Ultraviolet radiation and the skin: Photobiology and sunscreen photoprotection

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The efficacy of sunscreens can be measured by different methods, involving in vitro, ex vivo, or in vivo techniques. There is a need for a worldwide standardization of these methods to avoid misunderstanding and confusion among sunscreen users. The clinical benefits of sunscreens have been demonstrated in randomized controlled trials that established the role of sunscreens in the prevention of actinic keratoses, squamous cell carcinomas, nevi, and melanomas. Sunscreens also prevent photoimmunosuppression and signs of photoaging. Continued efforts in public education on the proper application of sunscreens and the practice of photoprotection in general are needed. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.09.038.)

Key words: cyclobutane pyrimidine dimer; DNA photodamage; photoaging; photoimmunosuppression; pyrimidine(6-4)pyrimidone; skin cancer; sunscreen; ultraviolet radiation.

Terrestrial solar ultraviolet (UV) radiation (UVR) (~295-400 nm) comprises UVA (320-400 nm) and UVB (280-320 nm).[1] UVC (100-280 nm) does not reach the Earth's surface because it is completely absorbed by stratospheric ozone. UVB accounts for no more than about 5% of terrestrial UVR, but its effects are typically much greater than those of UVA. The intensity of UVB peaks at around midday, whereas that of UVA remains fairly consistent throughout the day. The clinical effects of UVR on normal-appearing human skin, which are mostly adverse, may be acute or chronic. The acute effects include erythema (sunburn), pigmentation (tanning), suppression of acquired immunity, and enhancement of innate immunity, all mostly caused by UVB,[2] and reduction of blood pressure by UVA[3,4] (Table I). Chronic effects include photocarcinogenesis and photoaging.[5] All effects are underpinned by molecular or cellular effects such as DNA damage, the generation of reactive oxygen species (singlet oxygen, superoxide, peroxyl radicals, hydroxyl radicals, and peroxynitrite), melanogenesis, apoptosis,

Abbreviations used:

AK:	actinic keratosis
BCC:	basal cell carcinoma
CPD:	cyclobutane pyrimidine dimer
FDA:	Food and Drug Administration
ISO:	International Standards Organization
KC:	keratinocyte cancer
MED:	minimal erythemal dose
MMP:	matrix metalloproteinase
SCC:	squamous cell carcinoma
SED:	standard erythemal dose
SPF:	sun-protection factor
UV:	ultraviolet
UVR:	ultraviolet radiation

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depletion of Langerhans cells, and expression of many genes and related proteins. The only widely established benefit of UVR in the skin is the photosynthesis of vitamin D that is initiated by the UVB-induced conversion of epidermal 7-dehydrocholesterol into previtamin D_3.

PHOTOBIOLOGY

UVR sensitivity

Skin phototype, as described by the Fitzpatrick scale,[6] is among the most useful clinical determinants of UVR sensitivity. Lower number skin types are more susceptible to sunburn, tanning ability is poor, and skin cancer risk is higher (Table II).

Personal UVR sensitivity can be measured by visual assessment of the minimal erythemal dose (MED), which is the amount of UVR needed to induce just perceptible erythema after exposure (typically 24 hours). In general, the MED increases with Fitzpatrick skin type, but there is considerable overlap between skin types, so MED may not be consistently predictive of skin type.[7] The MED is widely used in experimental photobiology, phototherapy, and calculation of a sunscreen's sun-protection factor (SPF).

An action spectrum is defined as a plot of wavelength versus the reciprocal of the dose required for a given photobiological outcome (usually expressed on a log scale), such as erythema. Most international organizations have adopted the action spectrum proposed by McKinlay and Diffey[8] in 1987, including the Commission Internationale de l'Eclairage.[9,10] Using this schema as a weighting function for solar UVR shows that, when the sun is high, over 80% of the erythemal response of the skin is a result of the 5% or less UVB in solar UVR. The erythema action spectrum is also used as the biological weighting function for the standard erythemal dose (SED) that is increasingly used as the exposure unit in epidemiologic and laboratory studies. The SED is independent of personal UVR sensitivity and emission spectrum and is set as an exposure of 100 J/m^2.

Another measure of UVR exposure that is more easily understood is the UV index, which is used worldwide to promote public awareness of the risks of UVR exposure and sun protection.[11] The UV index, which is also based on the erythema action spectrum, is directly proportional to the intensity of erythemal UVR. The values vary with sun elevation, so by time of day, time of year, and latitude, and also with altitude, ozone, cloud cover, and ground reflection.

CAPSULE SUMMARY

- Acute effects of ultraviolet radiation exposure include erythema, pigmentation, suppression of acquired immunity, enhancement of innate immunity, and vitamin-D synthesis. Chronic effects include photocarcinogenesis and photoaging.
- Photoprotection, including the application of sunscreens, has been shown to inhibit many of the acute and chronic effects of ultraviolet radiation exposure.

DNA damage

The effects of UVR in the skin are initiated at a molecular level involving epidermal and dermal chromophores that absorb UV or visible radiation, each with a characteristic absorption spectrum. When such a chromophore absorbs photon energy, it moves to a higher energy ("excited") state and becomes unstable. This may result in either a structural change, binding to other molecules that define a "direct effect," or acting as a sensitizer generating reactive oxygen species that damage adjacent biomolecules such as DNA or proteins (indirect effects). In the excited state, chromophores are the initiators of all short- and long-term photobiological responses.[2,12] Endogenous skin chromophores include DNA, melanins, and their precursors, urocanic acid, aromatic amino acids, flavins, and porphyrins. Exogenous chromophores include photosensitizing drugs, eg, fluoroquinolones and azathioprine (inadvertent photosensitization), 8-methoxypsoralen as used in psoralen plus UVA therapy for psoriasis (deliberate photosensitization), and sunscreens. DNA, which absorbs solar UVB and some UVA, is probably the most important endogenous chromophore. The most frequent photolesions are cyclobutane pyrimidine dimers (CPDs) and pyrimidine (6-4) pyrimidones. These result in structural damage to the DNA helix inhibiting DNA replication and transcription. CPDs are the most common and the most damaging type of lesion. Relatively low and even suberythemal doses of UVB have been shown to cause a high amount of DNA damage in the epidermis.[13]

CPDs provoke cytokine-mediated inflammation leading to erythema and concomitant immunosuppression and transition mutations, such as C (cytosine) → T (thymine) or even CC → TT, which can lead to keratinocyte cancers (KCs). Less is known about the relationship of melanoma with CPDs, although intense, intermittent UVR exposure is significantly associated with melanoma risk.[14]