Sunscreens: Is Looking at Sun Protection Factor Enough?

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ABSTRACT

As mounting evidence points to the photocarcinogenicity and the photoaging potential of chronic ultraviolet A (UVA) exposure, broad-spectrum sunscreens that are effective against both ultraviolet B (UVB) and UVA radiation are obviously preferred. Older chemical filters are not effective against the longer UVA. Several chemical filters have been developed recently to provide invisible protection for the UVA spectrum. The sun protection factor (SPF) can only indicate the level of protection against UVB, but not UVA. There is not yet any widely accepted method to measure UVA protection.

Keywords: *Review, sunscreen, ultraviolet A*

INTRODUCTION

The sun protection factor (SPF) has widely been used to evaluate the protective value of sunscreens. However, SPF only reflects the effectiveness of the sunscreen to protect against acute sunburn which is mainly due to ultraviolet B (UVB) radiation. The deleterious effects of UVB are well known and UVB was believed in the past to be the spectrum responsible for the damages arising from ultraviolet radiation (UVR). However, there has been increasing evidence pointing to the photocarcinogenicity and the photoaging potential of ultraviolet A (UVA) radiation even at suberythemogenic doses. Therefore, broad-spectrum solar protection covering both the UVA and the UVB range is desirable, and choosing sunscreen products simply basing on the SPF value will not be adequate.

Ultraviolet filters developed in the past are mainly effective across the UVB wavelengths, though some extend into the short UVA spectrum. These offer little protection against the longer UVA radiation. Previously, broad-spectrum coverage could only be achieved by opaque sunscreens that are often cosmetically unacceptable. However, several organic UVA filters have been developed recently which aim to provide invisible protection against the whole UVA spectrum.

This review will examine the evidence for the harmful potential of UVA, discuss the safety issues concerning sunscreen use and the problems with UVA protection indicators, look at the UVA protective agents available commercially and advise on the choice and the use of sunscreen products.

ULTRAVIOLET RADIATION

Ultraviolet radiation (UVR) is defined as those electromagnetic radiation with wavelengths between 100 and 400 nm, and is divided into UVA (320-400 nm), UVB (290-320 nm) and UVC (100-290 nm). UVA can be further divided into UVA I (340-400 nm) and UVA II (320-340 nm). Solar UVR at the earth's surface comprises approximately 95-98% UVA and 2-5% UVB, all the UVC having been absorbed by stratospheric ozone.

Exposure to UVR has pronounced acute and chronic effects on the skin. The UVR-induced skin effects manifest as acute responses such as inflammation (sunburn or erythema), pigmentation, hyperplasia, immunosuppression, vitamin D synthesis, and chronic effects such as photocarinogenesis and photoaging. These acute and chronic effects are dependent of the spectrum, intensity and cumulative dose of UVR. The

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complete action spectrum for the majority of UVR-induced effects has not yet been completely defined in human skin. In addition, these responses have different thresholds such that the prevention of UVR-induced changes for an endpoint does not guarantee a similar level of protection for any other.

Effects of ultraviolet A radiation

Inflammation

Erythemal effectiveness declines rapidly with increasing wavelength, such that approximately 1000 times more UVA energy than UVB is required to produce the same erythema response.[1] However, due to its preponderance in terrestrial sunlight, UVA nonetheless contributes significantly to sunburn erythema.

Pigmentation

Ultraviolet A radiation causes immediate transient tanning which is believed to be due to the photo-oxidation of a precursor of melanin. The action spectrum is broad, extending from 320-400 nm, with a peak at around 340 nm. The physiologic significance of this immediate tanning response in humans is not known, as unlike neomelanogenisis, it does not confer photoprotective properties.[2] Delayed tanning, which is more persistent, is a result of increased formation of epidermal melanin. This is induced by UVB and the shorter UVA wavelengths.[1]

Photoageing

Ultraviolet A radiation, due to the longer wavelengths, can penetrate into and cause damage in the dermis. All UVA bands have been shown to be equally effective in inducing inflammatory changes in the dermis which can lead to connective tissue damage, whereas UVA II is more effective at inducing epidermal changes.[3] Although acute exposure to UVA may not lead to any detectable changes, repeated exposure to UVA, even at suberythemogenic doses, has been shown to have a cumulative effect in human skin causing significant photodamage and immunosuppression.[4]

Immunosuppression and carcinogenesis

In the past, it was thought that the cancer risk posed by UVA is negligible, as unlike UVB, it does not cause sunburn. Although we cannot subject humans for prospective studies to document the carcinogenicity of UVA using tumour occurrence as the study endpoint, there is now increasing evidence to suggest the pathogenic role of UVA in cutaneous malignancies.

It has been shown that UVA can have an immunosuppressive effect on the human skin.[4] UVR-induced immunosuppression is important as it occurs not only with environmental antigens but also with tumour antigens. It can be directly demonstrated in animals that UVA, including those with wavelengths >340 nm, induce skin tumours.[5] In human skin, UVA has been demonstrated to cause DNA breaks and accumulation of p53 protein in melanocytes.[6]

The epidemiological evidence for the photo-carcinogenicity of UVA is strong. Among individuals with long-term exposure to UVA tanning beds or psoralen plus UVA therapy (PUVA), increased incidence is observed for non-melanoma skin cancer.[7,8] However, the association is less consistent for melanoma.[8-10]

Protection by sunscreens

It has been shown that photodamage due to UVA can be reduced or abolished by broad-spectrum sunscreens or the UVA filters but not by sunscreens with attenuation spectrum mainly in the UVB range.[4,11]

Concerning protection against cutaneous malignancies, these endpoints are difficult to evaluate in humans for ethical reasons. However, it has been reported in humans that the use of a broad-spectrum sunscreen can effectively prevent and even reduce solar keratosis, and so by implication, possibly reduces the risk of skin cancer in the long term.[12] *In vivo* studies support that broad-spectrum sunscreens, compared with UVB filters, provide better protection against UV-induced cutaneous malignancies. Broad-spectrum sunscreens are more effective in the reduction of immunosuppression and skin tumours in mice,[13,14] and DNA breaks in human melanocytes.[6]

SAFETY OF SUNSCREENS

Acute adverse reactions

Acute adverse reactions to sunscreens are quite frequent and all sunscreen agents have been reported to cause contact or photocontact allergic reactions. However, most inflammatory reactions occurring after sunscreen application are irritant in nature, which can

be due to the active sunscreen agents or the base cream. For the small proportion of cases which are allergic in nature, as demonstrated by patch testing, photopatch testing or scratch testing, the offending agent is more often an ingredient in the base cream rather than an active sunscreen agent.[15]

Carcinogenicity and the melanoma-sunscreen controversy

Some *in vitro* studies have suggested that certain sunscreen agents could have a carcinogenic effect after UV irradiation. However, these findings have not been confirmed by *in vivo* studies using animals and humans. The results of the *in vivo* studies overwhelmingly demonstrated that sunscreen agents protect, instead of promote, skin cancers due to acute and chronic UVR exposure.

Despite laboratory evidence that sunscreens can reduce or prevent UV-induced malignancies, there are epidemiological studies which suggest that sunscreen use is associated with an increase in the frequency of malignant melanoma.[16] Other epidemiological studies either observed no association between sunscreen use and melanoma,[17] or demonstrated a protective effect by sunscreens.[18] A recent meta-analysis also found no significant association between melanoma and sunscreen use.[19] For the apparent increase in the incidence of melanoma in sunscreen users, the most widely accepted explanation is that sunscreens, by preventing sunburn, allow individuals to stay longer in the sun, which results in increased exposure to UVR. This is especially significant if sunscreens of low SPF or with inadequate protection against UVA are used.

Vitamin D deficiency

It has been raised that the chronic use of sunscreen could lead to vitamin D deficiency. This concern has not been substantiated by a larger study with the finding of normal vitamin D levels among all the adult subjects who used sunscreen regularly.[20]

THE IDEAL SUNSCREEN

The ideal sunscreen should provide good protection throughout the whole UV spectrum, even after sunlight exposure (photostable), and remain in place after perspiration or swimming. In addition, it should be non-toxic and does not cause irritation or contact allergy, and from this point of view, there is usually a maximum concentration recommended for each filter. The concentration is important because it determines the degree of protection of the final sunscreen product, and increasing this protection can be achieved by increasing the concentration of the filter (up to a certain point) or by combining different filters in the same product.

Protection against UVB

The sun protection factor

The sun protection factor (SPF) was first designed to indicate the level of protection offered by a sunscreen product against acute sunburn. According to the Food and Drug Administration of the United States, the SPF of a sunscreen product is calculated as the ratio of the minimal erythema dose (MED) of sunscreen-protected skin to the MED of unprotected skin. The light source used for SPF testing should provide a continuous emission spectrum from 290 to 400 nm similar to sunlight at sea level from the sun at a zenith angle of 10 degrees. The test sunscreen is applied at a thickness of 2 mg/cm^2, and the MED is defined as the energy required to produce the first perceptible redness reaction with clearly defined borders, evaluated at 22-24 hours after exposure.[21]

As UVB is 1000 times more erythemogenic than UVA, SPF reflects mainly the acute protection against UVB but it gives no indication of a product's protection against UVA. Products with the same SPF may have quite different absorption spectral profiles, and sunscreens with high SPF do not guarantee protection against UVA.[13,22,23]

Protection against UVA

There are many problems associated with the development of an indicator for UVA protection. Even the FDA still cannot issue guidelines in this area.[21] The ideal test for UVA photoprotection should use, as an endpoint, some biological event known to be mediated by these wavelengths. However, to date, an endpoint for use as a representative surrogate for UVA events has not yet been agreed on. Some of the methods used to assess UVA protection are discussed below.

Minimal erythema dose (MED)

As UVA is only mildly erythemogenic, using minimal erythema as an endpoint is often impractical as the time it takes to produce erythema by UVA at intensities similar to natural exposure is impossibly long. To determine the UVA protection factor of sunscreens, some studies use exaggerated intensities of UVA, with irradiance value of up to 100 mW/cm; others use 8-methoxypsoralen plus UVA irradiation (PUVA) which requires much less irradiation energy to produce discernable erythema. Protection factors obtained from the PUVA method are always higher than that from UVA irradiation. This is because 8-MOP-induced phototoxicity is maximal between 320-340 nm, and it is easy for sunscreens to filter out UVA of such wavelengths, but not UVA of longer wavelengths which is generated by the full-spectrum solar simulators. Exaggerated protection factors can be obtained when the absorption spectrum of the sunscreen coincides with the action spectrum of the sensitizer.

Immediate pigment darkening (IPD)

Immediate pigment darkening (IPD) is an endpoint often used in the assessment of UVA protection.[2] IPD refers to the transient brownish-grey discolouration that develops immediately following exposure to UVR and is predominantly caused by UVA wavelengths. This pigmentary response is believed to arise from photo-oxidation of a melanin precursor. This is a short-lived response in contrast to delayed UV-induced pigmentation, which results from the *de novo* synthesis of melanin pigment due UVB irradiation. One important practical problem of using the IPD method is that IPD response fades very quickly, which makes accurate reading of results difficult.[24]

Persistent pigment darkening (PPD)

Persistent pigment darkening (PPD) refers to the stabilized brownish-grey skin discolouration that follows IPD response read at two to four hours after exposure to UVA radiation. The response is thought to be caused by pigment produced in the basal keratinocytes as a photochemical conversion of pre-existing melanin/precursors and/or *de novo* migration of melanosomes. Good consistency of the PPD method with *in vitro* testing using physical filters points to the validity of using PPD as an endogenous dosimeter for UVA radiation. The PPD method has several advantages over using IPD as the endpoint. Pigmentation is stable and persistent for the PPD response, which allows easier observation. As the PPD response requires UVA doses of greater than 10 J/cm^2, the stability of sunscreens is also challenged during a PPD test procedure. Reciprocity can be demonstrated for PPD but not for IPD.[25]

The Protection Grade of UVA (PA) system is based on the PPD reaction and is now widely adopted on the labels of sunscreens. According to the Japan Cosmetic Industry Association PA+ corresponds to a UVA protection factor between two and four, PA++ between four and eight, and PA+++ more than eight.[24]

Critical wavelength

Apart from using certain biological endpoints to determine the UVA protection of sunscreen products, some authors advocated in vitro tests basing on spectophotometric measurements. The critical wavelength (CW) method has been proposed. The transmission through a substrate, both with and without the sunscreen, is measured on a wavelength-by-wavelength basis and the attenuation spectrum of the sunscreen is then determined. The critical wavelength is the wavelength at which 90% of the total area under the attenuation spectrum from 290 to 400 nm is obtained.[22]

Sunscreen agents effective against UVA

Apart from opaque sunblocks, the older sunscreen agents provide limited protection against UVA. The benzophenones provide only partial protection in the UVA range, covering the shorter UVA. Several chemical sunscreens have been developed recently which offer better protection against longer UVA.

Titanium dioxide and zinc oxide

These physical agents provide broad-spectrum protection but are not popular because of their opacity. By decreasing the size of the particles, they can be made to appear less obvious, though when applied at the recommended thickness of 2 mg/cm^2, micronized titanium dioxide can still appear white on the skin. The smaller particle size of the micronized titanium dioxide particle, although improves the cosmetic appearance, shifts the attenuation spectra towards the UVB end and significantly reduces its ability to protect against the longer UVA I radiation.

Compared with micronized titanium dioxide, micronized zinc oxide provides better protection against the longer UVA wavelengths.[26] Micronized zinc oxide,

however, is rarely found as an ingredient in the sunscreens commonly available in Hong Kong.

Butyl methoxydibenzoylmethane (=avobenzone= Parsol 1789)

This chemical sunscreen protects mainly against long UVA, with an absorption peak at 360 nm.[27] It is always combined with UVB filters as it provides little protection against UVB. It is now the most popular UVA filter. The major concern of this chemical is photolability. Fifteen minutes of solar simulated irradiation has been reported to destroy 36% of butyl methoxydibenzoylmethane.[26] The UV absorber, octocrylene, when used together with butyl methoxydibenzoylmethane, can significantly increase the protection in the UVA range, due to its ability to photostabilize the latter.[23]

Terephthalylidene dicamphor sulfonic acid (=Mexoryl SX)

Terephthalylidene dicamphor sulfonic acid is photostable and has an absorption spectrum of 290 to 400 nm and an absorption peak at 345 nm.[14] This compound is developed and patented by the L'Oréal Group, and is only found in the products manufactured by this group under different brand names (L'Oréal Paris, Lancôme Paris, Biotherm).

Drometrizole trisiloxane (=Mexoryl XL)

This compound is also patented by the L'Oréal Group. Drometrizole trisiloxane has two maximum absorption: 303 nm and 344 nm thus this filter is effective both in the UVB and the UVA range.

CHOOSING AND USING SUNSCREENS

The SPF value: is SPF 15 adequate?

Health professionals often recommend sunscreens with SPF 15. Theoretically, products with SPF 15 already block out more than 90% UVB, therefore sunscreens of higher SPF may confer little additional protection. However, it must be remembered that sunscreen efficacy is dependent on the adequacy of sunscreen application. The stated SPF of a sunscreen is based on the testing of the product when applied at 2 mg/cm^2. It is well known that in practice, the amount applied by individuals using sunscreen is much less, the median thickness has been shown to be around 0.5 to 1 mg/cm^2. With sunscreens applied at 0.5 mg/cm^2, the protection against UV-induced erythema is less than one-fourth of the labelled SPF.[28]

There is no evidence so far to suggest that sunscreen products with higher SPF cause more side effects, when the concentrations of the individual UV filters do not exceed that recommended by FDA. It should be born in mind that a SPF value of 15 only means that a sunscreen product will enable the user to stay 15 times longer in the sun without sunburn, without ensuring protection against other adverse effects due to UVR. It is known that to prevent UVB-induced immuno-suppression, the protection has to be much higher than that needed to prevent UVB-induced erythema.[29]

Using formulations with SPF higher than 15 is probably advisable for those who need better photoprotection. The most recent FDA guideline has set a maximum SPF of 30 on labels of sunscreens. Those with SPF greater than 30 will be labelled as "SPF 30+". There has been a lot of controversy over the setting of a maximum SPF, but FDA maintained its final rule.[21]

Substantivity also affects the efficacy of a sunscreen. The substantivity of the sunscreen reflects the ability of the sunscreen product to remain adherent or absorbed to the skin. According to the new FDA regulations, for products displaying the term "water resistant", the label SPF is the SPF value determined after 40 minutes of water immersion; for "very water resistant" products, the label SPF is the SPF value determined after 80 minutes of water immersion.[21]

Look for UVA protection

Descriptive terms such as "broad-spectrum", "UVB/UVA protection", "ultra/maximum protection" mean little as sunscreens labelled as such often does not contain agents that can effectively protect against UVA. It is important to look for specific UVA protection indicators, such as PA +++, or look for UVA filters in the ingredients. This is not always possible as not all sunscreen products display UVA protection factors or list their active ingredients. Table 1 shows the active sunscreen agents used in some formulations available in the two leading chain drug-stores in Hong Kong (products without labelling of ingredients are not reviewed). Sunscreen products by the L'Oréal Group are also included in the table, as these are the only ones the author could find among cosmetic products in Hong Kong that listed specific UVA filters. Table 2 shows the

Table 1. Active sunscreen compounds present in the more commonly available products in Hong Kong

	SPF / PA	Price*	2-ethylhexyl p-methoxycinnamate (Octyl methoxycinnamate)	Isoamyl methoxycinnamate	Benzophenone-3 (Oxybenzone)	Benzophenone-4 (Sulisobenzone)	Homosalate	2-ethylhexyl salicylate (Octyl salicylate)	Titanium dioxide	Micronised titanium dioxide	Zinc oxide	Octocrylene	Drometrizole trisiloxane (Mexoryl XL)	4-methylbenzylidene camphor	Phenylbenzimidazole sulfonic acid	Terephthalylidene dicamphor sulfonic acid (Mexoryl SX)	Butyl methoxydivenzoylmethane (avobenzone / Parsol 1789)
Banana Boat Baby Block	50	$$	+		+			+	+								
Banana Boat Faces Plus Sunblock	23&31	$$	+		+			+									
Banana Boat Maximum Sunblock	50	$$	+		+			+				+					
Banana Boat Sport Sunblock Lotion	15	$	+		+			+									
Banana Boat Ultra Sunblock	30+	$$	+		+			+									
Biotherm High Protection Sun Block#	30+	$$$$$							+					+		+	+
Biotherm High Protection Sun Block# Lotion	25	$$$							+					+		+	+
Coppertone Kids Sunblock Lotion	40	$$	+		+		+	+									
Coppertone Oil-free Sunblock Lotion	15	$$	+		+												
Coppertone Oil-free Sunblock Lotion	30	$$	+		+		+	+									
Coppertone Sport Ultra Sweatproof Dry Lotion	15	$$	+		+			+									
Coppertone Sunblock Lotion	15	$$	+		+												
Coppertone Sunscreen Lotion#	45	$$			+		+	+				+					+
Coppertone Water Babies Sunblock Lotion	45	$$	+		+		+	+									
Ego Sunsense Daily Face	30+	$$$	6%							3%				2%			
Ego Sunsense for Dry Skin	30+	$$	7.5%		3%					3%							
Ego Sunsense Face Milk	30+	$$$	6%		2%					3%							
Ego Sunsense Low Irritant	20	$								8%							
Ego Sunsense Sport	30+	$$	7.5%		3%					2.6%				2.5%			
Ego Sunsense Toddler Milk	30	$$$	3.5%	3.5%	1.5%					3.2%							
Ego Sunsense Ultra	30+	$$	7.5%		3%					2.8%							

Table 1. Active sunscreen compounds present in the more commonly available products in Hong Kong (Cont'd)

Lancôme UV Expert Double Daily Protection Fluid#	20/+++	$$$$$$										+				+	+
Lancôme UV Expert Extra Large Double Protection#	50/+++	$$$$$$	+		+				+				+		+	+	
L'Oréal Plénitude UV Perfect Double Protection Screen #	40/+++	$$$$$	7.4%		2%				2.4%							3.9%	
L'Oréal Plénitude White Perfect Multi-action Whitening Moisturizer# (Cream)	15	$$$$										7%			2%	0.7%	
L'Oréal Plénitude White Perfect Multi-action Whitening Moisturizer# (Lotion)	15	$$$										7%			1.7%	0.7%	
Neutrogena Intensified Day Moisture (Cream)	15	$$$$	7.5%												1.0%		
Neutrogena Fine Fairness Hands	15	$$$	7.5%		5.0%												
Neutrogena Fine Fairness UV Block	30	$$$	3%						4%								
Neutrogena Moisture (Lotion)	15	$$	+												+		
Neutrogena Sensitive Skin UVA/UVB Block	17	$$							4%								
Neutrogena UVA/UVB Sunblock#	30	$$	7.5%		3.3%		6.5%	5.0%									2.0%
Nivea Visage Natural Day Moisturizer	15	$$	+		+				+								
Nivea Visage Natural Tinted Moisturizer#	20	$$$$	+						+						+		+
Oil of Olay White Radiance UV Natural Lightening Lotion/Cream	15	$$	6%						+		+						
Oil of Olay UV Natural Lightening Cream	15	$$$	6%						+		+						
Palmer's Skin Success Anti-darkening Cream	30	$$$$$	+		+			+				+					
Sebamed Sun Protection Face Cream#	20	$$$$	+			+								+			+
Sebamed Sun Protection Face Cream#	28	$$$$	+			+			+								+
Sebamed Sun Protection Lotion#	20	$$	+			+								+			+
St. Ives Hand Renewal	15	$	7.5%		4.5%												
Super-C UV Lightening Lotion/Cream	15	$$$	+					+	+								
Watson's Hand & Body Lotion	15	$							+								

* Hong Kong dollars per millilitre or milligram: $: <0.5; $$: 0.5-0.99; $$$: 1-1.49; $$$$: 1.5-1.99; $$$$$: 2 -4.99; $$$$$$: ≥5

Sunscreen products containing organic UVA filters

Table 2. The absorption spectra of some commonly used active sunscreen agents[14,26,27]

Name of compound	Absorption spectrum, nm
2-ethylhexyl salicylate	280-320
2-ethylhexyl p-methoxycinnamate	280-320
Benzophenone-3	270-360
Benzophenone-4	260-360
Butyl methoxydibenzoylmethane	320-400
Homosalate	290-320
Micronised titanium dioxide	290-340
Octocrylene	290-360
Phenylbenzimidazole sulfonic acid	290-320
Terephthalylidene dicamphor sulfonic acid	290-400
Titanium dioxide	250-380

absorption spectra of the more commonly used sunscreen agents.

Proper use of sunscreens

Proper application of sunscreen is necessary to obtain the expected protection. A complete coverage of even and adequate thickness is essential. To achieve the standard thickness of 2 mg/cm^2 or 2 ml/cm^2, about 1.6 ml (around half-teaspoon) is required to cover the whole face and 35 ml for a single whole-body application. The product should be applied 15 minutes before going into the sun. Frequent reapplication – every one to two hours is advisable as sunscreen products are frequently removed by the constant touching, rubbing, sweating or swimming. To minimize photoaging and the risk of UVR-related malignancies, daily use of a broad-spectrum sunscreen is preferred, as suberythemogenic doses of UVR has been shown to cause cumulative photodamage and immunosuppression. Individuals with photosensitive dermatoses will also benefit from broad-spectrum coverage.

Sun avoidance

Even when using high protection factor broad-spectrum sunscreens, individuals should not be complacent and prolong their stay in the sun. Even potent sunscreens cannot prevent all the changes induced by UVR.[30] The energy not filtered out by sunscreens is of unknown significance. Moreover, theoretically, chemical sunscreens can pool beneath the stratum corneum allowing UVR to reach the photoreceptor, urocanic acid, at the stratum corneum, which initiates UVR-induced events despite sunscreen use. Physical means to reduce UVR exposure, for example avoiding the sun in mid-day, staying in shade and wearing protective clothing, should always be stressed, especially when the intriguing relationship between sunscreen and melanoma awaits further clarification.

CONCLUSION

Increasing evidence points to the deleterious effects of chronic UVA exposure. It is therefore advisable to choose sunscreen products that protect against both UVB and UVA. With the development of new chemical filters, UVA protection can be now achieved without solely relying on physical filters, which are often found to be cosmetically unacceptable. It is not enough to look at the SPF value alone when evaluating sunscreens, as SPF cannot reflect the level of protection against UVA. So far, no side effects have been confirmed to be associated with long-term sunscreen usage. Regular use of high protection factor broad-spectrum sunscreen, and proper application, can probably reduce the chronic effects of sunlight exposure, namely photoaging and photocarcinogenesis, although physical means to reduce UV exposure are still important.

Learning points:

Chronic exposure to UVA can have deleterious effects. The SPF value of sunscreens cannot indicate the level of protection against UVA.

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