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Evidence for a New Paradigm for UV Exposure: a Universal Schedule that is Skin Phototype-Independent

Sharon A. Miller¹, Sergio G. Coelho², Scott W. Miller¹, Yuji Yamaguchi², Vincent J. Hearing², and Janusz Z. Beer¹

¹Center for Devices and Radiological Health, Food and Drug Administration, Silver Spring, MD 20993 USA

²Laboratory of Cell Biology, National Cancer Institute, National Institute of Health, Bethesda, MD 20892 USA

Summary

Background—The Food and Drug Administration has published guidelines for manufacturer-recommended exposure schedules for UV tanning, intended to limit acute and delayed damage from UV exposure. These guidelines recommend that exposure schedules be adjusted for skin phototype. However, it has been shown that the dose necessary to produce tanning is similar for phototypes 2 to 4.

Methods—We observed tanning in phototypes 2 and 3 from repeated UV exposures over a 5-week period. Pigmentation was evaluated visually, instrumentally and through Fontana-Masson staining of biopsies.

Results—The resultant pigmentation was equal or greater in phototype 3 compared to phototype 2 – both visually and instrumentally - measured on day 31 of the exposure protocol. The amount of melanin measured in biopsies taken 24 h post-exposure was also greater in phototype 3 compared to phototype 2.

Conclusion—Published data on tanning in phototypes 4 and 5 supports our findings that higher phototypes can develop pigmentation more efficiently than lower phototypes.

Therefore, a universal exposure schedule (based on sensitivity of phototype 2) can be used for all phototypes that are expected to engage in indoor tanning. This approach will result in a reduction of the UV burden for skin phototypes 3 and above.

Keywords

ultraviolet; indoor tanning; skin phototype; exposure schedule

The Fitzpatrick system of skin phototyping (1) has been used for decades, mainly to determine appropriate phototherapy treatment regimens. It is also used in the indoor tanning industry for adjusting the exposure time and, therefore, the UV dose. The Fitzpatrick system assigns human skin to one of 6 distinct phototypes and is based on responses to 2 questions about an individual's sensitivity to sunburn and ability to tan. The indoor tanning industry has developed its own questionnaire [<http://www.tanningtraining.com/btf/>]

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[stQuestionnaire.pdf](#)] that uses responses to 8 questions, including questions on phenotype and racial background.

The US Food and Drug Administration (FDA) has regulated indoor tanning equipment since 1979 (2). The deleterious effects of UV exposure are well known and the purpose of the FDA regulations is to limit both acute and delayed damage from such exposure. Current regulations (3) stipulate that the manufacturer of the tanning equipment provide a recommended exposure schedule based on the UV output of the device. FDA provided additional guidance in a policy letter (4) which recommends that exposure schedules be tailored to different skin phototypes. This was largely based on the photobiological knowledge at the time, which indicated that UV sensitivity was significantly associated with skin phototype. According to Pathak and Fanselow (5) phototypes 2, 3 and 4 had mean Minimal Erythema Doses (MED) of 210 J/m², 360 J/m² and 780 J/m², respectively. As a result, tanning exposure schedules were designed to expose skin phototype 2 to doses lower than the MED for the most sensitive individuals in this group, and allowed higher doses for higher skin phototypes. Skin phototype 1 individuals were not included, as they are not able to tan. This exposure scheme operates under the paradigm of giving the highest dose possible, while avoiding erythema.

There was a limited amount of data on melanogenesis available at the time the FDA guidelines were written. The minimal melanogenic dose (MMD) is defined as the dose of UV radiation that produces detectable pigmentation of the skin 5 to 7 days after exposure. Pathak and Fanselow (5) found that the MMD was essentially the same for skin phototypes 2, 3 and 4. When exposures are repeated, a much lower UV dose (per exposure) can induce melanogenesis as compared to what is needed for a single exposure (6).

The efficiency of the tanning process strongly depends on the UV spectrum used. UVA (320 – 400 nm) radiation (especially UVA1 (340 – 400 nm)) is more melanogenic than UVB (290 – 320 nm) or solar simulated radiation (7, 8). We found that a 2% UVB/98% UVA tanning source produced darker pigmentation more rapidly than did a 5% UVB/95% UVA source for equally erythemogenic doses (9).

In a survey of over 29,000 adults, it was reported that the majority of indoor tanners in the US are UV-sensitive non-Hispanic whites (10) which includes phototypes 1 thru 4. In this study, we compared the tanning ability of skin phototypes 2 and 3. We employed equally erythemogenic repeated doses, as determined by spectral weighting with the CIE reference erythema action spectrum (11). Our exposure protocols followed both the FDA guidance for sunlamp exposure schedules (5) and the International Electrotechnical Commission (IEC) standard (12) in defining the first and maximum allowable doses using an erythema action spectrum. However, as shown in our previous publication (9), the exposure protocols employed in this study result in cumulative doses that are a factor of 2 to 3 lower than that recommended by current FDA guidelines. We used two different UV sources, one with a relatively high proportion (5%; Source 1) and the other with a relatively low proportion (2%; Source 2) of UVB. Both lamps are commonly used in tanning devices. We believe that a new paradigm should be used when designing exposure schedules for indoor tanning, i.e. the exposure schedule should be based on the minimum dose necessary for tanning, not burning. This paradigm leads to a universal exposure schedule for all skin phototypes that are expected to engage in indoor tanning. In addition, the use of such a schedule would reduce the UV burden for all phototypes, especially 3 and above, which should result in a reduction of the long-term deleterious effects of UV exposure for this population.

Subjects and Methods

Subjects

We recruited 40 healthy human subjects from the Washington, DC metropolitan area. These subjects gave informed, written consent prior to enrolling in the study. After signing the consent document, each subject was screened by a dermatologist.

The FDA Risk Involving Human Subjects Committee (the IRB of record) approved this study (#01-026R).

Fitzpatrick Phototyping

We determined the skin phototype on the basis of answers to the following questions:

1. After your first midday exposure of 45 to 60 minutes to summer sun, would your unprotected and previously unexposed skin:

- B1 always burn easily
- B2 burn slightly
- B3 rarely burn
- B4 never burn

C. One week later, would your skin develop:

- C1 no tan
- C2 slight tan
- C3 light brown tan
- C4 moderately brown tan
- C5 dark brown tan
- C6 black tan

Responses of B1 and/or C2 qualified as skin phototype 2. Responses of B2 and/or C3 qualified as skin phototype 3. Only subjects qualifying as skin phototypes 2 or 3 were enrolled.

Predicting photosensitivity using Tanning Industry Questionnaire

To explore real-life practices, we also used a questionnaire that was developed by the indoor tanning industry (National Tanning Training Institute (NTTI) - <http://www.tanningtraining.com/btf/stQuestionnaire.pdf>—originally provided to us by Donald Smith, Non-ionizing Radiation Research Institute, personal communication). This questionnaire interrogates 7 characteristics: (1) color of untanned skin, (2) natural hair color, (3) eye color, (4) number of freckles, (5) ethnic origin, (6) sunburn potential and (7) tanning potential. Each question gives a choice of 4 to 6 responses that increases in point value; with decreasing sensitivity to UV. Scores of 4 to 21 points are categorized as skin type 2, and scores of 22 to 41 are categorized as skin type 3. A score > 85 points is categorized as skin type 6. This questionnaire was used in our study only for analyses, i.e. not as a criterion for inclusion/exclusion.

Procedures

At each visit, the subjects underwent the following procedures: (1) visual assessment, (2) digital and conventional photography, (3) diffuse reflectance spectrometry and (4) UV exposure on the study areas (as indicated by the specific exposure protocol). The subjects

were exposed in a supine position under the tanning canopy with a custom-made template, attached to the mid-back of the subjects. The rest of the subject's body was protected from UV exposure. Skin biopsies were taken from UV-treated areas on day 24 for protocols A and B and on day 31 for protocol C and the unexposed control area, X. For details see (9, 13).

Photographic Documentation

Photographs were taken at the beginning of each visit to document the appearance of the skin over time as described in (9).

Ultraviolet radiation sources and measurements

For the evaluation of each subject's minimal erythema dose (MED), we used an array of eight Kodacel-filtered FS lamps (FSX24T12/UVB/HO, National Biological Corporation, Twinsburg, OH) as described in (9).

For the tanning exposures, we used a 12-lamp tanning canopy (SunQuest Model SQ 2000S, ETS, Indianapolis, IN) designed for home use. The canopy was equipped with 12-100 watt tanning lamps that are commonly used for tanning (Beach Sun, Light Sources, Orange, CT for subjects T7 – T30 defined as Source 1 (5% UVB/95% UVA); Cosmolux VLRT, Cosmedico, Germany for subjects T31 – T52, defined as Source 2 (2% UVB/98% UVA)). The emission spectra of all lamps used in this study are shown in (9). Daily measurements of the UV intensity at each 3×3 cm exposed site on the subjects' backs were used to determine exposure time as described in (9).

Determination of Minimal Erythema Dose (MED) and Minimal Melanogenic Dose (MMD)

Exposures were administered on one side of the back to determine each subject's Minimal Erythema Dose (MED) as described in (9). Briefly, eight 2×2 cm areas were exposed to arithmetically increasing UV doses from an array of Kodacel-filtered FS lamps (see UV sources). We used the CIE reference action spectrum for erythema (11) to calculate the wavelength-weighted administered doses. All doses reported in this paper are erythema-effective doses. The actual MED of each subject was determined by a visual assessment (performed by trained observers) of the redness in each area 24 hr after exposure.

We used a grading scale for erythema that ranged from 0 for no reaction to 5 for a 'violaceous red' reaction. The subject's MED was defined as the dose that produced a grade of 2 - pink erythema with at least one distinct border. The MMD was determined using the same sites. MMD was defined as the lowest dose that produced a light brown pigmentation (grade = 2, see below) eight days after exposure.

UV Exposure Schedules

Table 1 shows the three UV exposure protocols designed for this study. Each protocol used an initial dose of 100 J/m^2 (equivalent to one Standard Erythema Dose, or SED, as defined by the CIE (11)). In protocols A, B and C, doses increased by increments of 25% up to 380 J/m^2 , with exposures ceasing on day 23 at a cumulative dose of 1900 J/m^2 ; by increments of 40% up to 600 J/m^2 , with exposures ceasing on day 23 at a cumulative dose of 2900 J/m^2 ; and by increments of 50% up to 600 J/m^2 , with exposures ceasing on day 30 at a cumulative dose of 4200 J/m^2 , respectively. These protocols were used for 21 subjects treated with Source 1 and for 19 subjects treated with Source 2.

Visual evaluation of changes in skin pigmentation

At each visit, the skin pigmentation, or tan, was evaluated visually prior to that day's UV exposure using the grading scale shown below:

- 0 No reaction
- 0.5 Observer indecisive
- 1 Minimal perceptible pigmentation, faint or no borders
- 2 Light brown
- 3 Moderately brown
- 4 Dark brown

Diffuse Reflectance Spectrometry (DRS)

We measured the skin color using a Minolta CM-2002 spectrophotometer (Minolta Corporation, Ramsey, NJ). The Minolta CM-2002 measures the diffuse reflectance (DR) from 400 to 700 nm at 10-nm increments using an integrating sphere with an 8-mm aperture and a target mask that minimizes pressure in the measured area. The CM-2002 was calibrated according to the manufacturer's recommendations. At each visit, 3 readings of spectral reflectance were taken of all 4 study areas and the 3 readings were averaged.

The Minolta CM-2002 uses the spectral reflectance data to calculate the $L^*a^*b^*$ values of the CIE system of color quantification (14). L^* , luminous reflectance (quantity of reflected light weighted with the spectral response of the human eye), indicates lightness. Therefore, the lower the L^* value, the darker the sample appears. Changes in the L^* value (ΔL^*) over time, are reported in this paper. Additionally, using a previously described algorithm (15), the spectral data were transformed into apparent melanin concentrations. The change in apparent melanin concentrations over time are also reported.

Skin Biopsies

Modified shave biopsies (4 mm diameter) of skin were taken from the 3 UV-exposed sites 1 day after the last UV exposure, i.e. after 8 exposures (day 24) for protocols A and B, and after 10 exposures (day 31) for protocol C, and from an adjacent unirradiated area – X – as a control. Each biopsy was placed dermis side down on a Millipore filter and fixed with 4% formaldehyde, embedded in paraffin, sectioned at 3 μ m-thickness and mounted on silane-coated glass slides.

Determination of Melanin Content in Skin Biopsies

Melanin content was measured in fixed and sectioned skin samples from the integrated density in given areas of the epidermis in each section, using the Fontana-Masson method (16) as described previously (17- 19). Melanin content was determined using a Leica DMRB/DMLD microscope (Leica Microsystems, Bannockburn, IL, USA), a Dage-MTI 3CCD 3-chip color video camera (Dage-MTI, Michigan City, IN, USA), and ScionImage software (Scion Corp, Frederick, MD, USA). Using this approach, melanin contents were measured at the end of the UV exposure protocols, and for the unexposed control and are reported in arbitrary units (AU). This analysis was conducted for 17 Fitzpatrick phototype 2 subjects and 10 Fitzpatrick phototype 3 subjects.

We compared the apparent melanin concentrations derived from the DRS data with the Fontana-Masson measurements performed on biopsies to obtain melanin concentration values at times for which the biopsy data were not available.

Statistical Evaluation

SAS Proc NPAR1WAY [SAS Institute, Inc., v 9.2] was used to analyze pigmentation at day 31 via Friedman's test (a nonparametric analog of the 2-way ANOVA) (20). Day 31 was selected as a convenient time point to observe maximum pigmentation for all subjects. The median change in luminous reflectance (ΔL^*) between skin phototypes 2 and 3 was examined, using exposure protocol (A, B, C, or control - X) as the independent variable.

To compare the pigmentation behavior over the entire course of the study, an analysis using a mixed effects linear model was conducted using SAS Proc MIXED (SAS Institute, Inc., v 9.2, Cary, NC, USA). The analysis used a random block, repeated measures design with mean change in L^* as the response variable. Independent variables were skin phototype (2 or 3), and exposure protocol (A, B, C or X) as fixed effects and subject as a random effect. As each subject had four exposure protocols, and was assessed multiple times, the results were correlated within subject. This analysis adjusted the standard errors by using a compound symmetry covariance matrix in order to account for this correlation.

Results

Skin types and basic characteristics of subjects

In this study, only skin phototypes 2 or 3 were enrolled. By the Fitzpatrick method, there were 27 skin phototype 2 subjects and 13 skin phototype 3 subjects. The NTTI method categorizes individuals into one of 10 sub-phototypes. Phototype 2 is further divided into types 2A – 2C and phototype 3 into types 3A - 3C. Using the NTTI method, there were 9 skin phototype 2 subjects and 31 skin phototype 3 subjects.

The sex, age and skin phototype (both Fitzpatrick and NTTI), MED and ratio of MMD to MED of all enrolled subjects are shown in Table 2.

The mean value of L^* prior to exposure (in the test area) for Fitzpatrick phototype 2 was 69.94 (SD 2.79), while for phototype 3 it was 68.56 (SD 4.17); 2-sample independent t -test $t_{38} = 1.25$, $p = 0.22$. Thus, the difference in constitutive pigmentation was not statistically significant between the two Fitzpatrick phototypes. Similar results were obtained when the NTTI scale was used for Phototyping (data not shown).

The mean MED was 280 J/m² (SD 60) for Fitzpatrick phototype 2 and 310 J/m² (SD 130) for phototype 3; mean difference 26 J/m², $t_{14} = 0.68$, $p = 0.51$. The mean MMD was 410 (SD 65) for phototype 2 and 470 (SD 150) for phototype 3; mean difference 60, $t_{12} = 1.38$, $p = 0.19$. Thus there was no evidence of a statistically significant difference between Fitzpatrick phototypes 2 and 3 in either MED or MMD.

Effect of UV source

We examined the change in pigmentation over time for all subjects, and found that Source 2 produced slightly higher increases in pigmentation (ΔL^*) than Source 1, but the effect of exposure schedule (A, B, or C) was similar for both sources. Further, the difference between the UV sources was not statistically significant when UV source was included as an independent variable in the model. Hence, the data from the two UV sources were pooled for the analysis.

Changes in pigmentation – Visual Assessment

Fig. 1 shows examples of visible changes for one Fitzpatrick phototype 2 and one phototype 3 subject at five time-points during the study. By visual grading (Fig. 2, top row), skin phototype 3 subjects developed pigmentation as well or better than skin phototype 2 subjects

for all 3 exposure schedules and for both lamps. Table 3 shows the mean and standard deviation of the visual grade for the pooled data, evaluated at day 31. Phototype 3 subjects tended to achieve higher levels of pigmentation (as measured by visual grading) than subjects with phototype 2; Friedman's test for a difference in skin phototypes, blocked for exposure schedule: $X^2=6.605$, $p=0.0102$.

Changes in pigmentation – Diffuse Reflectance Spectrometry (DRS)

Using the DRS data, we evaluated the change in L^* and in apparent melanin concentration (according to (15)) over time for all 40 subjects. The apparent melanin concentration data showed high correlation (R^2 of 0.98 for phototype 2 and 0.99 for phototype 3) with the Fontana-Masson measurements performed on biopsies taken of all exposed sites and of the unexposed control. The effect of UV exposure on L^* (middle row) and apparent melanin concentration (bottom row) over the time-span of the study is shown in Fig. 2 for phototypes 2 and 3. Table 3 shows the mean and standard deviation of the change in L^* and melanin concentration, between the beginning of the study and day 31. There appears to be a consistent trend for subjects with skin phototype 3 to have a larger absolute increase in L^* than subjects with skin phototype 2. The results of the Friedman test suggest that this trend between skin phototypes 2 and 3 is statistically significant ($p<0.0001$).

Regarding the apparent melanin concentration, the data in Fig. 2 (bottom row) indicates that there is little difference between phototypes 2 and 3 for exposure protocols A and B. The difference for protocol C is more pronounced and phototype 3 shows a consistently larger mean melanin level over time compared to phototype 2.

Melanin content: Fontana-Masson staining of skin biopsy

We determined the melanin content by Fontana-Masson staining in skin biopsies taken 24 hrs after the final UV exposure and from the unexposed control area. The results presented in Table 4 correlate with our findings on apparent melanin concentration derived from the DRS data at several time-points throughout the study. They strengthen our findings that more pigmentation is produced in phototype 3 than in phototype 2 for the 3 exposure protocols used in this study. The difference is statistically significant after adjusting for exposure protocol: on average, the mean melanin content in Fitzpatrick skin phototype 3 subjects was 1.30 units greater than Fitzpatrick skin phototype 2 subjects, with a standard error of 0.50 ($p=0.0095$).

Discussion

All UV exposure causes DNA damage and induces other potentially carcinogenic molecular and cellular lesions. Hence, UV tanning represents an avoidable risk factor for melanoma and nonmelanoma skin cancer (21) and the FDA discourages this practice (<http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm186687.htm>). Our previous studies (9, 13) showed that repeated UV exposures produce significant DNA damage. Interestingly, the levels of cyclobutane pyrimidine dimers decreased while the numbers of p53-positive cells increased as the cumulative dose of UV increased. These measurements were taken at the end of the exposure series and compared with an unexposed control site. It would be useful to assess UV damage at multiple times during the course of the repeated exposures. Such data would help to fully assess the differences in UV damage caused by different exposure protocols.

There are at least two approaches that can be used to reduce the cumulative dose to UV tanners: (1) reduce the frequency of exposures and/or (2) reduce the absolute dose per exposure. Because it is well-known that a tan takes up to 5 days to develop (5), we chose to

reduce the frequency of exposure to two times per week. In addition, de Winter *et al.* (22) showed that it takes 3 to 4 days for DNA damage from a 1.2 individual MED dose to return to background levels. Dowdy *et al.* (23) propose a universal indoor tanning exposure schedule, based on 3 exposures per week; but using a maximum dose of 500 J/m², instead of the 600 J/m² used in our study. Even with the reduced maximum dose, their cumulative dose over a 4-week time period is 20% higher than that resulting from our exposure protocol B. Our previous publication (9) showed that exposure protocol B produced similar pigmentation to protocol C, which used a 46% higher cumulative dose. Thus, merely reducing the maximum allowable dose does not achieve the same savings in cumulative dose as does reducing the frequency of exposure. Nevertheless, any means of reducing the UV burden should be explored and, in fact, our studies (9, 24) have shown that the cumulative dose required to produce a moderate tan can be reduced by a factor of 2 to 3 below the doses used in current practices. The fact that higher skin phototypes can tan as well, or better, than lower phototypes (5) prompted us to study the differences in pigmentation caused by repeated UV exposures in humans of different phototypes.

To our knowledge, this is the first study that compares resulting pigmentation levels when different skin phototypes are given identical repeated, physical doses. As early as 1983, Pathak and Fanselow found similar MMDs for skin phototypes 2 to 4. Since that time, most studies of UV-induced pigmentation in different skin phototypes have used doses that increased according to skin phototype. In 2000, Caswell (25) exposed phototype 3 and 4 subjects to UV radiation from tanning beds using the 1986 FDA guidelines. He administered three exposures per week over a period of eight weeks. Slight adjustments were made to the exposure time for different skin phototypes, resulting in a cumulative dose of 92.4 SED (9240 J/m²-eryth. eff.) for phototype 3 and 94.4 SED (9440 J/m² – eryth. eff.) for phototype 4. However, he saw no significant differences in tanning response of phototypes 3 and 4 (26). Sheehan *et al.* (27) saw higher levels of tanning in skin phototype 4 compared to phototype 2, when daily, equally erythemogenic doses of 0.65 MED (pre-determined for each individual) were administered. The physical doses given to phototype 4 were approximately 30% higher than those given to phototype 2 subjects.

Ravnbak and Wulf (28) exposed skin phototypes 2 to 5 to four different UV sources. Their exposure protocol was based on the individual MMD, which was 5.3 SEDs for phototype 2 and 10.5 SEDs for phototype 5, with intermediate values for phototypes 3 and 4. After five daily repeated exposures, they found that the MMD was independent of pre-exposure pigmentation and skin phototype, except when a solar simulator and narrow-band UVB sources were used. Their study provides useful supplementary data on skin phototypes 4 and 5 that supports our findings on skin phototypes 2 and 3.

To categorize the UV sensitivity of the study subjects, we used the classic Fitzpatrick Phototyping system and the industry-developed NTTI system. Our results did not find any statistically significant relationship between Fitzpatrick phototype and the MED or MMD. This has been reported by others (29). Regardless of the phototyping approach, our final results were very similar. It is interesting to note that there were more subjects who were categorized as phototype 3 using the NTTI system than there were when using the Fitzpatrick system (31 vs 13). This indicates that the NTTI system is more liberal in assigning skin phototype than the classic Fitzpatrick system.

In summary, using different analyses, we showed that the propensity of phototype 3 to develop UV-induced pigmentation is the same or greater than phototype 2, when identical exposure schedules are administered. Hence, there is no reason to differentiate guidance on developing a tan for different phototypes. This indicates that the FDA Guidance of 1986 (4) should be revised – not only by allowing the use of a universal schedule for all phototypes -

but also to decrease the frequency of exposure and, thereby, reduce the cumulative dose (24). The use of our phototype-independent schedules can substantially reduce the UV burden to those who, in spite of medical advice and educational efforts, use UV for intentional tanning and, in particular, for skin phototypes 3 to 5.

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Fig. 1. Digital images of changes in pigmentation over time (days 1, 9, 16, 26 and 44) for phototype 2 (top - subject T45) and phototype 3 (bottom – subject T35). The doses administered to sites A, B and C are as shown in Table 1. The control area received no UV exposure.

Fig. 2. Visual grading (top), change in L^* , and change in apparent melanin concentration (derived from DRS data) vs day for Fitzpatrick phototypes 2 and 3. The cumulative doses (in erythema-effective kJ/m² are shown at the lower right corner).

Exposure schedules designed for this study. Doses are in erythema-effective J/m² (i.e. weighted with the 1998 CIE Reference Action Spectrum for Erythema (11).

Table 1

# of week			Dose (J/m ²)		
	Visit	Day	A	B	C
1	1	2	100	100	100
	2	3	130	140	150
	3	5	160	200	230
2	4	9	200	280	340
	5	12	250	400	500
3	6	16	300	560	600
	7	19	380	600	600
4	8	23	380	600	600
	9	24	0	0	0
	10	26	0	0	600
	11	30	0	0	600
5	12	31	0	0	0
	13	37	0	0	0
6	14	44	0	0	0
	Total		1900	2880	4200

Table 2

Study subjects and their basic characteristics.

Subject #	Sex	Age (years)	Skin Phototype Fitzpatrick	Skin Phototype NTTI	MED J/m ²	MMD/MED
T7	F	32	2	3A	385	1.1
T8	F	40	2	2C	205	1.6
T9	M	33	2	3A	185	2.2
T10	F	28	2	2B	330	> 1.3
T11	F	23	2	3A	345	> 1.5
T12	M	24	2	3A	285	> 1.5
T13	F	50	3	3A	355	> 1.5
T14	M	40	3	3A	170	1.7
T16	M	45	2	2C	335	1.2
T17	F	38	2	3A	330	1.4
T18	F	36	2	3A	290	> 1.5
T19	M	34	2	3B	195	1.7
T20	F	30	3	2C	185	1.0
T21	F	38	2	2B	320	> 1.5
T22	M	24	2	3A	330	> 1.5
T24	F	22	3	3C	615	> 1.2
T25	M	29	2	3A	200	1.5
T26	F	26	2	3A	295	> 1.5
T27	F	41	3	3B	220	2.0
T28	M	31	2	3A	210	1.7
T30	F	27	2	2C	225	1.6
T31	M	41	2	3A	250	1.25
T32	M	26	2	2C	300	1.5
T33	F	28	3	3A	225	1.7
T35	F	26	3	3A	450	> 1.5
T36	M	32	2	3A	190	1.7
T37	M	57	3	3A	300	1.5

Subject #	Sex	Age (years)	Skin Phototype Fitzpatrick	Skin Phototype NTTI	MED J/m ²	MMD /MED
T38	M	39	2	3A	250	1.5
T40	F	34	2	3A	315	1.4
T41	F	62	3	3A	450	1.5
T42	F	24	2	2C	300	1.3
T43	M	35	2	3A	300	1.25
T44	F	65	2	3A	375	1.4
T45	F	25	2	2C	225	1.7
T47	M	47	3	3A	200	2.0
T48	M	47	2	3A	375	1.2
T49	F	45	2	3A	250	1.5
T50	F	35	3	3B	300	1.0
T51	F	29	3	3B	300	1.25
T52	F	33	3	3B	225	2.0

* In some cases, the MMD was greater than the highest dose given, hence the use of the '>' sign for some subjects.

Table 3

Change in pigmentation between beginning of the study and day 31 as assessed visually and measured by DRS; mean and (standard deviation); ΔL^* and melanin concentration in arbitrary units.

Exposure Protocol	Fitzpatrick Phototype 2			Fitzpatrick Phototype 3		
	Visual Grade Mean (Std. Dev.)	ΔL^* Mean (Std. Dev.)	Melanin Concentration Mean (Std. Dev.)	Visual Grade Mean (Std. Dev.)	ΔL^* Mean (Std. Dev.)	Melanin Concentration Mean (Std. Dev.)
A	2.13 (0.33)	5.34 (1.24)	0.32 (0.11)	2.35 (0.38)	6.1 (1.81)	0.34 (0.15)
B	3.04 (0.31)	8.92 (2.49)	0.53 (0.18)	3.12 (0.22)	9.66 (2.40)	0.58 (0.16)
C	3.69 (0.28)	12.07 (3.10)	0.73 (0.21)	3.90 (0.25)	13.63 (3.45)	0.86 (0.20)

Table 4

Mean melanin content (AU) measured by Fontana-Masson and (standard deviation) shown for Fitzpatrick phototypes 2 and 3, for the 3 different exposure protocols and unexposed control, X. Biopsies were taken on day 24 for schedules A and B, and on day 31 for schedules C and X.

Fitzpatrick phototype	Melanin Content vs. Exposure Protocol			
	A Mean (Std. Dev.)	B Mean (Std. Dev.)	C Mean (Std. Dev.)	X Mean (Std. Dev.)
2	7.41 (2.0)	9.75 (3.0)	9.84 (2.7)	4.48 (1.4)
3	8.07 (2.4)	10.17 (3.1)	11.89 (2.6)	6.54 (3.0)
Difference (type 3 -type 2) $p = 0.0095$	0.66	0.42	2.05	2.06