SUNSCREENS WITH HIGH SPF VALUES ARE NOT EQUIVALENT IN THE PROTECTION FROM UVA INDUCED POLYMORPHOUS LIGHT ERUPTION

H. STEGE [1], M. BUDDE [1], S. GRETHER-BECK [1], A. RICHARD [2], A. ROUGIER [2], T. RUZICKA [1], J. KRUTMANN [1]

[1] *Clinical and Experimental Photodermatology, Department of Dermatology, University of Düsseldorf, GERMANY* [2] *- La Roche-Posay Pharmaceutical Laboratories, Asnières, FRANCE*

INTRODUCTION

Polymorphous light eruption (PLE) is the most frequent photodermatosis with an estimated incidence of approximately 3-17% (1). Photoprovocation testing has revealed that the vast majority of PLE patients (> 80%) is sensitive to longwave ultraviolet (UV) radiation, that is radiation in the range of 340-400 nm (UVA1) (2). Strategies directed at prevention of PLE therefore include sunscreens which preferentially absorb in the UVA range.

The efficacy of sunscreens is usually indicated by their protection factors (3). Accordingly, the sun protection factor (SPF) reflects the capacity of a given sunscreen to prevent solar radiation-induced erythema, and the pigment darkening factor serves as a measure for the UVA protective capacity. Measurement of the SPF follows clear rules that have been defined and standardized by the COLIPA. In contrast, the pigment darkening factor may be determined by two different methods, that is the immediate pigment darkening method and the persistant pigment darkening method. The relationship between these factors and the capacity of a given UVA-absorbing sunscreen to protect PLE patients from developing skin lesions is currently unknown. Here we have therefore compared three different and commercially available sunscreens with defined SPFs for their capacity to prevent the development of skin lesions in PLE patients undergoing photoprovocation testing. The sunscreens that we have compared were characterized by very high SPFs and thus did not differ significantly in their capacity to reduce the amount of UVB radiation penetrating into the skin (between 2 and 4%; table 1). Two of them were also known to have a high UVA-PF, reducing the amount of UVA radiation penetrating into human skin by 94% - 96%.

MATERIAL AND METHOD

Patients:

Thirteen patients (6 female, 7 male) with a history of PLE and positive photoprovocation testing were enrolled after written informed consent was obtained.

Photoprovocation testing:

In order to provoke the development of skin lesions in PLE patients, individual predilection sites (forearms and back) were exposed on three consecutive days to 100 J/cm^2 UVA radiation from a Sellamed 2000 irradiation device (Sellas Systems) at an intensity of 60 mW/sec. Irradiated skin sites were evaluated for the development of skin lesions immediately and 24 hours after each exposure.

Sunscreens:

Three different sunscreens were assessed. Details including the type of absorber present in each sunscreen, SPF, UVA-PF, and the capacity of each sunscreen to reduce the amount of UVB or UVA radiation penetrating into skin are given in table 1. Each sunscreen was applied 20 minutes prior to irradiation on a given test area of 6 x 6 cm according to the COLIPA norm.

RNA Extraction and RT-PCR Analysis. In 3 of 13 patients, 4 mm punch biopsy specimens were obtained from unirradiated control skin, from an unprotected and from a sunscreen C-pretreated photoprovocation test site 24 hours after the last irradiation. Intercellular adhesion molecule-1 mRNA expression was assessed in a semiquantitative manner by differential RT-PCR. This method has previously been used for analysis of in-situ expression of specific mRNAs and found to be highly sensitive and reliable (4-6). Each PCR of each sample was carried out at least two times. Products were visualized by gel analysis using ethidium bromide staining.

Table 1:
Description of the tested sunscreens

Sunscreen	UVB Absorber	SPF (UVB)	Reduction of UVB in %	UVA Absorber	UVA-PF	Reduction of UVA in %
A	Eusolex® 6300 Parsol® MCX Uvinul® T 150 Neoheliopan	> 75	> 98.6	Parsol® 1789 TiO_2	15 (IPD method)*	93.3
B	Eusolex® 6300 Parsol® MCX Uvinul® T 150	35	97.1	Parsol® 1789 TiO_2	unknown	unknown
C	Octocrylene	> 60	> 98.3	Mexoryl® SX Mexoryl® XL Parsol® 1789 TiO_2	28 (PPD method)**	96.43

* **Immediate Pigment Darkening method (IPD method)**
** **Persistent Pigment Darkening method (PPD method)**

RESULTS

Photoprovocation testing was positive in all patients assessed. The capacity of the three sunscreens tested to provide protection against the development of skin lesions in these patients markedly differed (Photo 1). Sunscreen A provided protection in 6 out of 13 patients, sunscreen B in 3 out of 13 patients, and sunscreen C in 13 out of 13 patients.

Development of skin lesions in irradiated skin areas was associated with an increased expression of keratinocyte ICAM-1 mRNA expression (Photo 2). Application of sunscreen C to test areas prior to photoprovocation testing completely prevented not only the development of skin lesions, but also the increase in ICAM-1 mRNA expression (Photo 2).

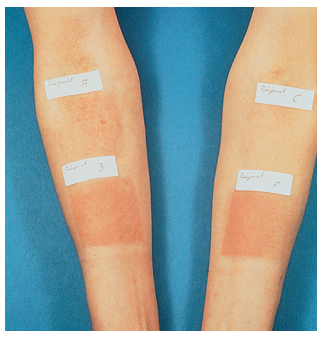

Photo 1:
Photoprovocation test reactions 24 hours after the 3rd UVA radiation exposure in a patient with polymorphous light eruption. Prior to irradiation, test sites were either left unprotected (left arm, lower test site) or protected with suncreens A, B or C as indicated.

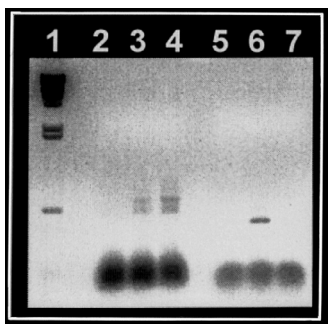

Photo 2:
Semiquantitative RT-PCR for ICAM-1 mRNA expression in photoprovocation test areas 24 hours after the 3rd UVA radiation exposure of a PLE patient. Biopsies were obtained from unirradiated control skin (no UVA), unprotected, UVA-irradiated skin (UVA) or sunscreen C-pretreated, UVA-irradiated skin. ICAM-1 mRNA expression was assessed by semiquantitative RT-PCR as described in Material and Method and visualized by gel analysis. Lane 1: lambda HindIII standard; lane 2: b-actin mRNA expression in unirradiated control skin; lane 3: b-actin mRNA expression in unprotected, UVA-irradiated skin; lane 4: b-actin mRNA expression in sunscreen C-pretreated, UVA-irradiated skin; lane 5: ICAM-1 mRNA expression in unirradiated control skin; lane 6: ICAM-1 mRNA expression in unprotected, UVA-irradiated skin; lane 7: ICAM-1 mRNA expression in sunscreen C-pretreated, UVA-irradiated skin.

DISCUSSION

In the present study we have compared the capacity of three different sunscreens to protect PLE patients by employing a photoprovocation protocol, in which predilection sites are exposed for 3 consecutive days to daily exposures with 100 J/cm^2 of UVA radiation. All patients tested had a history of positive photoprovocation testing using this standard protocol. We have selected UVA-sensitive PLE patients, because they represent the vast majority of cases and may thus be regarded as prototypic for this particular photodermatoses (2). By employing the above mentioned standard photoprovocation protocol it was observed that positive photoprovocation results could be obtained in 100% of tested patients. This observation indicates that the photoprovocation protocol used is characterized by a high intraindividual reproducibility. It is therefore ideally suited to evaluate measures directed at the prevention of UVA radiation-induced skin lesions in PLE patients.

Among these measures, sunscreens have previously been reported to be of benefit for PLE patients (1). This is in agreement with the present observation that topical application of sunscreens prior to photoprovocation testing prevented the development of skin lesions in PLE patients. The capacity of the 3 sunscreens tested in the present study to provide protection, however, varied markedly. This finding was somewhat surprising, since the tested sunscreens did not differ significantly when compared for their ability to reduce the amount of UVB or UVA radiation penetrating into the skin, as indicated by their high SPF and UVA-PF values. The major difference between the 3 sunscreens is given by the type of UV-filtering systems present in each sunscreen. It appears that Mexoryl® SX plus Mexoryl® XL is the most efficient combination providing 100% protection.

Effective prevention of clinically apparent skin lesions in PLE patients through application of sunscreen C was associated with complete inhibition of UVA radiation-induced expression of ICAM-1 mRNA expression in human keratinocytes. This observation further supports the concept that PLE represents an abnormal response of human skin towards UVA radiation that differs at a quantitative level by showing an overshooting and sustained expression of proinflammatory molecules such as ICAM-1 (7). Recent *in vitro* studies indicate that UVA radiation-induced keratinocyte ICAM-1 expression is mediated through the generation of singlet oxygen (8,9). It is therefore tempting to speculate that sunscreen C, that contains the combination of Mexoryl®XL and Mexoryl®SX, is particularly well suited to protect human skin from UVA radiation-induced generation of singlet oxygen. The combination of these two UV-filtering systems may thus not only be of benefit for protection of PLE patients, but may also be superior to conventional sunscreens in protecting against other UVA radiation-induced, singlet oxygen-mediated biological effects. These could possibly include protection against singlet oxygen-mediated upregulation of matrix metalloproteinase I, II and III (10) expression in human dermal fibroblasts or the UVA radiation-induced generation of large scale deletions in mitochondrial DNA in dermal fibroblasts (11,12). Both effects are thought to be pivotal to UVA radiation-induced actinic damage in human skin, thus making sunscreen C a prime candidate for prevention of photoaging.

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