UV AND SKIN: THE BIOLOGICAL EFFECTS OF UVA AND UVB

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INTRODUCTION

Almost all of the photobiological reactions that occur in the skin are induced by radiations between 290 and 380 nm. These radiations correspond to the wavelengths from the solar emission which are received at the earth surface after absorption by the terrestrial atmosphere. However, from artificial sources, used at work or in domestic environment, the complete spectrum of UV may present a potential hazard.[1]

After considering the optical properties of the human skin, acute effects of UV on the skin will be considered, followed by the potential phototoxic and photoallergic consequences of UV exposures and finally, the adverse cutaneous reaction to sunlight.[2] Protective measures will be considered.

THE OPTICAL PROPERTIES OF THE SKIN

To establish a photobiological reaction, three components are necessary: the biological system, the radiation and a radiation absorber in the biological system. All the components of the tegument are potentially able to react with the incident UV and, as a consequence, a protective filter for the constituents located below.

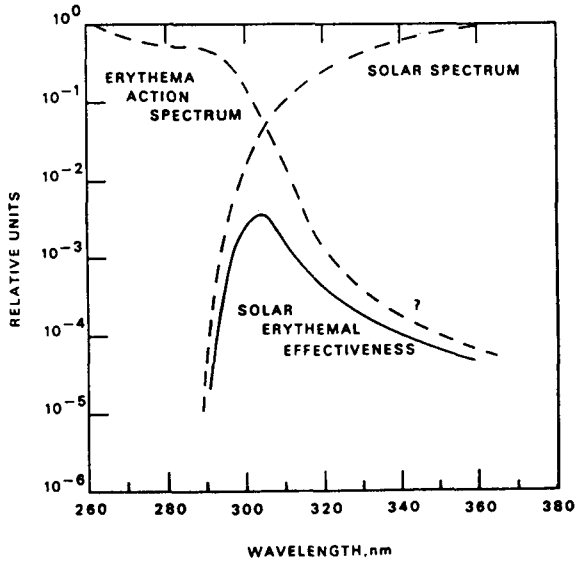

Figure 1. The human solar erythemal effectiveness is obtained by the convolution of the human skin erythema action spectrum and the solar spectrum. It clearly presents a maximum at 307 nm which is the most efficient wavelength to induce sunburn. For artificial sources the erythemal effectiveness shape of the curve may be completely different. The same holds for chemicals with different absorption spectrum.

Skin reflects a large amount of incident visible and near infrared radiation and to a lesser degree, some UVA. Scattering and absorption play a greater role in the attenuation of radiation than reflection. Melanins and melanosomes, nucleic acids, proteins, lipids, urocanic acid, cholesterol, and histidine do limit the penetration of UV.

UVC are absorbed by the stratum corneum and the upper layers of the stratum Malpighi. UVC has only indirect impact on the living layer of the epidermis (melanocytes and keratinocytes), but are able to generate the cytokin production responsible for erythema and to alter the immune function of Langerhans cells.

UVB has indirect impact on the full thickness of the epidermis, 10 to 15% of the longer UVB are reaching the papilla (the upper part of the dermis).

UVA are absorbed at 50% by the epidermis, the rest is able to penetrate the dermis up to 2 mm depth. Because of the importance of the shorter wavelength UV, in the production of the photobiological reaction, the acute effects will be mostly produced at sea level by radiation around 307 nm.

After repeated insults from UVR, and particularly UVB, the thickness of the epidermis is increasing with direct consequences on the UVB absorption, making the basal layer of the epidermis (where keratinocytes, able to divide, are located) out of direct reaction with UVB radiations. Soluble mediators produced by maturing keratinocytes are still efficient.

BIOMOLECULAR EFFECTS OF UVA AND B

The complexity of these reactions are out of the scope of this document. However, it is enough to say that DNA is one of the most important chromophores for both direct and indirect (activated oxygen species mediated) effects of UV. Once a DNA molecule has been altered by either of these processes, the damages have to be repaired by more or less complex pathway. The repair processes may be error-free or error-prone, depending on the severity of the DNA damages. Schematically, UVB are essentially inducing DNA dimers which are, most of the time, error-free repaired. UVA induce DNA strand breaks much less frequently than UVB, but the strand breaks are error-prone lesions. As a consequence, after long term exposures, the genetic code is altered equally by UVA and UVB. UVA-1 (340-400 nm) , considered for long time as inefficient in producing damages, are responsible for only strand breaks, while UVA-2 and UVB are inducing mixture of dimers and strand breaks (the 50/50 ratio being obtained around 320 nm).[3-4]

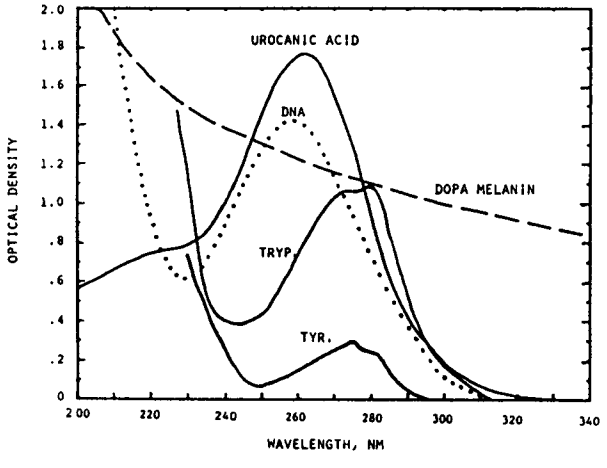

Figure 2. Absorption spectrum for different chromophores of the epidermis. The peaks of absorption for urocanic acid and DNA lie in the UVC and the small tails in the UVB are responsible for most of the deleterious biological effects, when human skin is exposed to sunlight.

The second most action of UV is on lipids which undergo peroxidation through indirect mechanisms. Other chromophores are able to absorb and react with UVB and UVA leading to activated molecules responsible for the production of several cytokins, biological inducers of mitosis, vascular changes, and systemic distant effects. The urocanic acid (maximum absorption at 265 nm) is still absorbing up to 315 nm

and is thought to play some role as an "endogenous sunscreen" of the epidermis. The energy of the photons are transferred to the chemical *cis-trans* isomerization of the urocanic acid.[5]

ACUTE EFFECT OF SUNLIGHT ON THE SKIN

- **Sunburn reaction and minimal erythemal dose.**

The sunburn reaction is the most common adverse effect produced by sunlight. The cutaneous changes induced by the erythemogenic radiation depend on the amount of radiation, the degree and the quality of melanins and the thickness of the stratum corneum. The erythema (reddening of the skin) is a visual aspect of the sunburn response. It is delayed 2-4 hours after the irradiation and peak at 14-20 hours, persisting normally for 72 hours. A severe sunburn is usually followed by an increase of the epidermal thickness and desquamation of dead epidermal cells. A minimal sunburn is light red and not painful. An extremely severe sunburn is followed, 48 hours after, by blisters. The UVA sunburn is more violaceous with prominent vasodilatation.

Based upon their personal[6] and previous works[7], McKinlay and Diffey proposed an action spectrum for a minimal sunburn. The action spectrum was adopted by CIE and, later, by several international agencies. This action spectrum is very closed in the UVB range to the absorption of UV by DNA and several other biological events like bacteria mutagenesis, cell toxicity, delayed pigmentation. It has also a good correlation in the UVB range with the ACGIH action spectrum[8], adopted by IRPA and ICNIRP for UV-induced biological hazards including eye hazards. It should be noted that in the UVA, the erythema action spectrum is not representative of pigmentation or mutagenesis.

The minimal erythemal dose (MED) is a useful tool to define the biological effects of a UV dose. It is generally expressed in mJ.cm^{-2} or J.m^{-2}. Unfortunately, international agreement has not been reached on the value of the MED. However, it is commonly set à 21 mJ.cm^{-2} when normalized at 297 nm which corresponds to the dose necessary to induce a minimal redness on the back of a very sensitive skin. This value has been adopted by most of the agencies to calculate for example, the UV risk for indoor/outdoor workers or the potential consequences of changes in the ozone layer thickness.

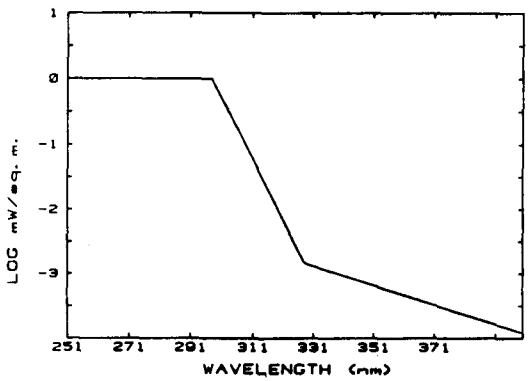

Figure 3. CIE human skin erythema action spectrum adopted after McKinlay and Diffey proposals.

For epidemiological inquiries related to skin cancers, melanocompromized subjects have an average MED of 25 ± 5 mJ.cm^{-2}, and melanocompetent subjects, an average MED of 45 ± 15 mJ.cm^{-2}. These values are characteristic of Caucasian subjects, mongoloid and metis have values closed to 90 mJ.cm^{-2}, and Negro skin, closed to 180 mJ.cm^{-2}.

- **Skin pigmentation**

Skin pigmentation is considered as an adaptation process, a direct consequence of UV radiations for a sufficient dose. It takes at least 24 hours to notice an increased pigmentation and it culminates at 8 days for a single irradiation. This **delayed pigmentation** is a consequence of an increased production of melanin pigment and its transfer to surrounding keratinocytes. In the UVB range, the induced division of the keratinocytes increases the thickness of the epidermis and so, the total content in melanin. This photoadaptative complex mechanism may be enhanced by further consecutive irradiations to an equilibrium state reached by almost doubling the total epidermal thickness, including the stratum corneum and a large load of melanin which increases the basic MED by a factor 4 to 10. In the UVA range, the multiplication of keratinocytes is

minimum while the increased pigmentation is provided directly by stimulation of melanogenesis. In this case, the basic MED is only increased by a factor 2. Phaeo and eumelanins coexist in melanocytes and keratinocytes in different ratios rendering the protection by melanins very much dependent on the quantity of phaemelanins which have been found more phototoxic than photoprotective when irradiated by either UVA or UVB. Melanocompromized subjects[9] have a large load of phaeomelanins which increases after irradiation and it is believed nowadays that the phenomenon is responsible for greater actinic damages and their consequences.

If the erythema action spectrum and the delayed pigment action spectrum for melanocompromized and melanocompetent subjects are nearly same in the UVB range, and in the shorter part of UVA, the action spectrum for pigmentation of melanocompetent subjects is diverging from the action spectrum for pigmentation of melanocompromized subjects. The same pigmentation is achieved for 5 times less dose of UVA in melanocompetent than in melanocompromized which remain closed to the UVA erythema dose[7].

The **immediate pigment darkening** reaction, a skin color observed immediately after UVA irradiation, is a totally different phenomenon which is believed to be the consequence of rapid oxidative reaction of colorless precursors of eumelanins. This transient phenomenon is nearly fully reversible with few hours and does not have any protective effect[10]. Only melanocompetent subjects are able to exhibit clearly this phenomenon which is readily perceptible after a 10 J.cm^{-2} UVA irradiation. The action spectrum has been obtained in the UVA range and is nearly flat from 330 to 380 nm, extending into the visible blue band.

- **Immunological effects**

The epidermis being an interface between environment and the body, it is naturally presenting a physical defense against external chemical or xenobiotics, but also an immunological organ able to control through immunological processes, the penetration of xenobiotic agents or the emergence of abnormal cells within the epidermis. The Langerhans cells located underneath the stratum corneum is the major afferent pathway toward a central lymphnode system, immunologically competent cells circulating by and through the capillary vessels, constituting the afferent pathway (response). For UV doses as low as half MED, the Langerhans cell functions are deeply altered within 24 hours and it takes almost 3 weeks to restore these functions[11]. Cytokins produced by other epidermal constituents, including the UV absorbing urocanic acid in its *trans* form, are able to modify either the afferent or efferent pathways, inducing a state of tolerance vis à vis any foreign substance. Several action spectra for this UV-induced tolerance have been proposed but are not yet acknowledged by the international scientific community.

In the modern vision of skin cancer initiation, promotion, and diffusion, the immunological consequences of UVR play an important role in favorishing the emergence of abnormal clones of cells[12].

- **Vitamin D_3 synthesis**

This important beneficial effect of solar radiations on the skin has been extensively studied: the UVB irradiation of 7-dehydrocholesterol by UVB produces previtamin D_3 which later will be converted into vitamin D_3 by thermal energy. The hyperproduction of previtamin D_3, by excess of UVB, is prevented by the conversion of previtamin D_3 by the production of lumisterol and tachysterol when previtamin D_3 is further irradiated. Upon continued irradiation, a photoequilibrium state is reached. As a consequence of the prevention of rickets, the production of vitamin D has probably been responsible for the establishment of skin variegated color population at the surface of the earth. Without supplementation of the diet in vitamin D_3, dark skin population children will be affected by rickets in countries with low level of UVB radiations (Nordic countries)

ADVERSE CUTANEOUS REACTIONS TO SUNLIGHT

Most of the cutaneous effects of sunlight are injurious. Beside the constitutional effects that we have already exposed, true pathogenic effects have been observed[13]. Two types of photomediated reactions may occur: phototoxic or photoallergic. Some molecules, either naturally produced, or absorbed through the skin or by the diet, present in the skin (epidermis/dermis) may absorb UVR and most of the time in the presence of oxygen, become toxic for the tissues. Clinically, **phototoxic reactions** are characterized by erythema and edema occurring within a few minutes to several hours after exposure. These chromophores may absorb at the maximum in any wavelength of the UV spectrum. For example, furocoumarins, following UVA radiation, are in their triplet state which is able to react with DNA to form adducts. Chlorpromazine reacts to form similar adducts with RNA. After the excitation, the photosensitizing molecule will return to the ground state and will be structurally unchanged, ready for more phototoxic reactions. Most of the photosensitizing molecules present this type of reaction in the UVA range.

Photoallergy can be defined as an acquired capacity of the skin to react in the presence of the photosensitizer by the development of circulating antibody or cell mediated immune response. These reactions are generally uncommon, not depending on the concentration of the photosensitizer and extend beyond the

exposed areas. Usually, less radiation exposure is required to induce a photoallergic response than a phototoxic response, the later being dose-dependent.

Among the adverse cutaneous reactions, **photo-induced diseases or photo-aggravated diseases have been** described. The spectrum of the diseases is very large from viral activation like herpes, to unknown agents responsible for polymorphic light eruptions which are afflicting 10% of the women population of clear skin complexion. The course of systemic diseases, metabolic disorders (porphyry) and complex immunological disorders (lupus), may be severely altered.

PROTECTIVE MEASURES

It is desirable to provide skin protection against acute and hypothesized chronic exposure hazards. In order to reduce the ambient solar aggression or the leisure/vacation overexposures, several measures should be taken[1]. Education should play a great role. The education programs should start very early at school and be regularly repeated for adults, through publicity campaigns, using all media. Staying in the shade during the most solar aggressive hours, wearing adapted clothing, hat with minimal 7 cm brim, applying adapted protective sunscreens, are elementary measures. The concept of a protection factor is useful to characterize items such as sunscreens, clothing. Generally, the protection factor is defined as the ratio of effective dose (unprotected) to effective dose (protected). It should take in account the spectral irradiance and the relative spectral effectiveness, the spectral transmission of the protective item. To communicate for the protective measures, the global UV-Index established in 1996, is a very effective tool.

CONCLUSIONS

International guide lines on exposure to ultraviolet radiations have been based on the same basic criteria of ACGIH (1993) and IRPA / ICNIRP (1991). The basic exposure limit (EL) for general public and occupational exposure to UV incident on the skin is 30 $J.m^{-2}$ effective when the spectral irradiance on skin surface is mathematically weighted by the hazard relative spectral effectiveness factor from 180 nm to 400 nm. Several tables express the relative spectral effectiveness of each wavelength and the maximum values of radiant UV exposure incident upon the unprotected skin with an 8-hour period.

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