

Oral Sunscreen *Reduces* Skin Cancer Risk

In a recent advance, researchers showed that a vitamin B nutrient called **nicotinamide** can reduce the risk of skin cancer by **23%**!¹ This is a rate of protection unparalleled by **any** known compound.

What researchers have confirmed is **nicotinamide** plays a significant role in producing **ATP**, which facilitates **DNA repair** in skin cells damaged by solar radiation.² Rapidly restoring sun-damaged DNA provides powerful protection against malignant transformation.

When combined with two other natural ingredients, the protection from harmful **solar rays** is expanded as these tropical **plant extracts** defend against sun damage and further promote **DNA repair**.³⁻⁷

This discovery is timely and important since skin cancer is now the most common form of malignancy in the United States, affecting over **3 million** Americans each year.⁸⁻¹¹

It is now possible to prevent DNA damage, promote DNA repair, and impede ultraviolet radiation immune suppression by taking **oral** nutrients.^{2,3,12,13}

This discovery can help reduce the epidemic of **skin cancers** that impact a greater number of individuals each year.

Skin Cancer Surgery How To Reduce Scarring and Pain

The vast majority of skin cancers are not fatal. They all require treatment by a qualified physician and the earlier skin cancer is diagnosed and treated, the better the outcome.

The two most common non-melanoma skin cancers are basal cell and squamous cell. Basal cell skin cancer can be locally aggressive if neglected, but usually does not metastasize. Squamous cell skin cancer is typically slow growing, but does have the potential to metastasize, especially if neglected.

Various non-surgical treatment regimens for non-melanoma skin cancer include topical chemotherapy, cryotherapy, photodynamic therapy, and cutaneous surgery.

Mohs micrographic surgery is a specialized type of skin cancer surgery useful for both non-melanoma skin cancer as well as melanoma skin cancer.

Mohs micrographic surgery is performed by a dermatologic surgeon trained in this technique. The Mohs surgeon painstakingly excises thin layers of tissue, examining tissue margins for evidence of cancer after each successive round of tissue removal. The Mohs technique offers the highest rate of cure, with the best chance of tissue preservation.

For primary **melanoma** lesions between **1 mm** and **4 mm** in thickness, sentinel node biopsy is strongly suggested. If melanoma cells are not detected in the **sentinel node** (the lymph node most likely to drain from the primary lesion), then the adjacent lymph nodes are unlikely to be involved and no further surgery is necessary. If the sentinel node does reveal melanoma, then the adjacent nodes are usually removed in what is called a complete node dissection, because of the risk of metastatic melanoma in these lymph nodes.

If left untreated, any type of skin cancer can potentially cause localized damage and tissue destruction, as well as death (e.g. metastatic malignant melanoma).

Prevention and early evaluation of suspicious skin lesions are critical to avoiding potential surgical scarring and tissue mutilation caused by skin cancers left untreated over time. Once any form of **skin cancer** grows too large, extensive surgery is required that can produce tissue mutilation and post-surgical pain.

The Sun and Skin Cancer Connection

Ultraviolet radiation from sunlight is the primary cause of skin cancers of all kinds. In fact, sunlight and ultraviolet radiation are considered "complete carcinogens" for **squamous cell carcinoma** and its precursor, **actinic keratosis**. This means that no other initiating factor is required to produce these conditions.¹⁴

It is now clear that excessive ultraviolet exposure is associated with **65%** of cases of **malignant melanoma**, the deadliest skin cancer, and **90%** of non-melanoma skin cancers (squamous and basal cell carcinomas).¹⁵ According to the American Cancer Society, it is estimated that in 2016 more than **13,000** deaths will occur from different types of skin cancer.¹⁶ Nearly **5 million** Americans are treated with skin cancer annually, accounting for over **\$8.1 billion** in health care expenditures.¹⁰

The number of sunburns a person experiences increases the chances of getting one of these cancers.¹⁴

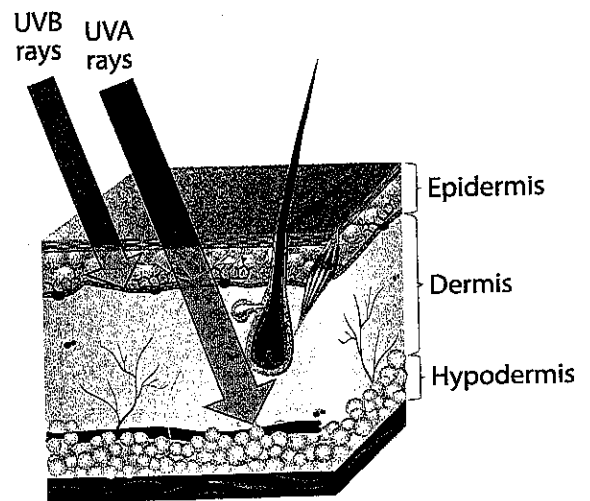
How Solar Ultraviolet Radiation Causes Cancer

So why is ultraviolet radiation so dangerous?

As sunlight reaches the earth and ultraviolet radiation strikes the human skin, changes characterized by the formation of cancer-producing compounds trigger DNA mutations.¹⁷⁻¹⁹

Our bodies have multiple **repair systems** that can remove the damaged portions of DNA and **restore**

Ultraviolet Radiation Penetration into the Layers of Skin



their normal sequence.^{20,21} To be effective, these repair systems require a steady and ample supply of *adenosine triphosphate* (ATP),²⁰ the energy-releasing molecule that fuels all cells to power their intracellular machinery.

Unfortunately, supplies of ATP tend to decrease with age, a problem that is compounded by the fact that ultraviolet radiation itself inhibits the production of ATP.^{17,22}

Insufficient ATP supplies means inefficient **DNA repair**. In other words, ultraviolet-exposed skin cells are not only at increased risk of DNA damage, but they are also **impeded** in their attempts to repair that damage before it triggers malignant transformation.^{2,17}

Further complicating matters, even small doses of ultraviolet radiation suppress the immune system in the skin, reducing the body's ability to identify and destroy potentially malignant cells before they go rogue.^{13,17,23-25}

The good news is that studies show that promoting rapid DNA repair is an effective means of preventing malignant transformation in skin cells.^{24,26}

Even better, science has identified **three specific nutrients** that work together to provide protection from the ill effects of solar radiation. Together, **nicotinamide**, **red orange extract**, and ***Polypodium leucotomos*** extract help prevent DNA damage, promote DNA repair, reverse immune suppression, and reduce the twin threats of oxidation and inflammation that arise from ultraviolet exposure.^{2,3,12,13}

Nicotinamide Protects against Skin Cancer

Nicotinamide (vitamin B3) is a safe vitamin that had shown promise in lab and animals studies in preventing skin cancers, especially the most common, non-melanoma variety.¹² In addition, studies in heavily sun-damaged people show that nicotinamide provides protection from precancerous **actinic keratosis**, as well as from new **non-melanoma** skin cancers.²

In the most compelling and important study to date, researchers enrolled 386 healthy subjects with a history of at least two non-melanoma skin cancers in the past five years. Subjects received either twice-daily nicotinamide (**500 mg** per dose) or placebo for 12 months.¹

The researchers were stunned at the results. At 12 months, the rate of new non-melanoma skin cancers was significantly reduced by **23%** in supplemented subjects compared to the placebo group.¹ It is almost unheard of for any single biological intervention to reduce the rate of cancer in people at risk by a figure as high as **23%** overall.



What You Need to Know

Oral Sunscreen Protects against Skin Cancer

- Skin cancer is the most common and most preventable cancer in American adults.
- The rate of skin cancer is rising as more and more people embrace the outdoors and experience greater exposure to sunlight.
- Topical sunscreens are useful and effective at skin cancer prevention, but most people apply them too lightly and inconsistently.
- Scientists have now identified a common intracellular substance, nicotinamide, that can reduce rates of skin cancer by up to **23%** overall when taken as an oral supplement.
- Nicotinamide boosts energy levels in cells, allowing them to repair their own DNA following ultraviolet light-induced damage, thereby reducing the risks of skin cancer.
- Nicotinamide also promotes immune system functions that are damaged by ultraviolet radiation, resulting in improved surveillance and destruction of emerging cancers.
- Red orange extract and *Polypodium leucotomos* extract serve as important adjuvants to nicotinamide, providing protection against reactive chemicals generated by ultraviolet light and reducing the resulting inflammation that can promote cancer.
- Topical sun protection along with the use of this nutrient combination should be part of a daily routine for a regular, year-round protection against the inevitable exposure to ultraviolet light.



Types of Skin Cancers

"Skin cancer" is a general term comprising several rather different types of malignancy. Like all organs, the skin contains a variety of cell types with differing functions, and several of those cell types produce readily recognized malignancies.

The most deadly, but fortunately least common, of the skin cancers is malignant **melanoma**.³¹ Two main types of skin cancers collectively referred to as "non-melanoma skin cancers" are discussed along with one precancerous lesion:^{31,32}

- **Basal cell carcinoma** is the most common human skin cancer, arising from the deeper (basal) skin layers that produce the protein keratin.
- Basal cell carcinomas represent about **80%** of skin cancers.
- They are most common in sun-exposed areas of skin, and, while once more common in middle-aged or older adults (whose lifetime exposure is higher), they now occur with increasing frequency in younger adults, presumably because of our sun-worshipping culture.
- **Squamous cell carcinoma** is the second most common skin cancer. It arises from flat (squamous) cells in the outer skin layer.
- These represent about **20%** of skin cancers found in sun-exposed areas but also in scars or chronic skin sores.
- Though metastatic or local invasion is unusual, squamous cell carcinomas spread by these means more commonly than do basal cell cancers.
- **Actinic (or solar) keratoses** are precancerous lesions produced by excessive sun exposure. These are small, rough/scaly lesions, most commonly seen on sun-exposed facial skin, though they can be found elsewhere.
- Though most remain benign (and some regress on their own), some actinic keratoses go on to produce squamous cell carcinomas, making them worth monitoring or removing.

All of these cancers and precancerous lesions result largely from excessive sun exposure, and can be prevented by taking steps to protect oneself from the DNA-damaging, immune-suppressing effects of solar ultraviolet light.

When the carcinomas were broken down by tumor type, supplemented subjects had **20%** fewer new diagnoses of basal cell carcinomas and **30%** fewer new diagnoses of squamous cell carcinomas.¹

In addition, supplemented individuals had an **11%** reduction in the rate of new premalignant actinic keratoses three months into the study. That reduction was **13%** at 12 months. Once supplementation was discontinued, however, no evidence of further benefit was seen. This lets us know the importance of continuous **oral** intake of **nicotinamide**, an inexpensive B vitamin that does not cause skin flushing.¹

How Nicotinamide Works

What makes nicotinamide so powerful against skin cancer?

The answer lies in two of nicotinamide's most fundamental properties: its role in producing **ATP** and its ability to protect against ultraviolet-induced **immunosuppression**.²

As stated earlier, the body relies on an ample supply of ATP to **repair** and remove the damaged portions of DNA and **restore** their normal sequence. By helping the body produce more ATP, **nicotinamide** helps to ensure continuous and efficient **DNA repair** mechanisms. In fact, nicotinamide has been shown to repair ultraviolet-induced DNA damage in two ways, making it extremely effective.^{2,12}

In a cell culture experiment, researchers treated skin cells with nicotinamide and then exposed them to low-dose simulated solar ultraviolet radiation. The nicotinamide treatment significantly increased the number of cells undergoing **DNA repair**. It accomplished this by removing and replacing damaged DNA and by increasing the repair *rate* in each cell.²

In a second portion of the experiment, researchers measured the production of molecular products of DNA damage within cells, which is another means of mea-

suring DNA damage and repair. They found that nicotinamide reduced the concentration of those marker molecules both in cells in culture and in human skin.²

A similar cell culture study using *melanocytes* (pigmented skin cells that can develop into deadly melanomas) showed virtually identical results. Nicotinamide treatment led to a reduction in markers of DNA damage and enhanced evidence of DNA repair.¹²

Immune Support

We learned earlier that ultraviolet radiation suppresses the immune system in the skin, which reduces the body's natural ability to identify and destroy potentially malignant cells. Ultraviolet radiation is so effective at suppressing the immune system that it is used in certain patients with severe autoimmune disorders to turn down their overactive immune system.

Human studies show that **nicotinamide** protects against ultraviolet-induced **immune suppression**.

In one such study, healthy volunteers took either a placebo or nicotinamide at doses of **500** or **1,500 mg** daily for one week. On the third day after supplementation, subjects underwent low-dose irradiation of distinct areas of their back for three days, at three fixed doses.¹³

As expected, the placebo recipients showed substantial *immunosuppression* of skin in the irradiated areas. When compared to placebo groups, subjects taking

either dose of nicotinamide showed significant reductions of **50%** to **66%** (depending on radiation dose), with no effects seen in unirradiated skin. It is important to note that all subjects tolerated the supplement well and that the low dose (**500 mg**) of nicotinamide delivered similar immune protection as the high dose (**1,500 mg**).¹³

The Problem with Topical Sunscreens

Skin cancers affect over 3 million Americans each year, killing tens of thousands. These shocking numbers continue to climb with each passing year.⁶⁻¹¹

Clearly, despite aggressive public education campaigns, Americans remain unable to protect themselves sufficiently from the cancer-inducing effects of solar radiation. That's not to say that taking protective measures such as wearing a hat, covering up, seeking shade, and wearing topical sunscreens aren't important. They are.

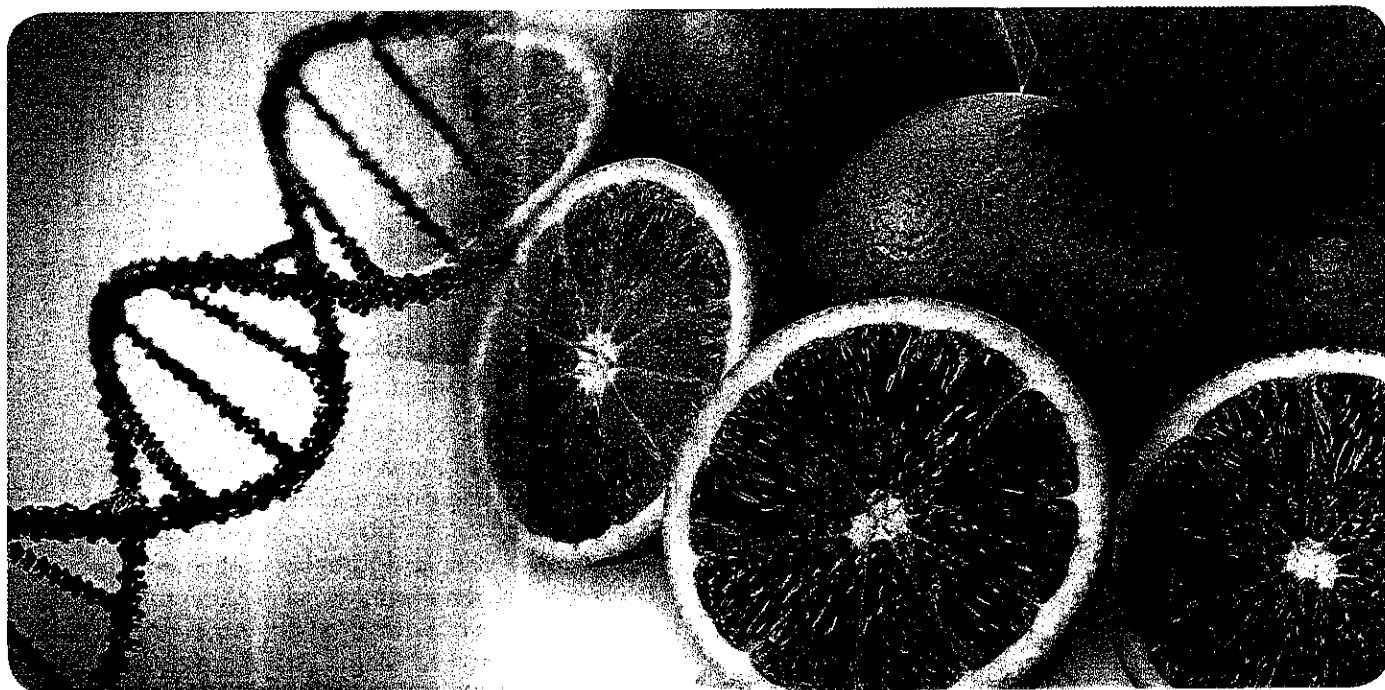
Unfortunately, most **topical sunscreens** have other limitations. They only block a portion of ultraviolet radiation from reaching the skin, they often break down under solar radiation (which reduces their effectiveness), and their content of free radical scavengers is woefully inadequate to deal with the intense release of oxygen free radicals deep within in skin exposed to ultraviolet light.²⁶

That's what makes the development of an **oral sunscreen** so revolutionary.

By avoiding the pitfalls of most topical sunscreens, oral sunscreens add a tremendous convenience factor that is likely to enhance people's willingness to use sun protection. In this way, daily oral sun protection can become routine, just like taking other supplements.

If thought of as **cancer prevention**, rather than simply sunburn protection, most people will take this regimen more seriously than they do topical sunscreens. The result will be more broad-spectrum protection against the negative effects of the sun—and likely a reduction in the risk of skin cancers.





Red Orange Extract for DNA Protection

Recent laboratory studies have demonstrated that **red orange extract** adds to nicotinamide's DNA-protective, immune-boosting effects.

Red orange extract is a powder obtained by a patented process from three pigmented varieties of *Citrus sinensis*. This extract is rich in anthocyanins, flavanones, and hydroxycinnamic acids. All of these nutrients have been found to enhance the body's natural ability to protect itself against ultraviolet radiation.³⁻⁶ These biomolecules also offer protection from the inflammation^{3,6} and oxidative stress caused by ultraviolet radiation.⁴

In one study, red orange extract has been clinically shown to reduce the intensity of sunburn by about **35%** after 15 days of treatment.²⁷ This demonstrated the ability of red orange extract to prevent skin damage and potentially reduce skin cancer risk. The ability to reduce the intensity of a sunburn is an important finding, given the close correlation between the number of lifetime sunburns and the risk of developing skin cancers.¹⁴

Let's take a look at a few of the studies that show these benefits.

In one study, when human skin cells (keratinocytes) were exposed to ultraviolet radiation, the application of red orange extract reduced ultraviolet-induced cell damage, helped prevent inflammation, and reduced cell death in response to ultraviolet radiation.⁵

Similar results were found in human cultured skin cells (keratinocytes and fibroblasts) exposed to powerful oxidants, demonstrating the ability of red orange extract to reduce oxidant stress.²⁸

Polypodium Leucotomos Extract Protects against Ultraviolet Radiation

Polypodium leucotomos extract is obtained from a tropical fern, which has a long history as a treatment for psoriasis and other inflammatory skin conditions.^{7,29} The extract is rich in polyphenols that potently inhibit oxidant stress and inflammation, while also protecting skin cells against ultraviolet radiation.⁷

In a study of 10 healthy volunteers aged 29 to 54, researchers randomly assigned patients to receive two **240 mg** doses of *Polypodium leucotomos* extract or a placebo prior to exposing them to a dose of ultraviolet radiation, then took skin biopsies.⁷ At a lower dose of ultraviolet light, placebo subjects had a dangerous increase in a marker of DNA damage (called the "common deletion") by **217%**. Subjects in the supplemented group had a decrease in the marker of **84%**. At a higher level of ultraviolet exposure, DNA damage increased by **760%** in placebo subjects, while increasing only **61%** in the supplemented group.

The impact of these results was seen in a human study in which subjects were given *Polypodium leucotomos* extract twice daily for 15 days. The researchers found that the subjects could tolerate a significantly **larger dose** of ultraviolet light before showing skin redness (a marker of exposure/damage) compared with their ultraviolet tolerance prior to supplementation. Subjects also recovered faster from ultraviolet-induced inflammation.³⁰

Summary

In a remarkable development, scientists have discovered that **nicotinamide**, a well-known natural supplement and essential cellular component, can reduce the rate of new skin cancers by **23%** following oral supplementation.

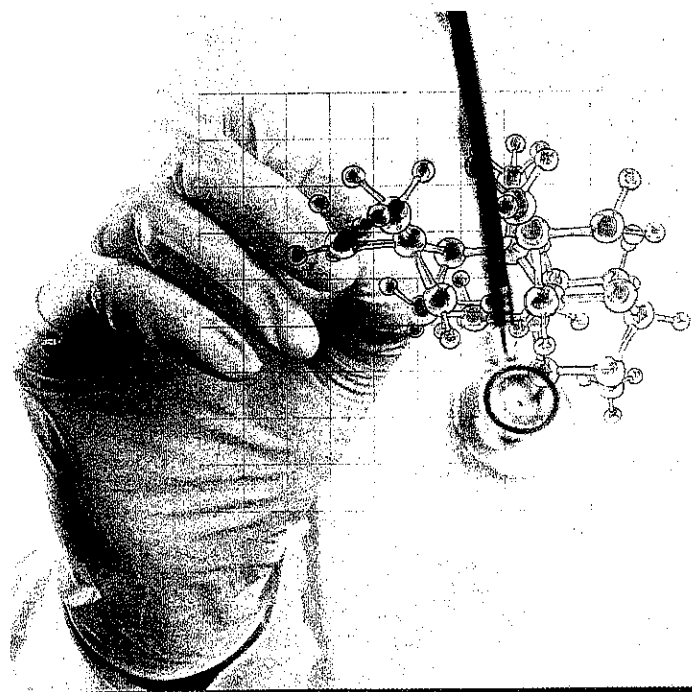
Nicotinamide appears to exert its beneficial efforts primarily through prevention of DNA damage and promotion of DNA repair, two early processes that can stop cancer initiation.

Two additional natural ingredients, **red orange extract** and ***Polypodium leucotomos* extract**, offer complementary benefits, providing protection against the reactive chemical compounds produced inside cells when exposed to ultraviolet radiation. These extracts also help to suppress the inflammatory response to radiation exposure, which is known to contribute to cancer progression.

What few people realize is that everyday exposure to solar rays causes cumulative DNA damage, accelerates skin aging, and increases skin cancer risk.

The advent of three natural compounds provides an **oral sun protection formula** that can be used daily to protect skin from routine solar exposure. These nutrients also complement any topical creams or lotions by protecting even hard-to-reach area of one's skin.

Daily supplementation should provide a strong baseline of protection against the sun's ill effects. However, when prolonged exposure to the sun is planned, the usual recommendations for sun protection still apply in order to provide maximum skin cancer-preventive effects. ●



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Photodynamic Therapy

Nicotinamide has been shown to powerfully prevent ultraviolet-induced immunosuppression. This makes it especially valuable in patients undergoing **photodynamic therapy**.³³

In this treatment for non-melanoma skin cancers, visible light is used in combination with chemical photosensitizers in an effort to specifically target skin cells affected by the cancer. Unfortunately, up to **45%** of people treated with this approach have resistant or recurrent tumors that are directly related to the light-induced immune suppression in the area of irradiation.^{33,34}

This makes photodynamic therapy a double-edged sword, since it potentially condemns nearly half of its recipients to further battles with malignancy. This presents an ideal scenario for the use of nicotinamide—and in fact, one study has already proven its benefits.

Subjects in this study received a placebo or **500 mg** of nicotinamide twice a day for seven days.³³ On day three, subjects received photodynamic therapy to discrete areas of the back, while adjacent, non-irradiated areas served as control patches. Immunosuppression in the skin was determined by injection of a known antigen to which volunteers were all sensitive, and to which they were expected to produce a reaction in the skin. (Skin redness as well as the diameter of the reaction were measured.)

Subjects receiving the placebo showed **50%** suppression of the skin reaction, as expected. But in those receiving nicotinamide, the immunosuppression was itself reduced, resulting in **66%** less redness and a **90%** reduction in diameter of the reaction site. A similar group of subjects received nicotinamide cream or a placebo cream, and again, immunosuppression was reduced in treated subjects by **59%** compared with placebo.

This study powerfully demonstrates nicotinamide's ability to combat immunosuppression and support the immune system's ability to detect and destroy developing cancers.

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