immunohistochemically in fibroblast MMP-2 expression in all biopsies".
    c) After week 6 of treatment: "Immunohistochemical expression level of MMP-2 in the surrounding tissue has dramatically decreased."

2. On the Radien website is "Ashcroft report "MMP in skin". As quoted: "To determine the spatial and temporal patterns and activities of MMP1, -2, -3 and -9, 132 healthy humans aged between 19 and 96 years underwent 4-mm punch biopsies followed by wound excision between day 1 and day 180 post wounding. ***Wounds showed an age-related increase in MMP-2 and MMP-9 immunostaining from day 3; this was associated with degradation of gelatin as shown by zymograms and with increased proteinase activity as shown by azocoll assays.***

    "These results indicate that: (1) intrinsic aging is associated with the up-regulation of MMPs previously associated with chronic wound healing; (2) wound-tissue proteinases are essentially active up to day 21 postwounding; and (3) ***intrinsic ageing may predispose to tissue breakdown disorders because of MMP-2 up-regulation in normal skin."***

3. On the Radien website is “Ashcroft – TIMP in aged skin – Cell & Tissue Research” (PDF). As quoted: “These results suggest that intrinsic cutaneous ageing is associated with reduced levels of TIMPmRNA both in normal skin and during acute wound repair. These levels may be instrumental in dermal tissue breakdown in normal skin, retarded wound healing, and the predisposition of the elderly to chronic wound healing states.”

Randomized Human Clinical Trials

Trials were conducted in 2005 in High Point, North Carolina, under the direction of Dr. Zoe Draelos using the development name InTon. The trial was to determine the “Efficacy of a Novel Topical MMP Regulator in Aging Skin”. Fifty women participated in the test, with 40 testing the active product against a placebo (a very good botanical base), and 10 testing the product against a cold cream-type placebo. During the study, Dr. Draelos commented “This data set was particularly challenging due to the excellent moisturizing characteristics of vehicle 1” (The Vehicle 1 cream is the same cream being used in our products today).

The study was double blind, randomized, placebo controlled human trials. Each woman used one cream (an active or a placebo) on each side of her face, and neither Dr. Draelos nor the participant knew which cream was active.

At the beginning of the study and at mid point, each participant was interviewed, photographed, and visually examined. Each side of her face was tested for skin moisture and skin conductivity, and a small silicone mask was taken from each side of her face. Each woman turned in unused product (which was weighed) and a diary of her experience.

Statistical superiority ($p=0.015$) of the active (with QXP) over vehicle 1 (cream without QXP) was achieved at week 6 in the overall investigator assessment. Dr. Draelos made very positive comments about the product in her report, and results were dramatic, particularly over the first six weeks.

Essentially all participants wanted more skin cream at the end of the study (which was provided), and all felt the moisturizing quality of the cream was outstanding.

A note regarding the study. In 2005, the scientific community was just beginning to learn about the many influences of MMP’s on skin aging. In addition, to test the actual level of MMP in skin required a skin puncture, (a wound) that could then be analyzed for MMP levels. Thus, the levels of MMP were not evaluated in the study.

Radien expects to update its clinical study to determine the true levels of MMP in skin and thus determine the amazing benefit of down-regulating MMP’s in skin.

Radien’s Product Line:

For any anti-aging product to be effective, you must lower your MMP levels using our proprietary QXP formula. Increased Collagen, Less Wrinkles

QXP, used in the entire Radien Ix product line, reduces the levels of MMP's, thus limiting the damage caused by the skin's enzymes and therefore, reduce the breakdown of collagen, laminin, elastin, and other components of the skin. The Radién Ix skin cream base is the finest combination of botanicals and moisturizers available today.

Women's Radién Ix™ Products

Radién Ix™ Eye Cream – Includes QXP and particular peptides effective in diminishing darkness and puffiness around the eyes and general skin discoloration.

Radién Ix™ Day Cream - Includes QXP and sesame protein as a skin-tightening agent that visibly smoothes the skin and is a very effective base for application of make-up.

Radién Ix™ Night Cream – Includes QXP and walnut extract is an excellent anti-oxidant which provides the skin with phytic acid, polyphenols, proteins, mineral salts, and vitamins. This protects the cell's antioxidant pool and has biostimulating properties while shielding from the consequences of oxidative stress. The walnut extract provides substantiated effects on extrinsic aging by reducing apoptosis and by reducing the inflammation processes. A custom peptide reverses the effects of photo-induced aging which is **extrinsic aging.**

Radién Ix™ Dejavu -- Includes QXP and peptides to tighten the elastins in the skin around your eyes to diminish the visible signs of aging. DeJaVu is formulated for instant gratification, but with longer term benefits. It is part of our anti-aging product line to work with our clients lifestyles. Apply anytime you want to be "Red Carpet Ready"!

Radien Ix Pore Reducer – Includes QXP and peptides to reduce larger pores and slows overactive oil production.

Radién Ix™ Cleanser (includes QXP) -- Properly cleaning the skin is the first step to the Radién Ix™ anti-aging system. The Cleanser is formulated for make-up removal and deep skin cleansing and is a mild exfoliate. This allows for faster and more efficient penetration of the Radién Ix™ creams.

Radién Ix Toner -- Using Radién Ix™ Toner is an essential part of the skin care regimen. Radién Ix™ Toner provides hydration to your skin, which is essential in maintaining elasticity, smoothness, moisture, and a more youthful appearance. Proper skin hydration reduces the signs of aging skin and provides an effective base for the application and absorption of skin care products. Large facial pores allow more dirt, oil, and toxins to enter the skin and can cause irritation, infections, and facial blemishes. Radién Ix™ Toner helps tighten your facial pores, allowing fewer oils and toxins to settle into the skin. This creates a fresher, cleaner, and less oily appearance while helping your skin prevent acne-related breakouts. This hydrating, balancing, and firming formulation provides instant hydration for thirsty skin while removing excess oil.

Men's Product

QXP™ Anti-Aging Treatment for Men - Includes QXP and a moisturizing peptide to allow increased skin volume by holding moisture, which is important as we age.

Radien Ix™ Skin Repair Cream and Serum Spray

The Radien Ix™ skin repair products include QXP and are designed to dramatically improve the quality of your skin after dermabrasions, laser treatments, acid peels or the use of products such as retinoid and other similar treatments that cause peeling. Great for general sunburns, minor burns, skin irritation, and bee stings.

Footnotes

(a) "Endogenous growth factors as cosmeceuticals" Mehta
(b) "Acne Scars: Pathogenesis, Classification and Treatment" Fabbrocini
(c) "Cosmetic Dermatology" Zoe Draelos, MD, clinical and research dermatolog