

Viewpoint: Anti-inflammation and Visible Skin Aging

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Skin care regimens recommended by professionals for reversing and preventing visible skin aging should include products with active ingredients focused on reversing and preventing chronic inflammation. This change in strategy should occur with all topical products, oral supplements and dietary recommendations. The driving force behind this strategic change is that cutaneous inflammation has now been linked to many diseases, including cancer, as well as visible skin aging. This article will review the compelling scientific story that resulted in the conclusion that chronic inflammation is a major culprit in visible skin aging. The two major proinflammatory stimulators are disruption of the skin barrier and ultraviolet (UV) light. Because of this, it becomes crucial that optimizing skin barrier structure and function to prevent or minimize the affect of UV radiation and other damaging molecules are absolute requirements for treatment and prevention regimens of skin aging and other skin conditions.

Public awareness

Denham Harmon first documented cellular destruction by reactive oxygen species (ROS) more than 50 years ago¹, and Kligman and Lavker documented that inflammation played a microscopic role in visible skin aging almost 20 years ago.² Perricone brought the information that inflammation induces skin damage into the public eye with his book, *The Wrinkle Cure*. In this book, he states that visible skin aging can be reduced and prevented by the daily use of antioxidant and/or anti-inflammatory cosmeceuticals, coupled with a diet rich in anti-inflammatory and antioxidant foods.¹ Articles published in several major news and industry magazines in recent years have further exposed the public to the concept that inflammation of the skin and other organs is the critical event in the development of diseases, cancers and aging. Wellness guru Andrew Weil, MD, has published his anti-inflammatory diet because he believes that, "Without question, diet influences inflammation." Weil and other researchers state that the link between inflammation and heart attacks; colon, esophageal, prostate and skin cancer; Alzheimer's disease; stroke; multiple sclerosis; rheumatic fever; rheumatoid arthritis; type I diabetes mellitus; systemic lupus erythematosus and scleroderma; as well as aging, strongly suggests a single inflammation-reducing remedy would effectively treat and prevent major debilitating and fatal conditions. This radically changes the medical community's concept of disease therapy.³⁻⁵ The idea of avoiding and reversing chronic inflammation for the prevention and treatment of aging cells also applies to the skin's surface. It follows that skin cells would be expected to benefit from direct exposure to anti-inflammatory and antioxidant-containing topical skin care products, oral supplements and foods.



The conclusion that chronic inflammation as the engine driving the most feared illnesses, as well as aging, has been reached by evaluating multiple historical, social and medical treatments. Importantly, the cellular/molecular mechanism links between inflammation, disease, cancer and aging have recently been established.¹⁻⁵

Historical and social implications

It is well-known that in modern American society the incidence of chronic inflammatory skin diseases is significantly increasing in all age groups, such as dermatitis in American children, which is now 15–30%. Occupational hand dermatitis has become the leading cause of lost days of work, not only in this country, but throughout the world.⁶ In 2005, it was reported that nearly 40% of American adults have suffered from a skin condition lasting longer than one month during their lifetime.⁷

In the last decade, the scientific community has gradually become more accepting that inflammation and malignant deterioration influence and predispose to each other. In American society, the incidence of skin cancer has reached epidemic proportions. During each of the past three years, more than a million Americans suffered from a skin cancer requiring surgery. About 50% of people over 65 are afflicted with premalignant solar keratoses. The most common procedures still performed today by dermatologists relate to skin cancer therapy. These surgical and destructive procedures treating skin cancer rose by 12% to include more than 1.7 million, despite massive public education on the relationship of sunlight to skin cancer. This trend is increasing, despite the introduction in the 1980s of sunscreens with a sun protection factor of 15 or higher, and a broadening of the protected UV light spectrum to include UVA exposure.⁸

During this same period, however, exfoliating strategies using alpha hydroxy acids (AHAs), retinoids and microdermabrasion have exploded in popularity. The number of exfoliating procedures performed by estheticians and spas has grown rapidly, yet skin cancer afflicts an increasingly larger number of Americans.

It has been documented that mild barrier disruption and suberythematosus doses of UV light each induce microscopic chronic inflammation and tissue destruction. Repeated chronic disruption of the skin barrier due to any cause has been documented to activate chronic inflammation.^{9,10} Acute inflammation followed by rapid complete repair of the skin barrier does not appear to induce skin damage, resulting in the aggravation of visible skin aging.

Chronic inflammation induced by both AHAs and retinoids appears to be primarily the result of barrier disruption. The United States Food and Drug Administration (FDA) in 2000 developed a warning for AHA products with a concentration more than 10% and pH under 3.0, due to increased photosensitivity and premalignant deterioration of skin cells. Since AHAs are not photosensitizers, unlike retinoids, the photoreactivity must be due to exfoliation of the barrier.^{5,11} Moreover, Halliday reported increased skin cancers with prolonged topical retinoid use, while short-term studies indicate the retinoids appear to reduce visible premalignant and cancerous growths in animal studies.¹²

This information strongly suggests to skin care professionals to adjust treatment and prevention strategies for reversing and preventing visible skin aging to one of reversing all causes of chronic inflammation, including skin barrier disruption.

The medical response

Prescriptions. Methotrexate and corticosteroids have been major therapies for treating psoriasis, dermatitis, certain skin cancers, and a variety of internal inflammatory diseases and malignancies, which strongly suggests a link between inflammation and cancer. A nonsteroidal anti-inflammatory drug, diclofenac, received FDA approval to treat premalignant solar keratosis with topical application. A similar agent, topically applied indomethacin, appears to improve visible skin aging in animal models.¹³

Examining the success of using medicine for treating a wide range of diseases supports the observations linking inflammation to diseases and cancer. Systemic lupus erythematosus, dermatomyositis and scleroderma are systemic diseases with characteristic skin damage. Epidermal atrophy and irregular pigmentation of the skin is present in these diseases, as well as visible skin aging.



Alternative/complementary medicine. The public's use of alternative and complementary medicine surpassed the volume of

traditional outpatient medicine in 1995.¹⁴ Half of the top 10-selling herbs have documented anti-inflammatory or antioxidant mechanisms of action in humans or animals.^{15,16} More than 100 herbs are being marketed in topical nonprescription skin care products, including cosmeceuticals. Many of these have documented anti-inflammatory or antioxidant activity, suggesting they may be beneficial in treating and preventing inflammatory diseases and skin aging. Of more than 8,000 documented antioxidant ingredients, only 14 have been incorporated into topical formulations that were documented in human clinical trials to improve parameters of visible skin aging.¹⁷⁻¹⁹ According to Perricone, all antioxidants act as anti-inflammatory agents, but not all anti-inflammatories—such as indomethacin and diclofenac—have antioxidant mechanisms of action.¹

Herbal ingredients with known antioxidant or anti-inflammatory activity are used as topical medicines for certain inflammatory skin diseases and skin care products for visible skin aging, including botanical extracts rich in AHAs, such as apple; retinoids including retinol, as in carrot; certain ascorbic acids, such as citrus; soy milk and total soy; arbutin;²⁰ date palm fruit as a solitary agent;²¹ green tea when applied topically and taken orally;²² colloidal oatmeal²³ and oat;²⁴ and proprietary formulations of date kernel, meadowfoam and flax;¹⁹ pycnogenol¹ and parthenolide-free extract (PFE).²⁵

Oral supplements containing herbs have become very popular, with the top 10 selling more than \$1 billion in 2004.²⁶ Many of these herbs contain multiple antioxidant or anti-inflammatory ingredients, and three of them—date, meadowfoam and pomegranate—have clinical studies documenting improvement of visible skin aging.¹⁹

Mechanisms

Environmental insults producing destructive ROS include smoking, pollution, harsh skin care regimens, medical and cosmetic procedures, preservatives, topical drug delivery recipients, irritants—including certain prescription topical therapies, allergens, blistering, wounds, and UV and X radiation.^{9,11} Skin barrier disruption activates the release of tumor necrosis factor alpha (TNF) and interleukins 1 (IL-1) and 8 (IL-8), as well as other proinflammatory molecules to induce protective acute inflammation and trigger repair of the damaged skin barrier.^{27,28}

Matrix metalloproteinases (MMPs) are enzymes that activate inflammation and degrade damaged dermal ground substance, collagen and elastin to remodel the skin after injury. These destructive enzymes are synthesized in several skin cells, including fibroblasts, keratinocytes and mast cells. Collagenase (MMP-1), stromelysin (MMP-3) and gelatinase (MMP-9) are the most important. Visible skin aging parameters, such as fine lines, wrinkles, fragility and laxity are due to solar elastosis, collagen destruction and tissue atrophy induced by damaging MMP activity. These enzymes play important roles in the premalignant and malignant deterioration of skin cells.²⁹

It follows then that preventing and reversing chronic inflammation should be a primary skin care strategy to treat and prevent skin conditions, such as visible aging, skin diseases and cancer, and to improve skin health. The ideal regimen would consist of topically applied skin care products that also optimize the stratum corneum barrier, combined with a diet rich in anti-inflammatory/antioxidant foods. Additional oral supplementation with these activities may also improve results. This regimen is especially important if the client lives, works or plays in a high-stress or harsh environment where healthy skin function is needed.

The linking of chronic inflammation to multiple cutaneous and systemic diseases, including skin aging and cancer, was suggested more than a century ago, but now has been scientifically accepted. Establishing chronic inflammation as the key cause is why anti-inflammatory medications are effective treatments for a variety of skin diseases, cancer and visible skin aging. It is now clear that destructive chronic inflammation can be prevented and reversed by the consumption of proper food and oral supplements, as well as the application of topical skin care products. This realization should stimulate skin care providers to be more focused on reversing and preventing inflammation with topical and oral products, including food. Optimizing the stratum corneum barrier function is necessary to prevent activation and reverse the skin damage caused by chronic inflammation. Returning the skin to its normal function and structure should reverse, prevent and minimize visible skin aging.



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