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How Ultra-Violet Light Causes Skin Cancer And Photo-Aging Of The Skin: The Protective Role Of Nutritional Antioxidants

- by Dr. James Meschino, DC, MS, ROHP

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Introduction

Non-melanoma skin cancer is the most common malignancy in the United States. The estimated lifetime risk of developing malignant melanoma in the U.S. has risen from 1 in 250, in 1981, to 1 in 87, in 1996. Cumulative lifetime sun exposure and decreased protection from the earth's shrinking ozone layer are considered to be the primary culprits for these disquieting statistics. More specifically, ultra-violet light from the sun is known to induce the production of free radicals within the epidermis and dermis layers of the skin. These free radicals, which are highly aggressive, reactive molecules, are known to damage skin cells and its connective tissues in various ways, leading to accelerated aging of the skin and increasing the risk of skin cancer. The following discussion outlines the biological mechanisms through which ultra-violet light creates these dangerous free radical species and outlines the most prudent and practical lifestyle steps individuals can employ to reduce ultra-violet light induced skin damage, with special emphasis on the emerging role of antioxidant supplements.

How Free Radicals Are Formed In The Skin

The presence of molecular oxygen (O2) within skin cells in the mid to lower levels of the epidermis is a primary target for ultra-violet light waves that penetrate the skin, primarily from exposure to sunlight. Molecular oxygen is a very unique and volatile substance in that it has outer electron shells that are not completely filled with orbiting electrons, and thus has a tendency to absorb additional electrons to fill up these two vacant orbits (electrons are negatively-charged wave particles that circle the nucleus of an atom in a specific orbiting pattern. Electrons with higher energy are found in the outer orbits of the atom whereas electrons with less energy have orbits that are closer to the nucleus of the atom). As such, the incoming ultra-violet light can donate an electron to molecular oxygen within skin cells of the epidermis. In this case, molecular oxygen will now have a single, unpaired electron in its outer orbit and this spells trouble, as electrons normally circle the nucleus of an atom in pairs. When molecular oxygen absorbs a single unpaired electron in this manner it becomes a very unstable, aggressive free radical known as the superoxide anion. In order to stabilize itself electrically, the superoxide anion will randomly steal an electron from another molecule that is close by. This not only damages the molecule, but also converts it into a free radical because it now will have an unpaired electron of its own. This sets off a chain reaction whereby the newly formed free radical steals an electron from a neighboring molecule, turning it into a free radical, which in turn steals an electron from another neighboring molecule and so on. This type of free radical propagation can damage many components of skin cells, such as its enzymes and the cell membrane (outer skin of the cell). Once damaged by free radicals the cell membrane loses some of its control in determining what chemicals can enter and exit the cell (loss of a key function in the health of the cell). Fortunately, skin cells possess an antioxidant enzyme known as the superoxide dismutase, which can quench and neutralize the superoxide anion. Vitamin E within skin cells can also intercept some of the free radicals created by the superoxide anion. However, when skin cells are exposed to a massive dosage of ultra-violet light (from excess sun exposure) then the normal antioxidant defense mechanisms within the cell can not keep pace with the generation of free radicals and severe free radical damage to skin cells is likely to occur, leading to accelerated aging and increased skin cancer risk.

The superoxide anion is not the only free radical created by ultra-violet light. What often happens is that a second electron from the ultra-violet light can be added to the superoxide anion, which creates a compound known as hydrogen peroxide (HOOH). Hydrogen peroxide is extremely dangerous to the cell because it can diffuse through the nuclear membrane and place itself next to the DNA of the cell. At this point hydrogen peroxide can be easily transformed into a very aggressive and damaging free radical known as the hydroxy radical. This occurs when a transition metal such as ferrous iron (Fe++) donates an electron to hydrogen peroxide, which splits hydrogen peroxide into two hydroxy radicals, and converts ferrous iron to ferric iron (HO- + -OH + Fe +++). Once formed, hydroxy radicals can do extensive damage to the DNA of the cell, creating mutations that are linked to cancer and accelerating the aging process of the skin. It is known that hydroxy radicals do most of the damage to our cells, compared to all other forms of free radicals generated from molecular oxygen. Hydroxy radicals can react with almost any compound in the body and are known to damage cellular enzymes, proteins, carbohydrates, lipids, DNA, and cause cross-linking of proteins (e.g. collagen) in the dermis (which results in decreased elasticity of the skin). Antioxidant enzymes such as catalase and glutathione peroxidase, as well as Vitamin E and Vitamin C, work synergistically to quench and neutralize hydroxy radicals. However, upon exposure to excessive amounts of ultra-violet light these antioxidant defense mechanisms are easily overwhelmed, allowing extensive DNA

mutations and other significant cellular damage to occur.
The other free radical generated from the interaction of ultra-violet light with molecular oxygen within skin cells is singlet oxygen. In this instance, an electron in a lower orbit is bumped up to a higher orbiting shell by the incoming energy from the ultra-violet light wave. This is known as an excited state of oxygen, which is also created in the body upon exposure to X-rays. The antioxidant Beta-carotene is a powerful quencher of singlet oxygen, as is one of its sister carotenoid compounds known as lycopene (a red carotenoid that provides tomatoes with its distinctive color).

The P53 Tumor Suppressor Gene And Pheomelanin

Free radicals generated by ultra-violet light within the skin can also damage the P53 tumor suppressor gene, which normally acts to prevent mutated cells from proliferating and initiating skin cancer development. When the P53 tumor suppressor gene is intact within the DNA of the cell, it identifies any serious mutations that have occurred to the genetic structure. If the damage to the DNA is severe then the P53 tumor suppressor gene prevents the cell from dividing and replicating. Thus, the mutated, potentially cancerous cell eventually undergoes programmed cell death or apoptosis. This is a safeguard mechanism that the body uses to encourage newly formed cancer cells to commit suicide, preventing them from replicating and spreading through the body. Unfortunately, free radicals can damage the P53 tumor suppressor gene within our DNA and thereby increase the risk that mutated and cancerous cells will continue to divide and spread. Damage to the P53 tumor suppressor gene has been shown to occur in more than 50% of all human malignancies. It has been shown that this applies to skin cells as well, as the free radicals induced by ultra-violet light have been shown to cause mutations to the P53 tumor suppressor gene in epidermal cells. Thus, free radicals in the skin can cause direct damage to cellular structures within skin cells and can also increase cancer risk by disabling other protective mechanisms such as the P53 tumor suppressor gene.

It should also be noted that individuals with fair skin and red hair tend to have red-brown or yellow pigment in their skin known as pheomelanin. Brown or black melanin (eumelanin) normally acts like a protective sunscreen (antioxidant), absorbing electrons from ultra-violet light to help reduce skin inflammation and free radical damage to skin cells as well as the connective tissues within the dermis. However, in fair skinned and red headed individuals the melanin molecule (pheomelanin) is altered in such a way as to allow it to easily become converted into a free radical itself upon exposure to ultra-violet light, generating the superoxide anion. In turn, the superoxide anion can damage nearby skin cells, including the DNA of melanocytes. Free radical damage to melanocytes is thought to give rise to melanomas – the most lethal form of skin cancer. Thus, individuals with red-brown or yellow pigment (pheomelanin versus eumelanin, which is brown or black in color) in their skin are known to be at higher risk for skin cancer due to the fact that the type of melanin in their epidermis can easily be converted into a cancer causing free radical upon exposure to sunlight.

Normal Skin Aging Versus UV-Light Induced Skin Aging

Free radical damage to the skin from ultra-violet light is known to produce accelerated aging of the skin. In fact, all changes due to normal aging of the skin can be distinguished from those due to UV-light induced skin damage, as UV-light induced skin damage produces a series of changes to the skin known as dermatoheliosis. The free radical damage characterized by dermatoheliosis produces distinctive changes to 5 parts of the skin (epidermis – actinic keratosis; dermis – solar elastosis;

blood vessels – telangiectasia; sebaceous glands – solar comedones; melanocytes – diffuse or mottled brown patches). Solar elastosis accounts for much of skin wrinkling due to exposure to ultra-violet light. In solar elastosis the free radicals generated in the skin from ultra-violet light cause up-regulation of the elastin promoter gene, which in turn increases synthesis and accumulation of elastin and fibrin in the upper dermis. This produces the characteristic deep wrinkle appearance of the skin. On the face, solar elastosis is visible as yellowish skin, criss-crossed by deep wrinkles, and on the neck and extended surfaces of the limbs as atrophied and dyschromic skin. Free radicals reaching the dermis also cause translocation of glycosaminoglycans and alter the main glycosaminoglycan dissacharide units. As a result, dermal glycosaminoglycans are repositioned from between collagen fibers (where they belong) to be deposited on the elastic material of the superficial dermis. As the correct structure and location of glycosaminoglycans within the skin is responsible for retaining water molecules and moisture, the repositioning and re-structuring of glycosaminoglycans results in less hydration and suppleness of the skin, further contributing to acceleration of skin aging.

How To Protect Yourself And Your Patients/Clients From Ultra-Violet Light Induced Free Radical Skin Damage

The four primary ways to reduce free radical damage to the skin generated from ultra-violet light is to avoid excess exposure to sunlight, wear protective clothing, use antioxidant-containing sun block creams and lotions and ingest antioxidant supplements at levels beyond that which food alone can provide. Taking antioxidant supplements is a less well known, but sound strategy to help defend the skin against free radical damage. Studies demonstrate that skin cells show rapid depletion of antioxidant enzymes and antioxidant nutrients (Vitamin E, Vitamin C, Beta-carotene, Coenzyme Q10) upon exposure to ultra-violet light. This indicates that these antioxidant defenses are being used up rapidly to protect skin cells and related structures from free radical damage. The same is true for skin surface lipids (a mixture of sebum and lipids secreted by epidermal cells), which represent the outermost protective layer of the skin. Upon exposure to ultra-violet light the antioxidant defenses within skin surface lipids have been shown to be rapidly depleted (e.g. Vitamin E and Coenzyme Q10) with the concurrent accumulation of lipid peroxides (free radical damaged fats) and other dangerous end-products of free radical damage to cholesterol and unsaturated fats found within skin surface lipids. Studies show however, that when individuals take antioxidant supplements prior to exposure to ultra-violet light, there is less free radical damage to skin cells and related structures (e.g. collagen, elastin, blood vessels, melanocytes, sebaceuos glands) and fewer free radicals created within skin surface lipids (skin surface lipids should then be viewed as the outermost antioxidant shield against free radicals from ultra-violet light). It is also known that individuals can increase the concentrations of antioxidant nutrients within their skin cells (epidermal cells) and within skin surface lipids by taking antioxidant supplements at levels beyond what can be obtained from food alone. In addition to Vitamin E, Vitamin C and Beta-carotene, the studies of JC Beani indicate that selenium and zinc are also important to boosting the antioxidant defense of skin cells. Selenium is required to activate the antioxidant enzyme glutathione peroxidase, and zinc has been shown to protect against cytotoxicity of UV-A and UV-B light, and against UV-B-induced DNA damage. Zinc is also required to activate the antioxidant enzyme superoxide dismutase within certain parts of the cell; a function it shares with the minerals magnesium and manganese. Beani showed that

better nutritional status of selenium and zinc within skin cells (and higher intracellular glutathione levels) resulted in significantly less free radical damage to these cells upon exposure to UV radiation than occurred in skin cells that displayed lower concentrations of these nutrients prior to UV radiation exposure. Beani concludes, "as DNA damage has a main place in photocarcinogenesis, our results point out the potential interest of photoprotection based on the support of endogenous antioxidants (food and supplement sources of antioxidants).... the research is indeed a necessity because sunscreens did not give convincing evidence of efficacy in preventing skin cancers."

Thus, it should be viewed as a prudent strategy to ensure that all patients and clients fortify the antioxidant defense mechanisms of the skin by choosing an antioxidant-rich diet (fruits, vegetables, legumes) and using an antioxidant-enriched multi-vitamin and mineral supplement each day. I would suggest the following levels of supplemental nutrients from a high potency multi-vitamin and mineral to help protect the skin from ultra-violet light induced skin damage:

Vitamin A:	2,500- 3,000 IU
Beta-carotene:	7,500 –15,000 IU
Vitamin C:	500-1,000 mg
Vitamin E:	200-400 IU
Selenium:	100-200 mcg
Zinc:	10-20 mg
Magnesium:	100-300 mg
Manganese:	5 mg
Copper:	1-2 mg

In conclusion, intensive investigation into this area of research indicates that free radicals produced in the skin from the interaction between UV-light and molecular oxygen (within skin cells) as well as from the interaction of UV-light and pheomelanin are primary factors in accelerated skin aging and increased risk of skin cancer. The biological mechanisms through which free radicals are created within the skin are largely understood, as are their deleterious effects on skin cells and related skin structures, and the ensuing depletion of skin antioxidant enzymes and nutrients that result from their presence in the skin. Recent evidence indicates that nutritional antioxidants (from diet and supplements) are critically important to optimizing the antioxidant defenses of skin cells and related skin structures and secretions (e.g. skin surface lipids), in addition to other standard lifestyle strategies that are commonly recommended to reduce risk of ultra-violet light induced skin damage. As such, health practitioners and skin care professionals should encourage their patients and clients to consume a diet rich in fruits, vegetables and legumes, and ingest an antioxidant-enriched multi-vitamin and mineral each day, that includes the above noted levels of antioxidant nutrients, as an integral part of lifelong protection against skin photoaging and to help reduce risk of skin cancer.

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