

CPD ARTICLE

Sunscreens – what’s important to know

C Antoniou,† MG Kosmadaki,† AJ Stratigos, AD Katsambas*

Department of Dermatology, University of Athens, School of Medicine, Andreas Sygros Hospital, Athens, Greece

Keywords

sunscreens, photoprotection, UVA, UVB

*Corresponding author, Department of Dermatology, University of Athens, Andreas Sygros Hospital, 5 Ionos Dragoumi Street, Athens 16121, Greece, tel. +30 210 3619542; fax: +30 210 3600196; E-mail: katsabas@internet.gr

†These authors contributed equally to the work.

Received: 19 July 2007,
accepted 12 December 2007

DOI: 10.1111/j.1468-3083.2007.02580.x

Corrections added after online publication
on 13 May 2008:
Questionnaire and information on authors.

Introduction

Extraterrestrial sunlight includes X-ray, ionizing, ultraviolet (UV), visible and infrared radiation, and radiowaves. The solar spectrum at the earth’s surface (sea level) consists of wavelengths of electromagnetic energy only between 290 and 3000 nm, whereas the spectrum implicated in human skin reactions involves wavelengths up to 1800 nm. UV radiation is arbitrarily subdivided into three bands: UVA (320–400 nm), UVB (290–320 nm) and UVC (200–290 nm). The total flux of UVA at the earth’s surface vastly exceeds that of UVB, with all the UVC being completely absorbed by stratospheric ozone. Depending on the latitude, the time of the day and the season of the year, the terrestrial spectrum of solar UV radiation consists of 1% to 5% of UVB radiation and 95% to 99% of UVA radiation. UVB radiation is fully absorbed by the stratum corneum and the top layers of the epidermis, whereas up to 50% of incident UVA radiation penetrates Caucasian skin deep into the dermis.¹ There is now a heightened concern regarding the depletion of the stratospheric ozone layer by the chlorofluorocarbons, halons and nitric oxides. This

Abstract

The popularity of sunscreens dramatically increased since ultraviolet irradiation was implicated in the pathogenesis of skin cancer and skin ageing. The absorption properties, safety, photostability of different organic and inorganic filters are reviewed: *para*-aminobenzoic acid, salicylates, cinnamates, benzophenones, butylmethoxydibenzoylmethane (Parsol 1789), drometrizole trisulphonic (Mexoryl XL), terephthalidene dicamphor sulphonic acid (Mexoryl SX), methylene bisbenzotriazol tetramethylbutylphenol (Tinasorb M), anisotriazine (Tinasorb S), titanium dioxide and zinc oxide. Furthermore, this review discusses the optimal methods for measuring the protection that a sunscreen offers, the role of sunscreen use in melanoma prevention and future trends in sunscreen filters development.

may result in an increased irradiance level of both UVB and UVC at the earth’s level that may eventually contribute to a higher incidence of skin cancer and other harmful effects to humans and to other life forms.

UV irradiation is involved in the pathogenesis of skin cancers and causes premature ageing of the skin and photoimmunosuppression. It also plays a role in the pathogenesis of photosensitive diseases such as chronic actinic dermatitis, polymorphous light eruption, actinic prurigo, hydroa vacciniforme and photoallergic or phototoxic drug reactions. Both UVB and UVA radiation may effect the biomolecules of the skin. Specifically, UVB is directly absorbed by DNA, giving rise to dimeric photoproducts between adjacent pyrimidine bases. Two types of lesions are produced: cyclobutane pyrimidine dimers (CPD) and pyrimidine (6–4) pyrimidone photoproducts.² Both may lead to mutations (if they are not repaired) that seem to have a role in photocarcinogenesis. A high proportion of p53 mutations is detected at bipyrimidine sites in skin tumours. Furthermore, UVB photoisomerizes *trans*- to *cis*-urocanic acid (a prominent candidate chromophore for mediating photoimmunosuppression)³ and generates

reactive oxygen species (ROS),⁴ suggesting that UVB also employs an indirect mechanism for its detrimental effects.

The contribution of UVA on the effects of UV on the skin is also currently recognized. It induces the formation of ROS that react with membrane lipids and amino acids. Membrane damage results in the release of arachidonic acid and leads to activation of secondary cytosolic and nuclear messengers that activate UV-response genes. UVA is further shown to induce photocarcinogenesis in mice.^{5,6} Basal keratinocytes from human skin squamous cell carcinomas contained UVA signature mutations.⁷ Exposure of normal human cultured fibroblasts to UVA induces the same type of DNA mutations (pyrimidine dimers) as UVB.^{8,9} UVA also results in immunosuppression,¹⁰ affecting both the induction (primary sensitization) and elicitation of immune responses,¹¹ and has an important role in photoaging.¹²

The avoidance of unwanted skin effects of the sun, termed photoprotection, has become very popular in recent decades and involved into a public policy concern. The protective measures that can be taken are avoidance of the sun, protection through clothing and the use of sunscreen filters. The latter are shown to have a protective role against photocarcinogenesis,¹³ photoimmunosuppression¹⁴ and photoaging¹⁵ and have become an essential armament for dermatologists in providing protection to human skin against adverse effects of solar radiation.

Sunscreens

Sunscreens have traditionally been divided into organic (chemical) absorbers and inorganic (physical) blockers on the basis of their mechanism of action. The organic compounds absorb high-intensity UV rays with excitation to a higher energy state. Excess energy is dissipated by emission of higher wavelengths or relaxation by photochemical process such as isomerization and heat release. They include *para*-aminobenzoic acid (PABA) and PABA esters, salicylates, cinnamates, benzophenones, butylmethoxydibenzoylmethane (Parsol 1789), drometrisole trisulphonic (Mexoryl XL), terephthalidene dicamphor sulphonic acid (Mexoryl SX), methylene bisbenzotriazol tetramethylbutylphenol (Tinasorb M) and anisotriazine (Tinasorb S). The inorganic agents, which protect the skin by reflecting and scattering UV, are titanium dioxide and zinc oxide.

PABA; (λ maximum, 283 nm) is one of the first widely available organic sunscreen ingredients. It is a very effective UVB filter when used in a 5% concentration in 50% to 60% alcohol base.¹⁶ It penetrates deep into the dermis with high resistance from water and perspiration. Because PABA was shown to be carcinogenic *in vitro*¹⁷ and to cause allergic reactions (contact and photoallergic), its current

Table 1 Popular sunscreen filters and protection against UV

Sunscreen filter	Wavelength protection
PABA	UVB
Octisalate	UVB
Homosalate	UVB
Octinoxate	UVB
Oxybenzophenone	UVB and some UVA
Avobenzene	UVA
Terephthalidene-dicamphor sulfonic acid	UVA and UVB
Drometrisazole trisiloxane	UVA and UVB
Methylene-bis-benzotriazolyl tetramethylbutylphenol	UVA and UVB
Bis-ethylhexyloxyphenol methoxyphenol triazine	UVA and UVB
Titanium dioxide	UVA and UVB
Zinc oxide	UVA and UVB

use in sunscreen formulations is limited. The most commonly used PABA derivate is octyl dimethyl PABA or padimate O (λ maximum, 311 nm). It is effective UVB filter with a good safety profile, although less effective than PABA (Table 1).

Salicylates absorb UV irradiation from 300 to 310 nm and are thus weak UVB filters. However, they are very stable and water insoluble. Skin sensitization and photocontact sensitization reactions to topical application of salicylates are rare. Octisalate (octyl salicylate; λ maximum, 307 nm) and homosalate (homomenthyl salicylate; λ maximum, 306 nm) are commonly used for improved substantivity and reduced photodegradation of other sunscreen ingredients, including oxybenzone and avobenzene.¹⁸ Less than 1% of the applied dose of octyl salicylate penetrates through human skin,¹⁹ and this is similar to dermal penetration of homosalate.

Octinoxate (octyl methoxycinnamate or OMC or Parsol MCX) is the most common cinnamate and probably the most common UV filter used globally (λ max, 311 nm). It is frequently used in combination with other UVB absorbers to achieve high SPF values in the final product. Topical application of OMC is tolerated well: skin irritation is almost negligible, and photocontact dermatitis is rare.²⁰⁻²² Upon exposure to sunlight, octinoxate degrades into a photoproduct with less UV-absorbing ability. Several studies suggest ways to improve the photostability of cinnamate. Encapsulation of ethylhexyl-*p*-methoxycinnamate into nanoparticles consisting of poly-D,L-lactide-coglycolide results in a reduction of the photodegradation of this from 52.3% to 35.3%,²³ and glyceridic esters of octinoxate have a longer photoprotective property *in vivo* compared with the native molecule.²⁴ Systemic absorption of octinoxate has been measured, but it is considered of no toxic concern.²⁵

Benzophenones absorb UVB and some UVA (to approximately 360 nm, with a peak at 290 nm). The most popular benzophenone and one of the most common sunscreen ingredients is benzophenone-3 or oxybenzone. It has been isolated in the blood and urine of humans^{25–27} after topical application. Compared with other UV filters, benzophenone-3 is the most bioavailable following topical application; however, this bioavailability is not of toxicologic concern.^{25,28} Moreover, it has the highest reported incidence of photodermatitis.²⁹

Parsol 1789 or avobenzone or butyl methoxydibenzoylmethane is a very efficient UVA filter because it absorbs across the UVR (290–400 nm). Importantly, however, it is not photostable. Inclusion of other filters that act as stabilizers can reduce its photodegradation. The systemic bioavailability of avobenzone is limited: its dermal penetration is less than or equal to 1% of the applied dose.^{30,31} It can cause photoallergy but apparently less frequently than other UV filters. Diethylamino hydroxybenzoyl hexyl benzoate is a successor of avobenzone that has similar UV-spectral properties but superior photostability.

Terephthalidene-dicamphor sulphonic acid (Mexoryl SX; λ maximum, 345 nm) is a photostable, broad-spectrum sunscreen, effective at absorbing irradiation between 290 and 400 nm. However, most of its UV-absorptive capabilities are within the UVA range. The systemically absorbed dose of Mexoryl SX is less than 0.1% of the applied dose.³²

Drometriazole trisiloxane (silatriazole; Mexoryl XL) is a hydroxybenzotriazole. It is the first photostable broad-UV filter against UVA and UVB. It consists of two chemical groups: 12-hydroxyphenylbenzotriazole, which absorbs both in the UVA and UVB range, and siloxane chain, which is liposoluble. It has two absorption spectra (290–320 nm, λ maximum, 303; and 320–360 nm, λ maximum, 344 nm). Allergic reactions to Mexoryl SX and Mexoryl XL seem to be very rare.³³

Methylene-bis-benzotriazolyl tetramethylbutylphenol (Tinasorb M) absorbs across the UVA spectrum but also has a strong absorption in UVB (λ max, 360 nm and 303 nm). It is the first of a new class of UV filters that combine the properties of both UV conventional filters (organic and inorganic): it scatters, reflects and absorbs UV light. It is manufactured as colourless organic microfine particles, which can be dispersed in the aqueous phase of sunscreen emulsions. It is proven very photostable. Because it is relatively large, its systemic absorption is small. Thus far, there has been one report of contact dermatitis due to Tinasorb M.³⁴

Bis-ethylhexyloxyphenol methoxyphenol triazine (anisotriazine; Tinosorb S) is an oil-soluble broadband absorber that protects against UVB (λ maximum, 310 nm) and UVA (λ maximum, 343 nm). It is photostable and can

increase the photostability of avobenzone and ethylhexyl methoxycinnamate.³⁵

The metal oxides titanium dioxide and zinc oxide are the physical sunscreens. They are very efficient, photostable sunscreens that offer protection extending into the UVA and visible ranges with almost negligible irritation and sensitization potential. However, these big molecules that reflect/scatter UV can cause whitening of the skin. Therefore, the metal oxides are now frequently processed as microfine or nanoparticles (10–50 nm compared with 200–500 nm of the non-micronized form). Nanoparticles reflect/scatter and absorb UV, and they are transparent on the skin, thus enhancing the cosmetic acceptability of the product. However, this happens at the expense of optimal protection in the UVA and visible ranges. Microfine TiO₂ has an absorption profile greater in the UVB but extends in the long UVA. Microfine ZnO has a flat absorption profile that spans UVB and UVA. Concern has been raised regarding possible systemic absorption of the nanoparticles.^{36,37} TiO₂ does not seem to penetrate the epidermis,³⁸ and ZnO has limited systemic absorption, if any.³⁹

New sunscreen technology

Sunscreen efficiency may further augment with the use of modern sunscreen technology. Exploiting microencapsulation active sunscreen ingredients can be entrapped within a silica shell.^{40,41} Using this technique, allergic or irritant reactions may be diminished because the active ingredient is not in direct contact with the skin. Microencapsulation may further solve incompatibility problems between different ingredients. Moreover, polymer materials that do not absorb UV irradiation but enhance the effectiveness of the active ingredients may be used. Specifically, sunspheres are tiny styrene/acrylates copolymers that are filled with water. When the product is applied to the skin, the water comes out of the sphere, leaving microscopic hollow beads. These beads scatter UV irradiation and increase the probability of contact with the active ingredients. They can boost SPF by 50% to 70%, making it possible to reduce the sunscreens active ingredients.

SPF – protection against UVA – immune protection factor

Sunscreens are very effective at preventing erythema, the endpoint used in sun protection factor (SPF) determinations. SPF is defined as the ratio of the dose of UVR (290–400 nm) required to produce 1 minimal erythema dose (MED) on sunscreen-protected skin (after application of 2 mg/cm² of product) over the dose to produce 1 MED on unprotected skin. Importantly, the

absence of erythema does not equal prevention of UV-induced damage.⁴² SPF is primarily a measure of UVB protection, as UVB is 1000 times more erythemogenic than UVA. Moreover, high SPF products allow individuals to spend greater amounts of time in the sun without developing erythema (burning). These products do not necessarily offer adequate UVA protection. Protection against UVA is becoming a major concern because UVA damage is now implicated in photocarcinogenesis,⁷ photoaging^{12,42} and immunosuppression.¹⁰

Currently, there is no consensus about the best method for measuring UVA protection. A variety of methods have been proposed. *In vivo* methods have been developed among which persistent pigment darkening (PPD) is more broadly used. PPD is measured 2 hours after irradiation of the skin with 30 J/cm² of UVA.

An *in vitro* method proposed by Diffey et al.⁴³ is based on the shape of the absorption spectrum of a sunscreen product, which is obtained using spectrophotometry. Critical wavelength is the wavelength where the integral of the spectral absorbance curve reaches 90% of the integral from 290 nm to 400 nm. It measures a sunscreen's extinction capacity in the UVA range in relation to its overall extinction between 290 nm and 400 nm. The critical wavelength determination does not promote the false notion of UVB and UVA as separate entities but rather as part of continuous electromagnetic spectrum. As the critical wavelength increases, so too must the protection against UVA. A complete description of a product's photoprotective characteristics results when critical wavelength is used in conjunction with SPF. However, although this *in vitro* spectrophotometry measurement is useful, it lacks the relevance to a clinical/biological endpoint easily grasped by the public.

Furthermore, immune protection factor (IPF) determination was introduced to measure the capacity of sunscreens to protect against immunosuppression.^{44,45} There are no standardized protocols to measure IPF. Current methods use solar simulated radiation (that contains UVA and UVB) and evaluate the ability of a sunscreen to inhibit UVR-induced local suppression of the contact or delayed-type hypersensitivity response. The induction or the elicitation arms of these responses are being evaluated *in vivo*. The induction arm of the contact hypersensitivity response is sensitive to a single suberythemal UVR exposure, but it requires sensitization, a large number of volunteers and is very time consuming. The elicitation arm of the contact or delayed hypersensitivity responses uses prior sensitization to antigens but repeated UVR exposures may be required making the use of this method difficult. A simpler method for measuring sunscreens' immunoprotective capacity is needed. IPF probably has a better correlation with the UVA protectiveness of sunscreen than with the SPF.^{46,47}

Photostability and water resistance

In addition to how efficiently sunscreens absorb UV irradiation, their photostability is also of major concern. The sunscreen ingredients should absorb or reflect and scatter radiation throughout the period of time they are intended to provide protection for and thus should remain stable photochemically. However, many chemical filters exhibit some photoreactivity (which may be minimal or significant) and lead to formation of a photoproduct(s) that might still act as a filter (e.g. photoisomerization reaction). Photostability depends on the filter itself, on the presence of other filters in the product and on solvent or vehicle. Many UV filters, especially avobenzone³⁵ octinoxate (OMC) and octyl dimethyl PABA, are photolabile.⁴⁸ Other UV filters are frequently used in the sunscreen as they are known to increase the photostability of the final product; these include ZnO, TiO₂, the salicylates and methylbenzylidene camphor. Furthermore, the newly developed filters are photostable: they include terephthalylidene dicamphor sulphonic acid (Mexoryl SX), drometriazole trisiloxane (Mexoryl XL), methylenebis-benzotriazolyl tetramethylbutylphenol (Tinosorb M) and bis-ethylhexyloxyphenol methoxyphenol triazine (Tinosorb S).

Resistance to water immersion and sweating is also an important aspect of a sunscreen performance. In the USA, this is measured *in vivo*, by the ability of a product to withstand water immersion. SPF has to remain unchanged after two 2-minute immersions for a 'water-resistant' product. A 'very water resistant' product will offer the same protection after four 2-minute immersions. Each 20-minute immersion interval is followed by a 20-minute rest/air dry period until the total water exposure time is reached. In Europe, the SPF after a 40- and 80-minute water immersion period is measured and compared with the original SPF before water exposure. A product is considered 'water resistant' or 'extra water resistant' if the SPF data after 40- or 80-minute immersions, respectively, is greater or equal to 50% of the pre-immersion SPF. Thus, the SPF number on the product label for European sunscreen products is pre-water exposure, whereas in the USA, the SPF on the label corresponds to the measurements after the water immersion cycles.

Sunscreens and melanoma

There are different reports in the literature regarding the relation of sunscreens and melanoma. Some studies have found a decreased melanoma risk with sunscreen use,^{18,49-51} and others increased melanoma risk among sunscreen users.⁵²⁻⁵⁴ Subsequently, the data have been meta-analysed to show little or no positive association of sunscreen use and melanoma.^{55,56}

The methodology used in the studies may explain the discrepancy. Frequency and quantity of sunscreen application and SPF of the specific products used are difficult to evaluate based on retrospective recall of participants.⁵⁷⁻⁵⁹ Furthermore, the sunscreens used probably protected only against UVB, whereas currently available sunscreens often have both UVA and UVB protection. In fact, individuals relying on sunscreens as their sole form of photoprotection in the past decades may have been subject to greater cumulative sun exposure, especially in the UVA range. Furthermore, although most studies include skin phototype and sun sensitivity, the results were not statistically adjusted on sun sensitivity of study participants (i.e. individuals with increased risk for sunburn and more likely to develop melanoma, but they are also most likely to use sunscreens).

Taking under consideration the above weaknesses of the conducted studies and the results from the meta-analysis showing no correlation between sunscreen use and melanoma, it is probably safe to suggest that predominantly UVB absorbing sunscreens do not prevent melanoma development in humans. The use of modern sunscreens offering broad UV protection remains to be evaluated. Despite the controversy, sunscreen use remains an important part of melanoma prevention because it can effectively block mutations^{60,61} and prevent sunburn,⁶² factors shown to be associated with melanoma. Moreover, recent small studies with short follow-up period suggest that sunscreens probably reduce the development of melanocytic naevi, a known risk factor for melanoma.⁶³⁻⁶⁶

Future trends

Novel substances with photoprotective potential are being investigated. Potent and long lasting derivatives of alpha-MSH have been synthesized and shown to induce synthesis of melanin (tanning) in humans when administered subcutaneously.⁶⁷⁻⁷⁰ Of interest, melanin synthesis appears to increase more in individuals with light skin that usually do not tan but burn when exposed to sunlight. The alpha-msh induced melanin may have a photoprotective effect. Specifically, it reduces the formation of epidermal sunburn cells and of thymine dimers after skin exposure to ultraviolet light.⁶⁸

T4 endonuclease V (T4N5) is a DNA repair enzyme in bacteria. It has also been shown to accelerate the repair of DNA in human cells when it is delivered intracellularly. The topical use of T4NV has been investigated in patients with xeroderma pigmentosum, a defect in nucleotide excision repair of DNA, and found to have a protective effect on the appearance of basal cell carcinoma and actinic keratosis.⁷¹ Application of T4N5 immediately after UV exposure partially protects against sunburn cell for-

mation. However, it has little or no effect on UV-induced skin oedema.⁷²

Thymidine dinucleotide (pTT) is a small DNA fragment that induces a photo-protective response in mammalian cells and intact skin. Specifically, topical pTT pretreatment enhances the rate of DNA photoproduct removal, decreases UV-induced mutations and reduces photocarcinogenesis in UV-irradiated hairless mice.⁷³ The protective effects of pTT are attributed to its partial sequence homology with the mammalian telomere repeat sequence 5'-TTAGGG-3'. In mammalian cells, telomeres are tandem repeats of a short DNA sequence TTAGGG that cap chromosome ends and form a large loop structure.⁷⁴ Disruption of this loop structure is hypothesized to lead to exposure of the 3'-overhang sequence (repeats of TTAGGG), digestion of the overhang, and signaling that induces DNA damage responses. It has been suggested that providing cells with DNA oligonucleotides partially or totally homologous to the telomere sequence (like pTT), initiates signalling for DNA damage-like responses without antecedent DNA damage.⁷⁴ The photoprotective potential of pTT remains to be evaluated in humans.

Summary

UV irradiation has deleterious effects that may be, at least partially, inhibited through the use of sunscreens. Development of new, highly effective sunscreens of both the traditional chemical kind as well as newer micronized physical blockers continues. It is an important task for dermatologists to educate patients regarding appropriate sun protection and to encourage prudent use of sunscreens.

Questions and multiple choices

- Which of the following regarding broad spectrum sunscreens is false?
 - they can be incorporated in cosmetic products
 - they protect against UVA and UVB
 - they can completely block the unwanted effects of the sun on the skin**
 - they can never be isolated in the blood/urine of humans
- Which of the following statements is correct?
 - UVA and UVB are implicated in the pathogenesis of skin cancer**
 - equal amounts of UVA and UVB reach the earth's surface
 - UVB is penetrates into the dermis
 - UVB but not UVA can cause photoaging
- Which of the following statements is false?
 - Para-aminobenzoic acid absorbs only in the UVB
 - Tinasorbs absorb in the UVA and UVB

- c) **Mexoryls absorb only in the UVA**
 d) titanium dioxide absorb in the UVA and UVB
4. Which of the following statements is correct?
 a) UVA is more efficient in inducing erythema than UVB
 b) UVA does not have carcinogenic effects on the skin
 c) UVA does not cause DNA damage in skin cells
 d) **Both UVB and UVA have immunosuppressive effect**
5. Which of the following statements is false?
 Parsol 1789 or avobenzone:
 a) is a very efficient UVA filter
 b) is an infrequent cause of photoallergy
 c) is photolabile
 d) **increases the photostability of other filters**
6. The concentration of sunscreen applied on the skin for SPF determination is
 a) 1 mg/cm²
 b) **2 mg/cm²**
 c) 2.5 mg/cm²
 d) 5 mg/cm²
7. Which of the following statements about ozone is false?
 a) Ozone absorbs large amounts of UVC and UVB
 b) Ozone depletion increases the risk of sunburn and skin cancer
 c) **Ozone absorbs large amounts of visible light**
 d) Ozone depletion is induced by chlorofluorocarbons, halons, and nitric oxides
8. Which of the following statements about microfine ZnO (Z-cote) is false?
 a) **it is a common cause of contact dermatitis**
 b) it is a visible light filter
 c) it is photostable
 d) it decreases photodegradation of other sunscreen filters
9. Decreasing the particle size of inorganic sunscreen results in:
 a) decreased cosmetic acceptability of the product
 b) **decreased scattering of visible light**
 c) shift of absorption peak toward the longer wavelength
 d) improved photostability
10. Which of the following statement about Tinosorb is false?
 a) It decreases photodegradation of avobenzone
 b) It is a broadband UV filter
 c) **It is an efficient antioxidant**
 d) It is photostable
11. The use of a sunscreen with SPF 25 means:
 a) **it takes 25 times more UV to develop erythema**
 b) 25% of UVB is blocked
 c) 25% of UVA is blocked
 d) 25% of total UV is blocked
12. Exposure of the skin to UVA
 a) induces more erythema than exposure to UVB
 b) **induces immunosuppression and photocarcinogenesis**
 c) is best blocked with octisalate
 d) is best blocked with high SPF products
13. All of the bellow filters are photolabile except:
 a) avobenzene
 b) octinoxate (OMC)
 c) octyl dimethyl PABA
 d) **drometriazole trisiloxane**
14. Persistent Pigment Darkening measures:
 a) skin pigment immediately after 30 J/cm² of UVA
 b) **skin pigment 2 hours after 30 J/cm² of UVA**
 c) skin pigment 4 hours after 30 J/cm² of UVA
 d) skin erythema 2 hours after 30 J/cm² of UVA
15. Which of the following is false?
 Critical Wavelength:
 a) **promotes the notion that UVA and UVB are separate entities**
 b) provides, in combination with SPF, a complete description of a sunscreens' photoprotective capacity
 c) is an in vitro method
 d) higher values correspond to a better UVA protection
16. All the bellow increase the photostability of other sunscreen filters except:
 a) ZnO
 b) **padimate**
 c) methylbenzylidene camphor
 d) homosalate
17. An extra water resistant European sunscreen filter
 a) **maintains at least 50% of its SPF after 80 min water immersion**
 b) maintains at least 80% of its SPF after 80 min water immersion
 c) maintains its SPF unchanged after a 40 min water immersion
 d) maintains at least 50% of its SPF after a 40 min water immersion
18. Which of the following is false?
 Microencapsulation of sunscreen filters:
 a) diminishes allergic contact dermatitis
 b) improves compatibility between different filters
 c) increases photostability
 d) **increases allergic contact dermatitis**
19. Which of the following is the mechanism of action of T4N5?
 a) absorption of UVA
 b) antioxidative property
 c) **repairs DNA**
 d) increases effectiveness of other filters

20. Thymidine dinucleotide (pTT) is a/an
- styrene/acrylates copolymer
 - DNA repair enzyme
 - UV filter
 - single-stranded DNA fragment**

Correct answers

- c
- a
- c
- d
- d
- b
- c
- a
- b
- c
- a
- b
- d
- b
- a
- b
- a
- d
- c
- d

References

- Bruls WA, Slaper H, van der Leun JC *et al.* Transmission of human epidermis and stratum corneum as a function of thickness in the ultraviolet and visible wavelengths. *Photochem Photobiol* 1984; **40**: 485–494.
- Cadet J, Sage E, Douki T. Ultraviolet radiation-mediated damage to cellular DNA. *Mutat Res* 2005; **571**: 3–17.
- De Fabo EC, Noonan FP. Mechanism of immune suppression by ultraviolet irradiation *in vivo*. I. Evidence for the existence of a unique photoreceptor in skin and its role in photoimmunology. *J Exp Med* 1983; **158**: 84–98.
- Heck DE, Vetrano AM, Mariano TM, Laskin JD. UVB light stimulates production of reactive oxygen species: unexpected role for catalase. *J Biol Chem* 2003; **278**: 22432–22436.
- Strickland PT. Photocarcinogenesis by near-ultraviolet (UVA) radiation in Sencar mice. *J Invest Dermatol* 1986; **87**: 272–275.
- Sterenberg HJ, van der Leun JC. Tumorigenesis by a long wavelength UV-A source. *Photochem Photobiol* 1990; **51**: 325–330.
- Agar NS, Halliday GM, Barnetson RS, Ananthaswamy HN, Wheeler M, Jones AM. The basal layer in human squamous tumors harbors more UVA than UVB fingerprint mutations: a role for UVA in human skin carcinogenesis. *Proc Natl Acad Sci USA* 2004; **101**: 4954–4959.
- Mouret S, Baudouin C, Charveron M, Favier A, Cadet J, Douki T. Cyclobutane pyrimidine dimers are predominant DNA lesions in whole human skin exposed to UVA radiation. *Proc Natl Acad Sci U S A* 2006; **103**: 13765–13770.
- Kappes UP, Luo D, Potter M, Schulmeister K, Runger M. Short- and long-wave UV light (UVB and UVA) induce similar mutations in human skin cells. *J Invest Dermatol* 2006; **126**: 667–675.
- Dumay O, Karam A, Vian L *et al.* Ultraviolet AI exposure of human skin results in Langerhans cell depletion and reduction of epidermal antigen-presenting cell function: partial protection by a broad-spectrum sunscreen. *Br J Dermatol* 2001; **144**: 1161–1168.
- Schwarz T. Mechanisms of UV-induced immunosuppression. *Keio J Med* 2005; **54**: 165–171.
- Krutmann J. Ultraviolet A radiation-induced biological effects in human skin: relevance for photoaging and photodermatosis. *J Dermatol Sci* 2000; **23** (Suppl. 1): S22–S26.
- Liardet S, Scaletta C, Panizzon R *et al.* Protection against pyrimidine dimers, p53, and 8-hydroxy-2'-deoxyguanosine expression in ultraviolet-irradiated human skin by sunscreens: difference between UVB + UVA and UVB alone sunscreens. *J Invest Dermatol* 2001; **117**: 1437–1441.
- Whitmore SE, Morison WL. Prevention of UVB-induced immunosuppression in humans by a high sun protection factor sunscreen. *Arch Dermatol* 1995; **131**: 1128–1133.
- Seite S, Colige A, Piquemal-Vivenot P *et al.* A full-UV spectrum absorbing daily use cream protects human skin against biological changes occurring in photoaging. *Photodermatol Photoimmunol Photomed* 2000; **16**: 147–155.
- Roelandts R. Shedding light on sunscreens. *Clin Exp Dermatol* 1998; **23**: 147–157.
- Gasparro FP, Mitchnick M, Nash JF. A review of sunscreen safety and efficacy. *Photochem Photobiol* 1998; **68**: 243–256.
- Moloney FJ, Collins S, Murphy GM. Sunscreens: safety, efficacy and appropriate use. *Am J Clin Dermatol* 2002; **3**: 185–191.
- Walters KA, Brain KR, Howes D *et al.* Percutaneous penetration of octyl salicylate from representative sunscreen formulations through human skin *in vitro*. *Food Chem Toxicol* 1997; **35**: 1219–1225.
- Fisher AA. Sunscreen dermatitis: Part II – The cinnamates. *Cutis* 1992; **50**: 253–254.
- Thune P. Contact and photocontact allergy to sunscreens. *Photodermatol* 1984; **1**: 5–9.
- Darvay A, White IR, Rycroft RJ, Jones AB, Hawk JL, McFadden JP. Photoallergic contact dermatitis is uncommon. *Br J Dermatol* 2001; **145**: 597–601.
- Perugini P, Simeoni S, Scalia S *et al.* Effect of nanoparticle encapsulation on the photostability of the sunscreen agent, 2-ethylhexyl-*p*-methoxycinnamate. *Int J Pharm* 2002; **246**: 37–45.

- 24 de Freitas ZM, dos Santos EP, da Rocha JF, Dellamora-Ortiz GM, Goncalves JC. A new sunscreen of the cinnamate class: synthesis and enzymatic hydrolysis evaluation of glyceryl esters of *p*-methoxycinnamic acid. *Eur J Pharm Sci* 2005; **25**: 67–72.
- 25 Janjua NR, Mogensen B, Andersson AM *et al.* Systemic absorption of the sunscreens benzophenone-3, octyl-methoxycinnamate, and 3-(4-methyl-benzylidene) camphor after whole-body topical application and reproductive hormone levels in humans. *J Invest Dermatol* 2004; **123**: 57–61.
- 26 Gustavsson Gonzalez H, Farbrot A, Larko O. Percutaneous absorption of benzophenone-3, a common component of topical sunscreens. *Clin Exp Dermatol* 2002; **27**: 691–694.
- 27 Hayden CG, Roberts MS, Benson HA. Systemic absorption of sunscreen after topical application. *Lancet* 1997; **350**: 863–864.
- 28 Benson HA. Assessment and clinical implications of absorption of sunscreens across skin. *Am J Clin Dermatol* 2000; **1**: 217–224.
- 29 Schauder S, Ippen H. Contact and photocontact sensitivity to sunscreens. Review of a 15-year experience and of the literature. *Contact Dermatitis* 1997; **37**: 221–232.
- 30 Weigmann HJ, Lademann J, Schanzer S *et al.* Correlation of the local distribution of topically applied substances inside the stratum corneum determined by tape-stripping to differences in bioavailability. *Skin Pharmacol Appl Skin Physiol* 2001; **14** (Suppl. 1): 98–102.
- 31 Simeoni S, Scalia S, Benson HA. Influence of cyclodextrins on *in vitro* human skin absorption of the sunscreen, butyl-methoxydibenzoylmethane. *Int J Pharm* 2004; **280**: 163–171.
- 32 Benech-Kieffer F, Meuling WJ, Leclerc C, Roza L, Leclaire J, Nohynek G. Percutaneous absorption of Mexoryl SX in human volunteers: comparison with *in vitro* data. *Skin Pharmacol Appl Skin Physiol* 2003; **16**: 343–355.
- 33 Hughes TM, Martin JA, Lewis VJ, Stone NM. Allergic contact dermatitis to drometrisole trisiloxane in a sunscreen with concomitant sensitivities to other sun screens. *Contact Dermatitis* 2005; **52**: 226–227.
- 34 Gonzalez-Perez R, Trebol I, Garcia-Rio I, Arrequi MA, Soloeta R. Allergic contact dermatitis from methylene-bis-benzotriazolyl tetramethylbutylphenol (Tinosorb M). *Contact Dermatitis* 2007; **56**: 121.
- 35 Chatelain E, Gabard B. Photostabilization of butyl methoxydibenzoylmethane (Avobenzon) and ethylhexyl methoxycinnamate by bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S), a new UV broadband filter. *Photochem Photobiol* 2001; **74**: 401–406.
- 36 Tan MH, Commens CA, Burnett L, Snitch PJ. A pilot study on the percutaneous absorption of microfine titanium dioxide from sunscreens. *Australas J Dermatol* 1996; **37**: 185–187.
- 37 Agren MS. Percutaneous absorption of zinc from zinc oxide applied topically to intact skin in man. *Dermatologica* 1990; **180**: 36–39.
- 38 Schulz J, Hohenberg H, Pflucker F *et al.* Distribution of sunscreens on skin. *Adv Drug Deliv Rev* 2002; **54** (Suppl. 1): S157–S163.
- 39 Derry JE, McLean WM, Freeman JB. A study of the percutaneous absorption from topically applied zinc oxide ointment. *JPEN J Parenter Enteral Nutr* 1983; **7**: 131–135.
- 40 Gogna D, Jain SK, Yadav AK, Agrawal GP. Microsphere based improved sunscreen formulation of ethylhexyl methoxycinnamate. *Curr Drug Deliv* 2007; **4**: 153–159.
- 41 Patel M, Jain SK, Yadav AK, Gogna D, Agrawal GP. Preparation and characterization of oxybenzone-loaded gelatin microspheres for enhancement of suncreening efficacy. *Drug Deliv* 2006; **13**: 323–330.
- 42 Lavker RM, Gerberick GF, Veres D, Irwin CJ, Kaidbey KH. Cumulative effects from repeated exposures to suberythemal doses of UVB and UVA in human skin. *J Am Acad Dermatol* 1995; **32**: 53–62.
- 43 Diffey B. A method for broad spectrum classification of sunscreens. *Int J Cosmet Sci* 1994; **16**: 47–52.
- 44 Fourtanier A, Moyal D, Maccario J *et al.* Measurement of sunscreen immune protection factors in humans: a consensus paper. *J Invest Dermatol* 2005; **125**: 403–409.
- 45 Young AR. Methods used to evaluate the immune protection factor of a sunscreen: advantages and disadvantages of different *in vivo* techniques. *Cutis* 2004; **74**: 19–23.
- 46 Young AR. Are broad-spectrum sunscreens necessary for immunoprotection? *J Invest Dermatol* 2003; **121**: ix–x.
- 47 Kelly DA, Seed PT, Young AR, Walker SL. A commercial sunscreen's protection against ultraviolet radiation-induced immunosuppression is more than 50% lower than protection against sunburn in humans. *J Invest Dermatol* 2003; **120**: 65–71.
- 48 Maier H, Schauburger G, Brunnhofer K, Honigsmann H. Change of ultraviolet absorbance of sunscreens by exposure to solar-simulated radiation. *J Invest Dermatol* 2001; **117**: 256–262.
- 49 Rodenas JM, Delgado-Rodriguez M, Herranz MT, Tercedor J, Serrano S. Sun exposure, pigmentary traits, and risk of cutaneous malignant melanoma: a case-control study in a Mediterranean population. *Cancer Causes Control* 1996; **7**: 275–283.
- 50 Espinosa Arranz J, Sanchez Hernandez JJ, Bravo Fernandez P *et al.* Cutaneous malignant melanoma and sun exposure in Spain. *Melanoma Res* 1999; **9**: 199–205.
- 51 Bakos L, Wagner M, Bakos RM *et al.* Sunburn, sunscreens, and phenotypes: some risk factors for cutaneous melanoma in southern Brazil. *Int J Dermatol* 2002; **41**: 557–562.
- 52 Westerdahl J, Olsson H, Masback A, Ingvar C, Jonsson N. Is the use of sunscreens a risk factor for malignant melanoma? *Melanoma Res* 1995; **5**: 59–65.

- 53 Westerdahl J, Ingvar C, Masback A, Olsson H. Sunscreen use and malignant melanoma. *Int J Cancer* 2000; **87**: 145–150.
- 54 Autier P, Dore JF, Schifflers E *et al.* Melanoma and use of sunscreens: an EORTC case-control study in Germany, Belgium and France. *The EORTC Melanoma Cooperative Group Int J Cancer* 1995; **61**: 749–755.
- 55 Huncharek M, Kupelnick B. Use of topical sunscreens and the risk of malignant melanoma: a meta-analysis of 9067 patients from 11 case-control studies. *Am J Public Health* 2002; **92**: 1173–1177.
- 56 Dennis LK, Beane Freeman LE, VanBeek MJ. Sunscreen use and the risk for melanoma: a quantitative review. *Ann Intern Med* 2003; **139**: 966–978.
- 57 Bastuji-Garin S, Diepgen TL. Cutaneous malignant melanoma, sun exposure, and sunscreen use: epidemiological evidence. *Br J Dermatol* 2002; **146** (Suppl. 61): 24–30.
- 58 Rigel DS. The effect of sunscreen on melanoma risk. *Dermatol Clin* 2002; **20**: 601–606.
- 59 Weinstock MA. Do sunscreens increase or decrease melanoma risk: an epidemiologic evaluation. *J Invest Dermatol Symp Proc* 1999; **4**: 97–100.
- 60 Rosenstein BS, Phelps RG, Weinstock MA *et al.* p53 mutations in basal cell carcinomas arising in routine users of sunscreens. *Photochem Photobiol* 1999; **70**: 798–806.
- 61 Ananthaswamy HN, Ullrich SE, Kripke ML. Inhibition of UV-induced p53 mutations and skin cancers by sunscreens: implication for skin cancer prevention. *Exp Dermatol* 2002; **11** (Suppl. 1): 40–43.
- 62 Miyagi T, Bhutto AM, Nonaka S. The effects of sunscreens on UVB erythema and Langerhans cell depression. *J Dermatol* 1994; **21**: 645–651.
- 63 Bauer J, Buttner P, Wiecker TS, Luther H, Garbe C. Effect of sunscreen and clothing on the number of melanocytic nevi in 1812 German children attending day care. *Am J Epidemiol* 2005; **161**: 620–627.
- 64 Lee TK, Rivers JK, Gallagher RP. Site-specific protective effect of broad-spectrum sunscreen on nevus development among white schoolchildren in a randomized trial. *J Am Acad Dermatol* 2005; **52**: 786–792.
- 65 English DR, Milne E, Jacoby P, Giles-Corti B, Cross D, Johnston R. The effect of a school-based sun protection intervention on the development of melanocytic nevi in children: 6-year follow-up. *Cancer Epidemiol Biomarkers Prev* 2005; **14**: 977–980.
- 66 Holly EA, Kelly JW, Shpall SN *et al.* Number of melanocytic nevi as a major risk factor for malignant melanoma. *J Am Acad Dermatol* 1987; **17**: 459–468.
- 67 Fitzgerald LM, Fryer JL, Dwyer T *et al.* Effect of MELANOTAN, [Nle(4), D-Phe(7)]-alpha-MSH, on melanin synthesis in humans with MC1R variant alleles. *Peptides* 2006; **27**: 388–394.
- 68 Barnetson RS, Ooi TK, Zhuang L *et al.* [Nle4-D-Phe7]-alpha-melanocyte-stimulating hormone significantly increased pigmentation and decreased UV damage in fair-skinned Caucasian volunteers. *J Invest Dermatol* 2006; **126**: 1869–1878.
- 69 Hadley ME, Sharma SD, Hruby VJ *et al.* Melanotropic peptides for therapeutic and cosmetic tanning of the skin. *Ann N Y Acad Sci* 1993; **680**: 424–439.
- 70 Levine N, Sheftel SN, Eytan T *et al.* Induction of skin tanning by subcutaneous administration of a potent synthetic melanotropin. *Jama* 1991; **266**: 2730–2736.
- 71 Yarosh D, Klein J, O'Connor A *et al.* Effect of topically applied T4 endonuclease V in liposomes on skin cancer in xeroderma pigmentosum: a randomised study. *Xeroderma Pigmentosum Study Group Lancet* 2001; **357**: 926–929.
- 72 Wolf P, Cox P, Yarosh DB *et al.* Sunscreens and T4N5 liposomes differ in their ability to protect against ultraviolet-induced sunburn cell formation, alterations of dendritic epidermal cells, and local suppression of contact hypersensitivity. *J Invest Dermatol* 1995; **104**: 287–292.
- 73 Gilchrist BA, Eller MS. The tale of the telomere: implications for prevention and treatment of skin cancers. *J Invest Dermatol Symp Proc* 2005; **10**: 124–130.
- 74 Kosmadaki MG, Gilchrist BA. The role of telomeres in skin aging/photoaging. *Micron* 2004; **35**: 155–159.

Information on authors



Andreas Katsambas M.D., is Professor and Chairman of the Department of Dermatology and Venereology at the 'A. Sygros' Hospital, University of Athens in Greece. He is Editorial Board member of many international medical journals and author of more than 180 peer reviewed published manuscripts. Prof. Katsambas has also co-edited two books, which have since been translated into Greek, Italian and Russian. He is a Board member of the International Committee of Dermatology (ICD) and Chairman of the ICD Awards Committee, as well as member and honorary member of many international dermatological societies. Prof. Katsambas is a long-standing member of the European Academy of Dermatology and Venereology (EADV), in which he served as Secretary General from 1992 to 2000 and was elected President-Elect in 2006.