Aesthetic Medicine 2025; Vol. 11, N. 2: 16289 DOI: 10.57662/am.v11i2.16289

Review

Sun exposure, onset of nonmelanoma skin cancers (NMSCS) and photoprotection: What's new?

Antonella Tammaro[1], Ilaria Demofonte[2], Pietro Pasquale Cozza[1], Ganiyat Adenike Adebanjo[3], Gabriella De Marco[4], Fabiola Luzi[5], Antonino Trischitta[6], Giovanni Pellacani[2]

[1]Department of Health Sciences, University Magna Grecia, Catanzaro; [2]Unit of Dermatology, Department of Internal Medicine and Medical Specialties, Sapienza University, Rome; [3]Department of Medicine and Surgery, University of Parma; [4]Department of Neuroscience, Mental Health and Sens Organs, NESMOS, Sapienza University of Rome; [5]IFO San Gallicano Institute Rome; [6]Federico II University of Naples

Abstract. *Introduction:* NonMelanoma Skin Cancers (NMSCs) are the most common types of skin cancers and are the most frequently diagnosed worldwide. Sun exposure is considered the major risk factor for the onset of skin cancers, particularly for NMSCs. The head and neck area appears to be the one most affected by skin tumors related to sun exposure. There are two main subtypes of NMSCs: Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC). Among the most frequent lesions of the head and neck area, there are also Actinic Keratoses (AKs), considered precancerous lesions. *Aims:* The purpose of this article is to highlight what's new in the field of photoprotection and reiterate the importance of protecting our skin from the potential risks of incorrect exposure to UV rays. *Results:* The frequency of AKs increases with age and with the cumulative dose of lifetime sunlight. Patients with multiple AKs are at higher risk of developing NonMelanoma Skin Cancers. *Conclusion:* The most effective tool in preventing the onset of these types of cancers persists being adequate photoprotection, both topical and systemic.

Key words: nonmelanoma skin cancers, actinic keratoses, basal cell carcinoma, squamous cell carcinoma, photoprotection, sun exposure

Introduction

Sun exposure is recognized as the primary risk factor for the development of skin cancers, particularly NonMelanoma Skin Cancers (NMSCs). Among these, tumours affecting the head and neck regions are most strongly associated with UV radiation. NMSC is the most prevalent type of cancer globally, with an annual incidence of approximately one million cases worldwide[1]. The two main subtypes of NMSCs are Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC). Actinic Keratoses (AKs), common lesions in the head and neck region, are considered precancerous with an estimated progression rate to invasive SCC of 0.075%–0.096% per lesion[2]. The frequency of AKs increases with age and cumulative lifetime sun exposure, and individuals with multiple AKs face a higher risk of developing NMSCs. Another tumour frequently found in sun-exposed areas, particularly on the face, is Lentigo Maligna Melanoma (LMM), a subtype of melanoma arising when Lentigo Maligna progresses into the dermis during its vertical growth phase. LMM is closely linked to NonMelanoma Skin Cancer and UV exposure. Effective sun protection and a prompt clinical evaluation of suspicious lesions remains the

most critical strategies for preventing and managing skin cancers[3].

Actinic Keratoses (AKs) and nonmelanoma skin cancers (NMSCs)

Actinic Keratoses (AKs)

AKs are considered precancerous lesions that present clinically as erythematous macules or plaques, sometimes crusted, that evolve in areas chronically exposed to sunlight. They are a very common condition to observed in individuals with a pale skin phenotype, in areas of the face that are commonly exposed to light, the scalp (in the absence of hair), auricles, neck, décolleté, forearms and dorsal portion of the hands, shins and less frequently eyelids and eye area. When the labial mucosa is involved, AKs are called Actinic Cheilitis.

They can be of various sizes, generally starting as "rough" areas that are perceived by touch but not easy to observe clinically, generally asymptomatic even if they can cause itching or discomfort. The frequency of AKs increases with age and with the cumulative dose of UV rays absorbed throughout life. Another important risk factor is immunosuppression which is more common in men.

Variants of AKs include hypertrophic (or hyperkeratotic) forms, as well as those that evolve as cutaneous horns. They can also be pigmented or Bowenoid lesions.

Clinically they may be graded as mild to severe in accordance with the 3-grade Olsen scale[4].

Patients with multiple AKs are more likely to develop Nonmelanoma Skin Cancers. In fact, AKs have the potential to evolve into Squamous Cell Carcinomas (SCCs). The term "Cancerization Field" is intended to describe the areas of the skin at risk of developing both AKs and SCCs[5].

Basal Cell Carcinoma (BCC)

Basal cell carcinoma (BCC) is considered the most common form of cancer in humans and the most common of skin cancers. It is estimated that every year, around 64,000 new cases of BCC in Italy and 2 million in America[6].

The prevalence is higher in males, although, especially in recent years, cases of BCC are increasing in women. They can present themselves at any age, although the highest incidence is in older individuals, with an average age at diagnosis of 68 years[6].

BCC is derived from basal keratinocytes. Various subtypes have been described, including nodular, superficial, pigmented, cystic (infundibular), fibroepithelial, morpheiform (also known as sclerosing or desmoplastic), infiltrative, micronodular, and basosquamous.

The major risk factor for the occurrence of BCCs is sun exposure, especially regarding individuals with a lighter phenotype. Intermittent sun exposure is considered a greater cause of development than a chronic cumulative exposure dosage.

Other risk factors include: environmental exposure to ionizing radiation, chemical agents such as arsenic, immunosuppression (e.g., following organ transplantation), and various genetically inherited syndromes such as Xeroderma Pigmentosum, Albinism or Gorlin-Goltz Syndrome.

BCC is a slow-growing tumour and metastasizes very rarely, with an estimated probability of 1 in 35,000 cases[6]. However, it can lead to the local destruction of the tissues surrounding the tumour and physical disfigurement.

Clinically, superficial BCC usually presents as a well-defined lesion, patch, or erythematous plaque with thin, slightly raised edges. The lesion expands horizontally, evolving over time with atrophy, hypo or hyperpigmentation. In nodular cases, they appear as a papule or nodule, soft, translucent, with raised edges and often surmounted by obvious telangiectasias. They can be pigmented and undergo ulceration.

Squamous Cell Carcinoma (SCC)

SCC is the second most common skin cancer in the world, with an increasing incidence in recent years. The lifetime risk of developing SCC is estimated to be 9-14% in men and 4-9% in women, usually occurring in later stages of life[7].

The most important risk factor associated with its development is the light phototype. Other factors include: ultraviolet exposure, immunosuppression, HIV infection, exposure to ionizing radiation, the consumption of tobacco, HPV (Human Papillomavirus) infection, chronic lymphocytic leukemia (CLL), exposure to chemicals (arsenic, coal tar, mechloretamine) and chronic ulcerations. About 10% of AKs turn into a skin cancer, most commonly an SCC[7].

Although SCC can develop anywhere on the body surface, including mucosal areas, the most common sites involved are photo-exposed areas, such as the head, neck, hands, and forearms. In individuals with a darker phenotype, on the other hand, they generally onset in areas where scarring or chronic ulceration occurs.

The clinical presentation of SCC is extremely variable. Most often it manifests as a papule or nodule, hyperkeratotic, firm or infiltrated, but can also evolve as a papule of soft or papillomatous consistency. The color also varies, from the individual's regular skin color to a more pigmented variant. It may undergo ulceration or erosion. Variants include: Marjolin Ulcer, Keratoacanthoma, Verrucosal Carcinoma (Busche-Lowenstein tumour), Lymphoepithelioma-like carcinoma of the skin (LECLS).

The lesion can grow slowly or, on the contrary, evolve very quickly (more aggressive variants). The risk of metastasis is estimated at 4%, locoregional lymph nodes are generally affected, but there may also be distal metastases[7] (Figures 1 and 2).

The importance of photoprotection: A first-line strategy in the prevention of skin cancer

Prolonged exposure to UVA and UVB radiation is a primary cause of premature skin aging (photoaging) and significantly elevates the risk of developing skin lesions, ranging from precancerous conditions to overtly malignant neoplasms. The increasing incidence of skin cancers, particularly NonMelanoma Skin Cancers, has become a pressing public health issue both in Italy and worldwide.

Preventing harmful solar exposure is therefore crucial to reduce of developing skin cancer. Effective photoprotection can be achieved through a combination of topical measures and systemic approaches, emphasizing the need for comprehensive skin care strategies.

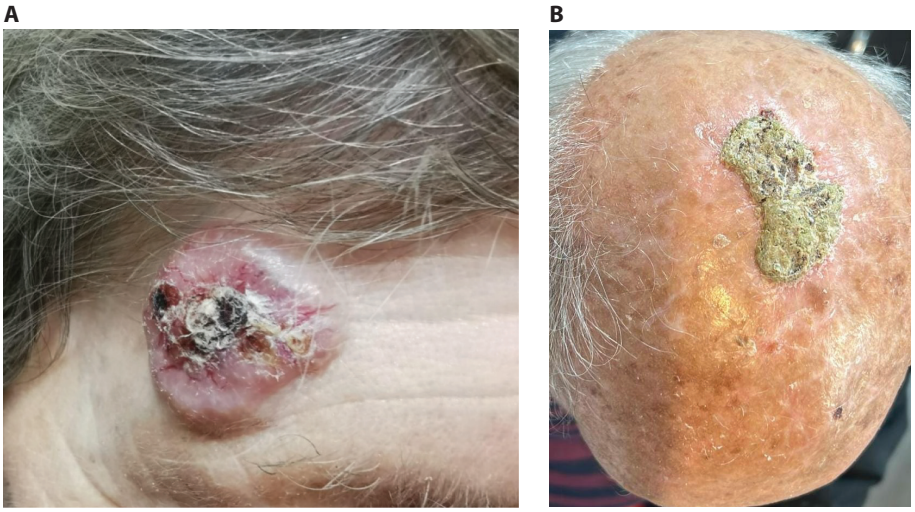

Figure 1. NonMelanoma Skin Cancers: clinical examples of manifestation of NMSCs involving the head and neck area.

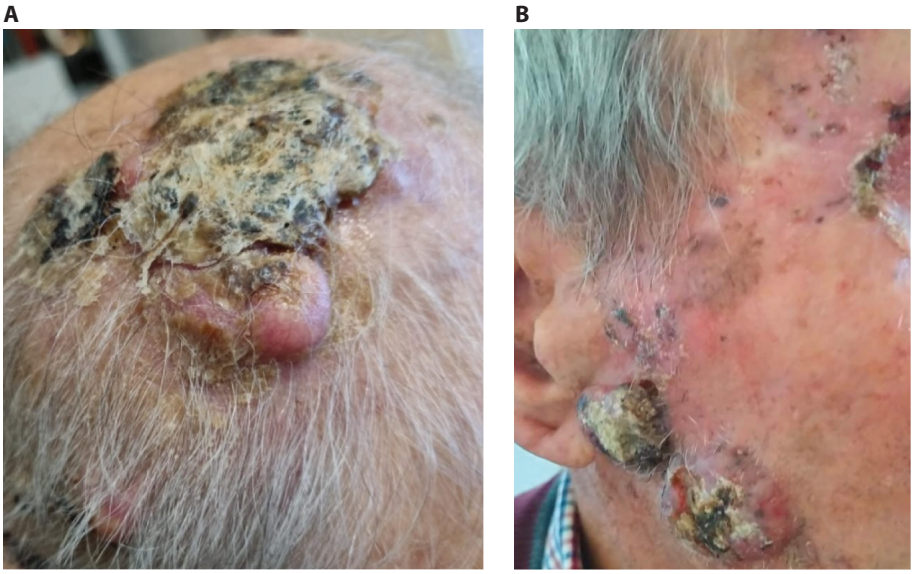

Figure 2. NonMelanoma Skin Cancers: clinical examples of manifestation of NMSCs involving the head and neck area.

Topical photoprotection

Local photoprotection can be achieved either through a chemical filter or using physical filters. Chemical filters are made up of substances that can absorb ultraviolet radiation, while physical filters are made up of substances that shield radiation, reflecting or diffracting UV rays.

Several forms of photoprotection are available, and new active molecules and delivery systems continue to be developed each year. Among the best-known chemical-based filters are Avobenzone, Oxybenzone, Octocrylene and Ecamsule, while among the most well-known physical-based filters are Zinc Oxide and Titanium Dioxide.

Topical photoprotectants should be applied not only in the summer, but also in the colder months, and not only near the seaside but also in an urban setting. Its application should also be repeated at least every 2-3 hours.

Another fundamental factor concerns the correct amount of product that must be applied to ensure adequate protection. The amount established by the SPF determination method, 2 mg/cm2, corresponds to about 36 g of product, or 6 teaspoons, which should be used to properly coat the body of an adult individual.

In more detail, the recommended amount is divided according to the body area on which the product is applied as follows:

HEAD-NECK district: one teaspoon, TRUNK: two heaped teaspoons, for each ARM: one teaspoon, for each LEG: two teaspoons[8].

New organic and inorganic solar filters

Over the last few years, new organic (or chemical) and inorganic (physical) molecules, which can be used as sun filters, were approved in Europe.

These new molecules guarantee broad-spectrum protection against UVB and UVA, even towards wavelengths above 400 nm. It has in fact been widely demonstrated that High Energy Visible Radiation (HEVR), which corresponds to wavelengths greater than 380 nm (including Blue Light up to 450 nm), are responsible for skin hyperpigmentation as well as oxidative stress and damage to cellular DNA. Thus, new effective sunscreens should be approved to offer

photoprotection beyond ultraviolet (UV) radiation to also prevent or limit BL-induced cutaneous effects.

Among the most recently approved organic sunscreens in the EU, in 2021, was Phenylene Bis-Diphenyltriazone (TriAsorB), a low molecular weight substance which, being both hydrophilic and water-soluble, can deeply penetrate the skin.

TriAsorb is the first organic filter that has a unique ability to absorb and reflect UVB, short-wavelength and long-wavelength UVA as well as High-Energy Visible Blue Light. Its effectiveness against High Energy Visible Radiation (HEVR) has been widely demonstrated, especially in its ability to reduce oxidative damage to DNA and the formation of dark cyclobutane pyrimidine dimers (CPDs). On the market, TriAsorB is found in formulations in which it is associated with other classic UVB and UVA sun filters[9,10].

Inorganic filters, however, have always played a secondary role and, until now, have essentially been based on two main elements, Titanium Dioxide and Zinc Oxide, mostly used in the photoprotection of children or patients sensitive to other types of sun filters.

Lately, however, physical filters have also rediscovered an important role, for their use both alone and in combination with other chemical filters. When combined with classic organic filters, inorganic filters achieve an absorption spectrum that includes both Visible Light (VL) and UV light.

Furthermore, in recent years, research in the pharmacological and cosmetological fields has taken an ecological turn, engaging in the development and creation of topical products based on natural substances with a low environmental impact.

Polyphenols, derived from herbs and medicinal plants, have shown positive effects against photoaging. Their action is based on the ability to reduce the production of Reactive Oxygen Species (ROS) after exposure to UVA and UVB rays, as well as their ability to stabilize the phenomenon of lipid peroxidation, inhibit the apoptosis of keratinocytes, barring collagen degradation, reduce inflammation associated with skin damage and promote the expression of key factors in cellular reparation. For this reason, Polyphenols are among the molecules that could play a future role in the field of photoprotection[11].

Among these, Resveratrol is a natural polyphenol with proven antioxidant and anti-aging properties. Its topical application can modulate the apoptosis of keratinocytes after exposure to UVB rays, increase the production of type I and III collagen and elastin and inhibit the gene transcription of metalloproteinases 1 and 9 (MMP1 and MMP 9). Other actions of resveratrol include the upregulation of antioxidant enzymes, reduction in the production of pro-inflammatory cytokines, and enhanced expression of anti-aging proteins, such as Sirtuin 1 (SIRT1) and various cellular growth factors[11].

Another promising natural substance belonging to the Polyphenol group is Silymarin, obtained from the milk thistle plant Silybum marianum. This molecule has been shown to possess antioxidant properties with a strong anti-inflammatory and photoprotective action. It protects the skin from damage due to photoaging, improves the skin's natural defense systems and prevents potential damage caused by chemical and environmental oxidants[9].

Already known for these antioxidant properties, Silymarin has also been shown to have the ability to absorb UV rays, when present in 10% topical formulations and especially when combined with Titanium Dioxide and Zinc Oxide[9].

Systemic photoprotection

Although local photoprotection is certainly the basis for fulfilling a key preventive goal, systemic photoprotection must also be considered, especially in subjects suffering from dermatological diseases or with a history of previous skin cancers or considered at high risk of developing them. In subjects at risk of photodermatosis, systemic protection should be started about 1 month before sun exposure and continued throughout the exposure period, while in subjects with previous skin cancers it is advisable to implement it throughout the year.

Systemic photoprotection is carried out by oral administration of molecules with strong antioxidant and photoprotective properties. The most widely used molecule is certainly Nicotinamide, also known as Niacinamide. This is a derivative of the water-soluble

vitamin B3 (Niacin) and its role is to be a precursor of essential coenzymes such as NAD+ (Nicotinamide Adenin Dinucleotide) or NADP (Nicotinamide Adenine Dinucleotide Phosphate)[12].

The action of Nicotinamide is based on its ability to prevent the decrease in NAD+ levels in response to exposure to ultraviolet rays; in this way, it prevents the reduction of ATP and enhances DNA repair processes and therefore protects the skin from actinic damage induced by photoexposure[12].

Due to its antioxidant, immunomodulatory and anticarcinogenic properties, Nicotinamide has been shown to significantly reduce the incidence of actinic keratoses and non-melanoma skin cancers.

The recommended intake of Nicotinamide varies according to age. In adults it ranges between 14 and 16 mg/day, is reduced by a few units in children (6-14 mg/day) and is increased in case of pregnancy and breastfeeding (up to 20 mg/day)[12].

According to the new updated ***2023 European consensus-based interdisciplinary guideline for invasive cutaneous squamous cell carcinoma EJC***, the administration of 500 mg of Nicotinamide twice a day is recommended in case of a history of multiple SCCs[13.]

Among the other types of systemic photoprotectors for oral administration, there is a lot of evidence on the use of systemic retinoids, especially Isotretinoin and Acitretin. Both are derivatives of vitamin A and have been shown to have strong antitumor properties, based on the regulation of proliferation, differentiation, and apoptosis of different cell types[13].

From a molecular point of view, however, these substances act by neutralising the effects produced by ultraviolet rays, especially by decreasing the UV-induced depletion of Langherans cells.

According to the EJC, the use of systemic retinoids should be considered in immunosuppressed patients with a history of one or more Squamous Cell Carcinomas. Recent systematic reviews have shown that patients treated with systemic retinoids showed a reduction in the incidence rate of SCCs[13].

Topical retinoids (Acitretin, Adapalene, Tazarotene, Tretinoin) have also been shown to play a role in photoprotection. In fact, they have a mechanism of action based on determining, at the molecular level, an increase in the proliferation of basal cells, and therefore a thickening of the stratum spinosum and granulosum and a thinning of the stratum corneum[14].

Role of NSAIDs

Non-steroidal Anti-Inflammatory Drugs (NSAIDs), such as Indomethacin and Celecoxib, have been shown to have protective effects against the onset of skin cancer. Several studies have indicated the protective effect of NSAIDs against carcinomas linked to keratinocyte and melanocyte proliferation, including SCCs, BCCs and Melanoma. A thoroughly developed Danish observational study on Cancer published in 2012 revealed that subjects who habitually used these drugs showed a significantly lower risk of developing melanoma and Squamous Cell Carcinoma (SCCs)[15], with an advantage proportional to the treatment duration and dosage of NSAIDs taken. In particular, the use of any NSAID was associated with a 15% reduction in the relative risk of SCCs[15]. The protective effect would be related to the inhibition of Cyclooxygenases (COX) and thus the production of prostaglandins, molecules with anti-apoptotic and immunosuppressive activity and the ability to stimulate angiogenesis and tissue invasion. They are also capable of limiting the growth of keratinocytes induced by UV rays[15].

Regarding the type of NSAIDs, Aspirin, non-selective NSAIDs, and older generation COX-2 inhibitors, have shown a similar effect on the risk of developing SCCs[15].

Furthermore, A case-control study of 1621 people achieved in South Queensland, Australia, found that regular NSAID users had a lower incidence of AKs and SCCs[13].

However, it is important to note that the most important preventive measure against the onset of skin cancer remains adequate and correct photoprotection, whereas the use of NSAIDs with the sole aim of protecting against sun damage is not justified.

Role of Polypodium Leucotomos: A tropical plant beneficial to the skin

Polypodium Leucotomos is a tropical fern native to Central and South America, used for medicinal

purposes in the traditional setting and currently being studied by researchers all over the world.

Clinical research has in fact demonstrated the beneficial properties of *P. leucotomos* extracts, due to the presence of compounds with high antioxidant and photoprotective properties, such as p-Coumaric Acid, Ferulic Acid, Vanillic Acid, Caffeic Acid and many others[16].

When taken systemically, it provides a high level of protection against the harmful effects of ultraviolet rays, also helping to reduce the effects of photoaging.

The capabilities of these active ingredients are based both on the reduction of oxidative damage of reactive oxygen species (ROS), and through the stimulation of collagen synthesis and the decrease in the expression of metalloproteinases, thus ensuring the integrity of the extracellular matrix[16].

When taken orally, *P. Leucotomos* is considered safe and effective at a dose of 240 mg twice daily for a period of 2 months[16].

A recent multicenter, prospective, case-control study has shown that the combined use of topical and oral photoprotection with a standardized extract of *P. Leucotomos* has been shown to provide near-complete protection against ultraviolet radiation, thus ensuring the reduction of the development of NMSC[17] (Table 1).

Future scenarios: Beyond repair towards cellular regeneration

A recent article published in *Cells* in early 2024 highlights promising advancements in photoprotection and the treatment of photodamage[18]. The study explores the therapeutic potential of Mesenchymal Stem Cells derived from the umbilical cord (HUCMSCs), both in vivo and in vitro, demonstrating their beneficial properties against skin photoaging[18]. Experimental evaluations utilized a Concentrated Supernatant of HUCMSCs (CHS), which exhibited significant protective effects against UVB-induced photodamage[18]. Specifically, CHS was shown to enhance cell migration, reduce senescence and apoptosis, and support cellular repair mechanisms after UVB exposure. These effects appear to result from the activation of autophagy, as evidenced by an increase in autophagic protein levels following UVB radiation[18]. Furthermore, CHS demonstrated reparative effects on collagen integrity by reducing wrinkle formation, enhancing collagen expression, and promoting immune cell activity in areas affected by actinic damage[18]. The application of Mesenchymal Stem Cells to initiate intrinsic skin regeneration may represent a groundbreaking approach to skin protection and the prevention of photoaging in the future[18].

This discovery holds immense potential for revolutionizing dermatological treatments, offering not only advanced strategies to combat photoaging but also the possibility of long-term skin rejuvenation and enhanced protection against UV-induced damage, paving the way for transformative developments in both preventive and therapeutic dermatology[18].

Photoprotection and healty eating: A combination of strength

The role of a proper diet in photoprotection from ultraviolet (UV) rays has become an increasingly significant topic of discussion. A balanced diet rich in essential macronutrients, such as collagen and elastin, as well as vitamins, minerals, and antioxidants, is vital for maintaining skin integrity and supporting cellular repair mechanisms.

As highlighted in the article *"Diet and Skin Cancer"*[19], Selenium emerges as one of the most effective substances with notable photoprotective properties. This essential element, found in foods such as Brazil nuts, seafood, chicken, and red meat, demonstrates remarkable photoprotective capabilities.[19]

Beta-carotene, abundant in orange fruits and vegetables such as carrots, pumpkin, sweet potatoes, mango, peaches, and apricots, also plays a key role in photoprotection[19].

Essential vitamins include Vitamin C, present in citrus fruits, strawberries, broccoli, peppers, and leafy greens, and Vitamin D, found in milk, cheese, and orange juice. Additionally, Vitamin E, contained in almonds, peanuts, spinach, chard, sunflower seeds, and soybean oil, offers significant photoprotective benefits[20,21].

Vitamin C, a powerful antioxidant, reduces lipid peroxidation, limits oxidative damage, inhibits NF-κB activation, and stimulates collagen production.

Table 1. Overview of filters and photoprotection strategies. A detailed synthesis of the main filters and photoprotection strategies categorized into topical, systemic, and adjunctive approaches, highlights each method's features, advantages, disadvantages, and corresponding action spectrum for targeted photoprotection.

A. Topical Photoprotection

Filter Type	Examples	Features	Advantages	Disadvantages	Action Spectrum
Chemical Filters	*Avobenzone*, *Oxybenzone*, *Octocrylene*, *Ecamsule*	Absorb UV radiation	Broad-spectrum protection (UVB and UVA); effective in advanced formulations	Potential for skin irritation; environmental impact	UVB and UVA
	New Filters: *TriAsorB*	Hydrophilic and deeply penetrating; absorbs UVB, UVA (short and long), and HEVR (blue light)	Reduces oxidative DNA damage; prevents cyclobutane pyrimidine dimer (CPD) formation	Limited availability; potentially high cost	UVB, UVA, and HEVR
Physical Filters	*Zinc Oxide*, *Titanium Dioxide*	Reflect and scatter UV rays	Safe for children and sensitive skin; low environmental impact	May leave a white cast on skin	UVB, UVA, Visible Light
Natural Filters	*Polyphenols (Resveratrol, Silymarin)*	Extracted from plants with antioxidant and photoprotective properties	Reduces free radicals; protects against photoaging; anti-inflammatory and cellular repair properties	Efficacy depends on concentration; needs combination with other agents for optimal protection	UVA, UVB, free radical protection

Abbreviations: UVB: Ultraviolet B radiation; UVA: Ultraviolet A radiation; HEVR: High-Energy Visible Radiation (includes blue light up to 450 nm); CPD: Cyclobutane Pyrimidine Dimers (DNA lesions induced by UV exposure); SCC: Squamous Cell Carcinoma; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs.

B. Systemic Photoprotection

Filter Type	Examples	Features	Advantages	Disadvantages	Action Spectrum
Systemic Antioxidants	*Nicotinamide (Vitamin B3)*	Enhances DNA repair processes; prevents actinic damage caused by UV exposure	Reduces actinic keratoses and non-melanoma skin cancer incidence	Requires consistent, specific dosing; incomplete without topical filters	Protection against DNA damage and UV-induced cancers
Systemic Retinoids	*Isotretinoin*, *Acitretin*	Vitamin A derivatives that regulate cell proliferation and apoptosis	Reduces SCC incidence; useful for immunocompromised patients	Side effects (skin dryness, photosensitivity); limited to high-risk individuals	Protection from UV-induced cellular damage and cancers
Plant-Based Antioxidants	*Polypodium Leucotomos*	Extracted from a tropical fern with antioxidant properties	Reduces oxidative stress; stimulates collagen synthesis; protects extracellular matrix integrity	Effectiveness depends on regular intake and correct dosages	UV-induced oxidative damage protection

C. Adjunctive Strategies

Filter Type	Examples	Features	Advantages	Disadvantages	Action Spectrum
NSAIDs	*Indomethacin, Celecoxib*	Inhibit cyclooxygenases (COX), reducing prostaglandin production associated with cellular damage	Reduces SCC relative risk. potentially protective against melanoma and actinic keratoses	Not justified as a standalone photoprotective measure;risk of gastrointestinal side effects	Limits UV-induced keratinocyte growth, anti-tumor effects

A study[21] showed that daily oral supplementation of 100 mg and 180 mg of Vitamin C reduces reactive oxygen species (ROS) production by 22% and 37%, respectively. Its effectiveness is enhanced when combined with Vitamin E, synergistically protecting the DNA from UV-B-induced damage[21]. Topical Vitamin C has also been shown to combat photoaging by inhibiting metalloproteinases, increasing collagen synthesis, and protecting against erythema and hyperpigmentation[22]. Sunscreens enriched with Vitamins C and E demonstrate superior efficacy against UV-induced oxidative stress, immunosuppression, and pigmentation compared to UV filters alone[22].

Omega-3 fatty acids, found in fatty fish such as mackerel, sardines, herring, and salmon, are crucial for maintaining the membrane lipid structure[19]. Lycopene, an antioxidant found in red and pink foods like tomatoes, watermelon, guava, and pink grapefruit, also offers significant protection against UV damage[19]. Zinc, another essential mineral for photoprotection, is found in red meat, shellfish, poultry, nuts, and legumes like chickpeas and baked beans[19,20].

How climate change can affect the occurrence of NMSCs

An emerging but extremely interesting topic concerns the interconnection between the increase in Basal Cell and Squamous Cell Carcinomas and the climate change that we have been facing in recent years.

We know that the amount of UV rays that reach the earth is influenced by several factors, such as time of day, latitude, season, and altitude. Other contributing factors include the ozone layer, relative humidity, and cloud cover. The latter are factors influenced by climate change. The harmful effect of UV rays is also enhanced by the increase in global temperature.

A landmark in understanding the relationship between climate change and the incidence of Non-Melanoma Skin Cancer (NMSC) is the article by Monfrecola et al.[23], one of the first to offer a pioneering and integrated perspective on how environmental and climatic factors interact to determine the prevalence of skin cancer. This study provides an essential foundation for the development of future prevention and mitigation strategies[23].

The research thoroughly examines the role of environmental factors in the global increase of these cancers, with particular emphasis on the effects of ozone depletion, ultraviolet (UV) radiation, and rising temperatures. Ozone layer depletion is identified as a key factor in the escalation of UVB radiation reaching the Earth's surface[23]. The authors estimate that a 10% reduction in stratospheric ozone could lead to a 30% increase in the incidence of BCCs and a 50% rise SCCs, highlighting the critical need to monitor and mitigate UV-related damage[23].

Climate change also plays a significant role through global temperature increases, which influence human behaviour and time spent outdoors, thereby exposing individuals to higher levels of UV radiation. Behavioral studies cited in the article[23] indicate that elevated temperatures promote increased outdoor activity, thereby raising the risk of sunburn - a well - established precursor to skin cancer. This effect is particularly pronounced in regions near the equator, where both UV irradiance and temperatures are naturally higher.

Another critical aspect analysed is the role of atmospheric pollutants, such as black carbon, which under certain conditions can mitigate UV exposure by

reflecting or dispersing solar radiation. However, this attenuation is counterbalanced by the synergistic effects of certain pollutants, such as benzo[a]pyrene, which, when combined with UVA radiation, exacerbates the risk of skin cancer by generating a reactive oxygen species[23].

Finally, the authors reflect on the potential impact of global warming in amplifying the carcinogenic effects of UV radiation. A 2°C increase in average temperatures could enhance the carcinogenic potential of UV radiation by approximately 10%. This phenomenon, coupled with climate-induced behavioural changes, suggests that climate change could significantly exacerbate the global burden of skin cancer[23].

A recent study assessed the close relationship between increased UV rays and skin carcinogenesis based on climate change from the year 2000 to 2100. According to the reported data, it is estimated that the incidence of non-melanoma skin cancers could increase by another 21.4% by 2100[24]. This study describes a worrying future scenario underlining how much climate change is a serious threat to our health and how it is essential to intervene as soon as possible to mitigate its negative effects and avoid future repercussions.

It is imperative to underscore the necessity of further epidemiological research to establish a clearer and more definitive causal link between climate change and cutaneous carcinogenesis[25]. Leveraging advanced climate modelling in conjunction with robust epidemiological data and integrating environmental and behavioural factors is pivotal to accurately assess the risk of skin cancer within specific populations. An interdisciplinary collaboration among climatologists, epidemiologists, and healthcare professionals would yield critical insights and practical tools, empowering international policymakers to implement comprehensive and effective preventive strategies.

Conclusions

Photo protection tips: What is true and what is false?

To enhance daily photoprotection and prevent skin damage, it is essential to adopt practical strategies. Avoid sun exposure during peak UV radiation hours (10 a.m.–5 p.m.) and prioritize early morning or late afternoon exposure. Seek shade whenever possible and wear protective items such as hats, sunglasses, and UV-specific clothing, especially during prolonged outdoor activities. Apply chemical and physical sunscreens correctly, ensuring an even coverage, and reapply every three hours or more frequently if swimming or sweating. Consider taking supplements to protect against UV-induced damage and avoid sun exposure if using photosensitizing medications or cosmetics. Minimal sun exposure from daily activities, such as walking outdoors or waiting for a train, is sufficient to meet Vitamin D requirements, even under low UV levels. Clinical studies confirm that sunscreen use, including high-SPF formulations, does not cause Vitamin D deficiency, but helps maintain adequate levels while reducing the risk of skin cancer[26].

Glass windows, while effective at blocking UVB rays, allow UVA rays to penetrate, particularly through non-tinted side windows and sunroofs, which can let up to 50% of UVA rays pass through, contributing to photoaging and skin damage. To mitigate this, it is recommended to use sunscreen while driving and keep windows closed[27].

By combining external measures - such as sunscreens, protective clothing, and avoiding peak sun hours - with internal strategies like supplementation and careful medication management, it is possible to protect the skin while making sun exposure a source of both physical and psychological well-being.

Conflict of Interest Statement: The authors declare no conflict of interest.

References

1. Gholizadeh N, Rokni GR, Zaresharifi S, Gheisari M, Tabari MAK, Zoghi G. Revolutioning non-melanoma skin cancer treatment: Receptor Tyrosin kinase inhibitors take the stage. J Cosmet Dermatol. 2024; 23(9):2793-2806.
2. Eisen DB, Asgari MM, Bennett DD, et al. Guidelines of care for the menagement of actinic keratosis. J Am Acad Dermatol. 2021; 85(4):e209-e233.
3. Ouyang YH. Skin cancer of the head and neck. Semin Plast Surg. 2010; 24(2):117-126.

4. Reinehr CPH, Bakos RM. Actinic keratoses: review of clinical, dermoscopic, and therapeutic aspects. An Bras Dermatol. 2019; 94(6):637-657.
5. Zalaudek I, Giacomel J, Schmid K, et al. Dermatoscopy of facial actinic keratosis, intraepidermal carcinoma, and invasive squamous cell carcinoma: a progression model. J Am Acad Dermatol. 2012; 66(4):589-597.
6. US Preventive Services Task Force; Mangione CM, Barry MJ, Nicholson WK, et al. Screening for Skin Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2023; 329(15):1290-1295.
7. Wysong A. Squamous –cell carcinoma of the skin. N Eng J Med. 2023; 388(24):2262-2273.
8. Sander Megan, Sander Micheal, Burbidge T, Beecker J. The efficacy and safety of sunscreen use for the prevention of skin cancer. CMAJ. 2020; 192(50):E1802-E1808.
9. Aguilera J, Gracia-Cazaña T, Gilaberte Y. New development in sunscreens. Photochem Photobiol Sci. 2023; 22(10):2473-2482.
10. Bacqueville D, Jacques-Jamin C, Dromigny H, et al. Phenylene Bis-Diphenyltriazine (TriAsorb), a new sunfilter protecting the skin against both UVB+UVA and blu radiations. Photochem Photobiol Sci. 2021; 20(11):1475-1486.
11. Cui B, Wang Y, Jin J, et al. Resveratrol Treats UVB-Induced Photoaging by AntiMMP Expression, through Anti-Inflammatory, Antioxidant, and Antiapoptotic Properties, and Treats Photoaging by Upregulating VEGF-B Expression. Oxid Med Cell Longev. 2022; 2022:6037303.
12. Park J, Halliday GM, Surjana D, Damian DL. Nicotinamide prevents ultaviolet radiation induced cellular energy loss. Photochem Photobiol. 2010; 86(4):942-948.
13. Stratigos AJ, Garbe C, Dessinioti C, et al. European consensus-based interdisciplinary guideline for invasive cutaneous squamous cell carcinoma. Part 1: Diagnostics and prevention-Update 2023. Eur J Cancer. 2023; 193: 113251.
14. Ramchatesingh B, Martínez Villarreal A, Arcuri D, et al. The Use of Retinoids for the Prevention and Treatment of Skin Cancers: An Updated Review. Int J Mol Sci. 2022; 23(20):12622.
15. Johannesdottir SA, Chang ET, Mehnert F, Schmidt M, Olesen AB, Sørensen HT. Nonsteroidal anti-inflammatory drugs and the risk of skin cancer. Cancer. 2012; 118(19): 4768-4776.
16. Nestor MS, Berman B, Swenson N. Safety and Efficacy of Oral Polypodium Leucotomos Extract in Healty Adult Subjects J Clin Aesthet Dermatol. 2015; 8(2): 19-23.
17. Pellacani G, Peris K, Ciardo S, et al. The combination of oral and topical photoprotection with a standardized Polypodium Leucotomos extract is beneficial against actinic keratosis. Photodermatol Photoimmunol Photomed. 2023; 39(4):384-391.
18. Cheng L, Liu J, Wang Q, Hu H, Zhou L. The Protective Effect of a Human Umbilical Cord Mesenchymal Stem Cell Supernatant on UVB-Induced Skin Photodamage. Cells. 2024; 13(2):156.
19. Katta R, Brown DN. Diet and Skin Cancer: The Potential Role of Dietary Antioxidants in Nonmelanoma Skin Cancer Prevention. J Skin Cancer. 2015: 2015:893149.
20. Evans JA, Johnson EJ. The Role of Phytonutrients in Skin Health. Nutrients. 2010; 2(8):903-928.
21. Lauer AC, Groth N, Haag SF, Darvin ME, Lademann J, Meinke MC. Dose dependent Vitamin C uptake an radical Scavenging Activity in human skin measured with in vivo electron paramagnetic resonance spectroscopy. Skin Pharmacol Physiol. 2013; 26(3):147-154.
22. Nusgens BV, Humbert P, Rougieret A, et al. Topically applied vitamin C enhances the mRna level of Collagenes I and III, their processing enzymes and tissue inhibitor of matrix metalloproteinase 1 in the human dermis. J Invest Dermatol. 2001; 116(6):853-859.
23. Fabbrocini G, Triassi M, Mauriello MC, et al. Epidemiology of skin cancer: role of some environmental factors Cancers (Basel) 2010; 2(4):1980-9.
24. Rubén D Piacentini, Lara Sofía Della Ceca, Adriana Ipiña. Climate change and its relationship with nonmelanoma skin cancers. Photochem Photobiol Sci. 2018; 17(12):1913-1917.

25. Eva Rawlings Parker [1] The influence of climate change on skin cancer incidence – A review of the evidence. Int J Womens Dermatol. 2020; 7(1):17–27.
26. Jonathan R Raymond-Lezman, Suzanne I Riskin. Benefits and Risks of Sun Exposure to Mantain Adequate Vitamin D levels. Cureus. 2023; 15(5):e38578.
27. De La Garza H, Maymone MBC, Vashi NA. Impact of Social Media on Skin Cancer Prevention. Int J Environ Res Public Health. 2021; 18(9):5002.

Correspondence:
Received: 6 August 2024
Accepted: 25 February 2025
Antonella Tammaro, MD, University Magna Grecia, Catanzaro, Italy
E-mail: tammaroantonella@gmail.com