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Outdoor Sunscreen Testing with High-intensity Solar Exposure in a Chinese and Caucasian Population

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Declarations

CG and CT are employees of ISDIN, Spain. PA, JK, TP, HL are consultants for ISDIN, GO was the investigator hired by the independent Clinical Research Organization (CIDP) who performed the clinical study. MH was appointed as a consultant by the CRO contracted to perform the clinical study. W Lai and W Lei have no conflict of interest.

Summary statement

Sunscreens are tested in laboratories, using artificial light sources to measure UVB or UVA protection, but in real life, sunlight contains other types of light that can also damage the skin. We tested an outdoor method to see if it could differentiate between the protection afforded by 3 different sunscreens (an SPF 15, SPF 30 and SPF 50+) in people from Chinese and Caucasian backgrounds. The method was able to identify differences in protection (levels of tanning and burning) among these products; we therefore think that it is a reliable method for categorizing sun protection. Chinese and Caucasian people might have different responses to sun exposure, but larger studies are needed.

Keywords: ethnic, racial, pigmentation, sunburn, erythema

Abstract

Background. Currently, sunscreens' sun protection factor (SPF) and ultraviolet (UV) A protection are tested separately under indoor conditions, without considering external conditions that may affect performance. Studies are often conducted in Caucasian individuals; other racial groups may respond differently.

Methods. An outdoor, double-blind, intra-individual study was performed in 63 healthy Chinese and Caucasian volunteers in Singapore. Subjects underwent one outdoor sun exposure lasting 2-3 hours. ISO reference products P3 (SPF 15), P5 (SPF 30) and P8 (SPF 50+) applied at 2 mg/cm^2 were compared against each other and against an untreated exposed area (positive control) and an unexposed area (negative control). Endpoints were investigator global assessment (IGA) of erythema at 24 hours, IGA of pigmentation at 1 week, and colorimetry (a*, L* and ITA) at 24 hours and 1 week.

Results. Clinical erythema and pigmentation scores were statistically significantly different among the three sunscreens, with the highest SPF product providing the highest protection, confirming the discriminatory capacity of the model used. Colorimetric assessment correlated well with clinical evaluation.

Conclusion

This study confirmed the feasibility of ranking sunscreens (at 2 mg/cm^2) based on clinical effects of high-intensity outdoor solar radiation. Larger studies are needed to look at differences in erythema and pigmentation reactions between Chinese and Caucasian individuals, which could be relevant for photoprotection.

Introduction

The ability of a sunscreen to prevent ultraviolet (UV)-induced erythema and pigmentation is assessed following the international validated indoor in vivo methods of sun protection factor (SPF) testing[1] (a measure of UVB protection) and UVA protection factor (UVAPF).[2] Of these, the SPF value is probably the most widely-recognized and widely-used measure of protection level. However, the testing methods use solar UV simulators that differ from real sunlight both in irradiance – the irradiance is higher than that of sunlight to avoid the need for prolonged exposure – and spectrum. Such indoor testing does not provide information on protection against other components of the light spectrum, such as visible light, which has been reported by several authors to induce both erythema and

pigmentation, nor how different components of the spectrum may interact to intensify such responses.[3-7] These aspects and how they affect the SPF value under conditions of real sun exposure remain unquantified. Some authors have argued that the overall protection level provided by a sunscreen in real life may be less than the reported SPF value,[8,9] be it due to the wavelengths,[9] or to suboptimal use, which is undoubtedly an issue in real-life use.[8,10-16] Likewise, the impact of environmental factors (such as atmospheric conditions or geographical location),[8,17,18] or sweat and heat[19,20] are not integrated in the indoor method.

Our group previously evaluated a method of outdoor sunscreen testing based on clinical erythema scoring and demonstrated that it could differentiate the level of sun protection provided by an SPF 50+ product versus the P3 (SPF 15) reference standard when applied at 2 mg/cm^2, based on evaluation of clinical erythema, colorimetry parameter a*, and immediate pigmentation by colorimetry parameter L* at 24 hours.[21] The limitations of that study included that the control products were limited to SPF 15 (*medium* protection) and SPF 50+ (*very high* protection). Previously, the ISO norm (24444: 2010)[22] for SPF testing used only the reference standards of SPF 4 (P7), SPF 16 (P2) and SPF 15 (P3); now, in the updated norm ISO 24444:2019, reference standard P7 (SPF 4) has been removed and three other reference standards, P5 (SPF 30), P6 (SPF 43) and P8 (SPF 50+), have been added to verify the test procedure.[1] Another limitation of our previous study was that it focused heavily on erythema, with no clinical scoring of light-induced changes in delayed pigmentation. Furthermore, the subjects we studied were all Caucasian. Sun protection strategies often target fair-skinned populations, due to an increased propensity to sunburn and high risk of skin cancers[23]; however, non-Caucasian skin types also require protection against skin cancer,[24] photoaging, and pigmentation changes. Asian, Latino and Black individuals are particularly susceptible to pigmentary disorders.[25,26] Thus, while photoprotection is required for individuals with skin of color, it is unclear if the recommendations should be the same as those for Caucasian individuals. In the English literature, there are only a few studies comparing the response of Asian and Caucasian skin to sunlight.[27-29]

The aim of the current study was to determine if this outdoor method would be able to differentiate more subtle differences between photoprotection levels by introducing an intermediate level of SPF, comparing products labelled as SPF 15 (P3), 30 (P5), and 50 (P8), as measured by erythema and delayed pigmentation. A secondary aim was to explore whether differences in skin responses to solar exposure between Chinese and Caucasian subjects could be observed.

Material and methods

Study design and population

This was a single-center, double-blind, randomized, intra-individual clinical study, conducted at an outdoor facility in Singapore in June-July 2019 (specifically, Sentosa island, very close to sea level). Seventy-nine healthy Caucasian and Chinese volunteers were recruited, aged 21-45 years, with skin colors from "light" "intermediate" and "tan" categories based on ITA determination[30] (**Table 1**). Individuals who had used a sunbed, or any depigmenting treatment within 3 months prior, or who had dermatological conditions (eg multiple nevi, freckles, excess hair or uneven skin tones, vitiligo, photodermatoses) or were using topical or oral medications (eg vitamin A derivatives, psoralen, aminolevulinic acid derivatives, anti-inflammatories, corticosteroids) that would affect assessment of efficacy or safety were excluded.

Sun exposure and protection

The methods followed those used in our previously-published study.[21] Briefly, on the backs of the volunteers, five 12 cm^2 squares were marked out with tape, while the rest of the back was protected with UV-protective clothing, including the non-exposed control area. Each square was randomized to receive one of three sunscreens, applied at 2 mg/cm^2: reference standards P8 (SPF 50+; UVAPF 20.2), P5 (SPF 30; UVAPF 9.2) or P3 (SPF 15; UVAPF 2.5) of ISO norm 24444:2019,[1] or no sunscreen (two squares). Of the two squares that had no sunscreen, one was exposed to sunlight for 1 hour (unprotected skin, positive control, 1-hour duration to minimize skin damage), and one was not exposed at all (unexposed skin, negative control). The investigator, technician, and subject were blinded to which areas were treated with which sunscreen. For safety reasons, if any area became erythematous during the experiment, it was to be covered with the same protective tape used to mark out the test areas.

Fifteen to 30 minutes after application, subjects spent 2-3 hours outdoors (earliest start time, 12.05; latest end time, 17.10), in a prone position, with the rest of the body covered with clothes, hats, and sunglasses, and facial sunscreen. To minimize unnecessary sunburn risk, the duration of exposure depended on the individual's skin color: those with intermediate or tan skin color were exposed for 3 hours, calculated as corresponding to a cumulative UVB dose of approximately 1800-2000 J/m^2 eff., while those with light skin color were exposed for 2 hours, or until they had received approximately 1200 J/m^2 eff, whichever occurred first. After exposure, subjects were instructed not to expose their

back again until the final evaluation (day 8). During this time, no topical cream (medical, cosmetic, or otherwise) was applied to the study areas and no oral anti-inflammatory drugs were allowed.

For each individual, the cumulative UVB and UVA doses received were measured with a PMA2100 radiometer along with PMA2101 erythema UVB and PMA2110 UVA sensors (all, Solar Light Company Inc, PA, USA), placed at the level of the subject's back. This radiometer reads the irradiance and through its software calculates the cumulative UVA (J/cm^2) and erythemally-weighted UVB (J/m^2 eff) dose received by multiplying irradiance and exposure time. The UV index was calculated from the values of erythemal UV irradiance measured by the radiometer. Irradiance was measured with the radiometer every 10 minutes of sun exposure. Temperature and hygrometry were recorded with a Testo 608-H1 thermohygrometer (Testo SE & Co.KGaA, Lenzkirch, Germany); both were measured in the same area where subject sun exposure occurred.

Outcomes

The primary outcome was the investigator global assessment (IGA) of clinical erythema at 24 hours after sun exposure, graded on a 6-point scale (0=none, to 5=very severe with blistering) (**Supplementary Table 1**).[21] This was performed by a trained physician under the supervision of a board-certified dermatologist. Failure of photoprotection was defined as erythema grade ≥2, that is, unequivocal erythema.

As a secondary outcome, IGA of delayed pigmentation was assessed 1 week after exposure (day 8, as a measure of light-induced increased melanogenesis) (0=no difference, to 4=intense dark brown) (**Supplementary Table 1**).

In addition to clinical scores, colorimetry assessment was performed at 24 hours and 1 week after sun exposure with the CR400 Chroma Meter (Konica Minolta Inc., Tokyo, Japan) for parameters a*=erythema, L*=pigmentation, and ITA°=skin color typing.[31] Colorimetry results are reported as percentage difference vs unexposed skin; absolute change (Δ) values[32] are also provided in supplementary material for completeness (**Supplementary Tables 3, 4 and 5**).

Before all assessments, subjects spent 15 minutes in a temperature- and hygrometry-controlled room. Safety was assessed through adverse event reporting and recording of signs or symptoms of skin irritation.

Ethics

The study was approved by Parkway Independent Ethics Committee (PIEC, 24/05/19), and conducted in compliance with the Declaration of Helsinki and its modifications, Good Clinical Practice E6(R1) (CPMP/ICH/135/95) and E6(R2) addendum, and according to local laws.

Statistical analysis

Analyses were performed on 63 subjects (see results below, and **Supplementary Figure 1**). Quantitative variables were summarized using measures of central tendency and dispersion. Qualitative variables were summarized using frequencies and percentages. In addition to treating the clinical scores of erythema as quantitative data, the frequency of each observation (erythema grade) was listed, by product.

For the clinical scores of erythema and pigmentation (ordinal in nature), the Wilcoxon signed rank test was used for pairwise comparisons between the concerned zones, while for colorimetry measurements (L*, a* and ITA°), which are highly numerical and fairly normally distributed, the paired samples t-test was used. Bonferroni's adjustment, a conservative method to adjust for the multiplicity problem, was used.

Statistical software SPSS 19.0 and Microsoft Excel 2010 or above were used. P-values <0.05 were considered significant.

Results

Seventy-nine subjects were enrolled in this study. Sixty-five participated in the exposure part of the study: weather conditions on one of the study days led to cancellation, and 13 subjects who had signed informed consent were unavailable to be rescheduled. One subject was found to have numerous solar lentigines on the back after having signed the consent form and therefore was rejected by the investigator before any study procedure. At the analysis stage, two subjects were deemed to have a baseline ITA value that was too low (<20) so were excluded. The results reported here are thus based on the 63 subjects with ITA>20 who received the sunscreens and sunlight exposure (**Supplementary Figure 1,** flowchart of participants). Participant characteristics are detailed in **Table 1**. Due to the small sample number in the Caucasian group, statistical analysis comparing the Caucasian and Chinese groups was not performed, but results are described. **Supplementary Table 2** contains detailed results of exposure times and durations and clinical scoring results. One subject had a zone where the SPF 15

product was applied, which required premature covering at 1 hour 36 minutes from the start of exposure; otherwise, the areas were exposed as per the protocol.

UV radiation doses

Depending on the day of exposure, the minimum UVB dose received during the study was 716.9 J/m^2 eff and the maximum was 1905.3 J/m^2 eff; the minimum UVA dose received was 11.41 J/cm^2 and the maximum was 42.22 J/cm^2. Eight subjects received less than 1000 J/m^2 effective of UVB radiation (5 *light* skin color, 2 *intermediate* and 1 *tan*) due to a change in weather conditions. All volunteers were exposed at some point to a high UV index (≥6); 35 subjects (53.8%) were exposed at some point to a very high UV index (8-10). The temperature ranged from 29.9°C to 48.4°C, and hygrometry from 29.5% to 75.3%.

Clinical erythema score at 24 hours

As expected, mean erythema score at 24 hours was highest in the positive control area (no sunscreen, exposed), where it showed an inverse relationship with skin color category (**Figure 1A and B**), despite the darker skin color categories being exposed for longer as part of the study design. There was a statistically significant difference in mean clinical erythema score among all test areas, except between the SPF 50+ and the unexposed area, confirming the capacity of the method to differentiate between sunscreen protection categories.

Erythema scores are presented in **Figure 1**. The Caucasian group appeared to have a higher mean erythema score than the Chinese group in the SPF 30 test area (**Figure 1A**). Also at SPF 30, the Chinese group had a greater proportion of subjects with no clinical evidence of burning (erythema score of 0) than the Caucasian group (**Figure 2A**). However, the limited Caucasian sample size prevents us from making meaningful comparisons between these groups.

In terms of failure of photoprotection (erythema score ≥2), overall there was one failure with SPF 50+ (grade 2 erythema in one individual with *light* skin color), three failures with SPF 30 (grade 2 erythema in two individuals with *intermediate*, and one with *tan* skin color), and 13 failures with SPF 15 (12 grade 2 and one grade 3 erythema; three *light*, six *intermediate*, four *tan*; the grade 3 erythema was in an individual with *tan* skin color). **Figure 2B** shows the proportion of subjects with failure of photoprotection by racial group.

Clinical pigmentation score at 1 week

The mean clinical pigmentation score at 1 week was significantly different among test areas (**Figure 3**). The Chinese group appeared to have greater pigmentation changes than the Caucasian group overall (despite having fewer subjects with *tan* skin color at baseline).

Colorimetry at 24 hours

At 24 hours, a* values aligned well with the clinical erythema scores, with mean a* values decreasing (less erythema) as SPF increased (**Figure 4A**). Data on absolute Δa* at 24 hours is provided in the supplementary material; the percentage of subjects with Δa* ≥2.5[33] decreased progressively as SPF increased.

Percentage differences compared to the unexposed control area showed statistically significant differences between adjacent photoprotection levels (**Figure 4A**). The percentage difference in a* between the unexposed control area and exposed unprotected control area was 101.2±58.3% in the Chinese group and 43.8%±32.5% in the Caucasian group.

Percentage changes in L* and ITA were more modest than changes in a* at this point (less than 10% change in L*, 30.8% change in ITA; **Figures 4B and 4C**). Both L* and ITA also showed statistically significant differences between adjacent SPF test areas at this point (**Figures 4B and 4C**).

Colorimetry at 1 week

The overall patterns in colorimetry (a*, L* and ITA) persisted at 1 week. The Chinese group appeared to show greater differences than the Caucasian group (**Figure 5**), though again, the small size of the Caucasian group severely limits interpretation. Percentage differences (vs unexposed) for all colorimetry parameters remained significant between adjacent areas (**Figure 5**).

Example photographs of the appearance of test areas are available in **Supplementary Figures 2 and 3**.

Discussion

The main objective of this study was to confirm the ability of this outdoor method to differentiate levels of protection from sunscreens with SPF 15, 30 and 50+ based on clinical erythema (typically, though not exclusively, linked to UVB) and pigmentation assessment (typically linked to UVA and high-energy visible light in skin phototype III and higher), taking into account the whole solar spectrum, with supporting colorimetry tests. An additional objective was to explore potential differences in sunscreen protection and responses to sunlight between Chinese and Caucasian populations living in Singapore.

This secondary objective was severely limited due to the drop out of Caucasian subjects, but some of the findings may stimulate further investigation.

It should be noted that this study was designed to test the discrimination between the three reference products of the ISO norm (24444)[1] in conditions of exposure to real sunlight. Although it used features of ISO testing methods as a baseline,[1,2] it did not strictly follow these methods. For example, the ISO for SPF testing,[1] which assesses erythema as an endpoint, requires a minimum ITA of 28 while the ISO for UVAPF testing,[2] which uses pigmentation as an endpoint, requires a minimum of 20. Other studies using outdoor methods of evaluating sun protection[21,34-39] have used criteria such as "phototypes" I-III, II-IV or I-IV. In the present study, which assessed both erythema and pigmentation, the initial inclusion criteria included subjects with "tan" skin color, corresponding to approximately phototype IV, and which has as its lower limit an ITA of 10; however, following review we excluded two subjects with a very low ITA (13 and 19, respectively), setting a minimum ITA of 20 in an attempt to bring it into line with the ITA used in ISO UVAPF testing.[2]

Overall, we found that all tested products, under these conditions, provided a level of photoprotection that aligned well with the reported SPF and UVAPF, in that it allowed sunscreens to be ranked in order of protection, based on both erythema (24 hours) and pigmentation (1 week). Colorimetry results also backed these results with statistically significant differences between all SPF levels both at 24 hours and at 1 week. This supports our previous findings[21] from a study that assessed SPF 15 vs 50+ based on erythema, but the present study adds a greater discriminatory capacity as it was possible to differentiate between SPF 30 (*high* protection) and the other categories of SPF 50+ (*very high* protection) and SPF 15 (*medium* protection).

Some results are worthy of further comment: under these high to very high UV-index conditions, the SPF 15 tested did not provide sufficient protection, since 20% of subjects experienced sun protection failure (erythema grade ≥2) including some subjects with *tan* skin color; the SPF 30 and SPF 50+ reference products had just a 4% and 1.5% failure rate, respectively. This confirms that SPF 15 is inadequate in this setting. Some previous outdoor studies have sought to determine whether SPFs above 50 provide additional benefit (generally finding that they do, under extreme outdoor conditions such as the beach or ski-slopes).[35-37,40] Ou-yang et al were able to determine that SPF 70 was more effective than SPF 30 in an outdoor study at the beach.[38] Lott et al assessed clinical erythema response with SPF30, 50 and 100, seeking to determine if SPFs above 50 offered clinically meaningful protection.[37] They concluded that SPF 50 and SPF 100 were "measurably better" than the SPF 30 product, but that neither offered complete protection, and noted that the SPF 30 did not offer good

protection in that fair-skinned study population. This is interesting because we also noted an apparent difference in skin reactions around the SPF30 mark, where there seemed to be a greater proportion of the Caucasian group with failure of sunscreen.

Previous outdoor studies[21,34-39] have used erythema as an endpoint, in line with the aim of preventing sunburn; naturally this is a key endpoint that must be assessed, but our study adds to this by including data on protection from solar-induced pigmentation. Interestingly, while we observed good protection against erythema, the protection against solar-induced pigmentation remain limited, even when using the SPF 50+ sunscreen. Thus, a further advantage of this method is that it allows simultaneous evaluation of erythema and pigmentation, which are usually tested separately with indoor in vivo methods.[1,2,41] It also takes into account the full solar spectrum including wavelengths of light outside the UV spectrum known to induce erythema and pigmentation in real life.[5,7,9,42]

Regarding potential differences between the Chinese and Caucasian groups, although the small sample size of the Caucasian group prevented statistical analysis and limits the generalizability of the findings, certain areas may warrant further larger studies on differences in sun protection requirements. In particular, it appears that, under the study conditions, "medium" SPF 15 offers insufficient protection for most, and "very high" SPF 50+ offers sufficient protection for most, whereas "high" SPF 30 may be enough for some population groups only, as reflected by differences in failure of photoprotection. We think that this difference is unlikely to be due to simple skin color differences between the groups, as the Chinese group did not have a greater proportion of darker skin color (based on ITA).

Another point that would warrant further study is the apparent greater pigmentation response in the Chinese group at 1 week on clinical scoring and supported on colorimetry parameters L* and ITA. This would need to be tested in a larger sample to determine if such a difference is maintained. If so, a possible explanation could be a higher susceptibility to the pigmenting effects of long wave UVA and HEV light[5] that are not well (or at all) protected with such sunscreens (low UVA protection for P5 and very low UVA protection for P3).

The lower clinical incidence of sunburn (greater proportion with grade 0 erythema) observed in the Chinese group in our study is in line with the reported lower rate of sunburn in Asian than White population groups (USA),[43] and the higher minimal erythemal doses required in Asian and particularly Chinese individuals, compared to Caucasians.[44] As described by Chan et al, Asian skin has a greater tendency to develop postinflammatory hyperpigmentation, and pigmentary disorders in general.[25] Indeed, melanogenesis can be stimulated with a suberythemogenic dose of solar radiation.[45]

Differences in pigmentation are due to melanin production and type,[46,47] melanosome stage, and melanin distribution in the epidermis.[48,49] This becomes clinically relevant because an inverse relationship exists between constitutive pigmentation and UV-induced DNA damage.[46,48] However, while clear differences in DNA repair have been demonstrated between Black and White skin, and even with Asian skin,[46] to our knowledge, direct comparison of DNA repair comparing Asian and Caucasian individuals with the same skin color category or phototype has not been studied. It is conceivable that different racial groups within the same skin color category or phototype could have different DNA repair mechanisms or inflammatory reactions, perhaps being more severe or prolonged once a threshold is reached.[50,51] This represents an appealing area for future investigation.

Outdoor studies can be difficult to standardize and are susceptible to many technical issues and weather conditions, but they help develop our understanding of photoprotection. This study was conducted on several days over a 3-week period, so there was some variation in conditions between subjects in terms of UV index, hygrometry etc, and some subjects (those with lighter skin color) received less exposure (2 hours rather than 3, to prevent severe sunburn); however, each subject served as their own control to try to reduce the effect of this variability. The study also provides some initial data on potential differences between Chinese and Caucasian groups, which could be used as a starting point for a larger study on this subject. Further studies could seek to prove or disprove potential differences between racial groups in response to solar exposure. This could help determine whether such population groups need the same level of UVB, UVA, and visible light protection, to provide a more personalized, effective protection.[42,52]

Conclusion

Under the conditions of this outdoor study, the proposed clinical model was able to discriminate and rank sunscreens of different protection categories based on clinical scoring of the key indicators of erythema and pigmentation and was supported with colorimetry. Larger studies are needed to analyze in more detail any potential differences in response to solar exposure between racial groups.

References

1. International Organization for Standardization. ISO 24444:2019. Cosmetics — Sun protection test methods — In vivo determination of the sun protection factor (SPF). Available at https://www.iso.org/standard/72250.html. Accessed 07 July 2020.

2. International Organization for Standardization. ISO 24442:2011 Cosmetics -- Sun protection test methods -- In vivo determination of sunscreen UVA protection. Available from: https://www.iso.org/standard/46521.html. Accessed 15 October 2020.
3. Schiecke SM, Ruwiedel K, Gers-Barlag H, Grether-Beck S, Krutmann J. Molecular cross-talk of the ultraviolet A and ultraviolet B signaling responses at the level of mitogen-activated protein kinases. J Invest Dermatol 2005; 124:857-859.
4. Mahmoud BH, Hexsel CL, Hamzavi IH, Lim HW. Effects of visible light on the skin. Photochem Photobiol. 2008;84(2):450-462.
5. Kohli I, Zubair R, Lyons AB, et al. Impact of Long-Wavelength Ultraviolet A1 and Visible Light on Light-Skinned Individuals. Photochem Photobiol. 2019;95(6):1285-1287.
6. Noda T, Kawada A, Hiruma M, Ishibashi A, Arai S. The comparison of sun protection factor values with different light sources. J Dermatol. 1992;19(8):465-469.
7. Kohli I, Chaowattanapanit S, Mohammad TF, et al. Synergistic effects of long-wavelength ultraviolet A1 and visible light on pigmentation and erythema. Br J Dermatol. 2018;178(5):1173-1180.
8. Lui H, Gallagher RP, Mclean DI. Use and Misuse of Sunscreens. In: Skin Cancer and UV Radiation. P. Altmeyer, K. Hoffmann, M. Stücker (Eds.) Springer-Verlag Berlin Heidelberg 1997. Chapter 9 pages 333-342.
9. Diffey B, Osterwalder U. Labelled sunscreen SPFs may overestimate protection in natural sunlight. Photochem Photobiol Sci. 2017;16(10):1519-1523.
10. Bech-Thomsen N, Wulf HC. Sunbathers' application of sunscreen is probably inadequate to obtain the sun protection factor assigned to the preparation. Photodermatol Photoimmunol Photomed. 1992;9(6):242-244.
11. Autier P, Boniol M, Severi G, Doré JF; European Organization for Research and Treatment of Cancer Melanoma Co-operative Group. Quantity of sunscreen used by European students. Br J Dermatol. 2001;144(2):288-291.
12. Lademann J, Schanzer S, Richter H, et al. Sunscreen application at the beach. J Cosmet Dermatol. 2004 Apr;3(2):62-8.
13. Brown S, Diffey BL. The effect of applied thickness on sunscreen protection: in vivo and in vitro studies. Photochem Photobiol. 1986 Oct;44(4):509-13.
14. Stokes R, Diffey B. How well are sunscreen users protected? Photodermatol Photoimmunol Photomed. 1997 Oct-Dec;13(5-6):186-8.

15. Faurschou A, Wulf HC. The relation between sun protection factor and amount of suncreen applied in vivo. Br J Dermatol. 2007 Apr;156(4):716-9.
16. Bimczok R, Gers-Barlag H, Mundt C, et al. Influence of applied quantity of sunscreen products on the sun protection factor--a multicenter study organized by the DGK Task Force Sun Protection. Skin Pharmacol Physiol. 2007;20(1):57-64.
17. Sayre RM, Kollias N, Ley RD, Baqer AH. Changing the risk spectrum of injury and the performance of sunscreen products throughout the day. Photodermatol Photoimmunol Photomed. 1994;10(4):148-153.
18. Hojerová J, Medovcíková A, Mikula M. Photoprotective efficacy and photostability of fifteen sunscreen products having the same label SPF subjected to natural sunlight. Int J Pharm. 2011;408(1-2):27-38.
19. Taylor CR, Stern RS, Leyden JJ, Gilchrest BA. Photoaging/photodamage and photoprotection. J Am Acad Dermatol. 1990;22(1):1-15.
20. Cho S, Lee MJ, Kim MS, et al. Infrared plus visible light and heat from natural sunlight participate in the expression of MMPs and type I procollagen as well as infiltration of inflammatory cell in human skin in vivo. J Dermatol Sci. 2008;50(2):123-133.
21. Granger C, Krutmann J, Bustos J, et al. New Methodology to Evaluate Sunscreens Under Outdoor Conditions: A Double-Blind, Randomized Intra-Individual Clinical Study of a Water-Based Broad-Spectrum SPF50+ Versus SPF15 (P3) and SPF50. Dermatol Ther (Heidelb). 2019;9(3):589-599.
22. ISO 24444:2010. Cosmetics — Sun protection test methods — In vivo determination of the sun protection factor (SPF). Available at https://www.iso.org/standard/46523.html. Accessed 07 July 2020.
23. Agbai ON, Buster K, Sanchez M, et al. Skin cancer and photoprotection in people of color: a review and recommendations for physicians and the public. J Am Acad Dermatol. 2014;70(4):748-762.
24. Sng J, Koh D, Siong WC, Choo TB. Skin cancer trends among Asians living in Singapore from 1968 to 2006. J Am Acad Dermatol. 2009;61(3):426-432.
25. Chan IL, Cohen S, da Cunha MG, Maluf LC. Characteristics and management of Asian skin. Int J Dermatol. 2019;58(2):131-143.
26. Ho SG, Chan HH. The Asian dermatologic patient: review of common pigmentary disorders and cutaneous diseases. Am J Clin Dermatol. 2009;10(3):153-68.

27. Rawlings AV. Ethnic skin types: are there differences in skin structure and function? Int J Cosmet Sci. 2006;28(2):79-93.
28. Kawada A, Noda T, Hiruma M, Ishibashi A, Arai S. The relationship of sun protection factor to minimal erythema dose, Japanese skin type, and skin color. J Dermatol. 1993;20(8):514-6.
29. Suzuki HS, Hammerschmidt M, Kakizaki P, Mukai MM. Phototype comparison between caucasian and asian skin types. Surg Cosmet Dermatol. 2011;3(3):193-6.
30. Del Bino S, Bernerd F. Variations in skin colour and the biological consequences of ultraviolet radiation exposure. Br J Dermatol. 2013;169 Suppl 3:33-40.
31. Ly BCK, Dyer EB, Feig JL, Chien AL, Del Bino S. Research Techniques Made Simple: Cutaneous Colorimetry: A Reliable Technique for Objective Skin Color Measurement. J Invest Dermatol. 2020;140(1):3-12.e1.
32. Healy ZR1, Dinkova-Kostova AT, Wehage SL, Thompson RE, Fahey JW, Talalay P. Precise determination of the erythema response of human skin to ultraviolet radiation and quantification of effects of protectors. Photodermatol Photoimmunol Photomed. 2009;25(1):45-50.
33. Ferguson J, Brown M, Alert D, et al. Collaborative development of a sun protection factor test method: a proposed European Standard. COLIPA Task Force 'Sun Protection Measurement', Europe. Int J Cosmet Sci. 1996 Oct;18(5):203-18.
34. Granger C, Sola Y, Gilaberte Y, Trullàs C. Outdoor testing of the photoprotection provided by a new water-based broad-spectrum SPF50+ sunscreen product: two double-blind, split-face, randomized controlled studies in healthy adults. Clin Cosmet Investig Dermatol. 2019 Jun 27;12:461-467.
35. Kohli I, Nicholson CL, Williams JD, Lyons AB, Seo I, Maitra P, Tian X, Atillasoy E, Lim HW, Hamzavi IH. Greater efficacy of SPF 100+ sunscreen compared with SPF 50+ in sunburn prevention during 5 consecutive days of sunlight exposure: A randomized, double-blind clinical trial. J Am Acad Dermatol. 2020 Apr;82(4):869-877.
36. Williams JD, Maitra P, Atillasoy E, Wu MM, Farberg AS, Rigel DS. SPF 100+ sunscreen is more protective against sunburn than SPF 50+ in actual use: Results of a randomized, double-blind, split-face, natural sunlight exposure clinical trial. J Am Acad Dermatol. 2018 May;78(5):902-910.e2.
37. Lott D. Testing SPF 15–100, Indoor vs. Outdoor. Cosmetics and Toiletries. 2013 Sept; Vol. 128, No. 9: 638-647.

38. Ou-yang H, Rzendzian RB. Sunburn Protection by Sunscreen Sprays at Beach. *Cosmetics* 2017, 4(1), 10.
39. Ou-Yang H, Jiang LI, Meyer K, Wang SQ, Farberg AS, Rigel DS. Sun Protection by Beach Umbrella vs Sunscreen With a High Sun Protection Factor: A Randomized Clinical Trial. JAMA Dermatol. 2017 Mar 1;153(3):304-308.
40. Russak JE, Chen T, Appa Y, Rigel DS. A comparison of sunburn protection of high-sun protection factor (SPF) sunscreens: SPF 85 sunscreen is significantly more protective than SPF 50. J Am Acad Dermatol. 2010 Feb;62(2):348-9.
41. ISO 24443:2012. Determination of sunscreen UVA photoprotection in vitro. Available at https://www.iso.org/standard/46522.html. Accessed 07 July 2020.
42. Krutmann J, Passeron T, Gilaberte Y, et al. Photoprotection of the future: challenges and opportunities. J Eur Acad Dermatol Venereol. 2020;34(3):447-454.
43. Hall HI, Saraiya M, Thompson T, Hartman A, Glanz K, Rimer B. Correlates of sunburn experiences among U.S. adults: results of the 2000 National Health Interview Survey. Public Health Rep. 2003;118(6):540-549.
44. Wee LKS, Chong, TK, Quee DKS. Assessment of skin types, skin colours and cutaneous responses to ultraviolet radiation in an Asian population. Photodermatology, Photoimmunology & Photomedicine. 1997;13(5-6):169-172.
45. Pathak MA, Fanselow DL. Photobiology of melanin pigmentation: Dose/response of skin to sunlight and its contents. J Am Acad Dermatol. 1983;9(5):724-733.
46. Tadokoro T, Kobayashi N, Zmudzka BZ, et al. UV-induced DNA damage and melanin content in human skin differing in racial/ethnic origin. FASEB J. 2003;17(9):1177-9.
47. Brenner M, Hearing VJ. The protective role of melanin against UV damage in human skin. Photochem Photobiol. 2008;84(3):539-549.
48. Del Bino S, Sok J, Bessac E, Bernerd F. Relationship between skin response to ultraviolet exposure and skin color type. Pigment Cell Res. 2006;19(6):606-614.
49. Nielsen KP, Zhao L, Stamnes JJ, Stamnes K, Moan J. The importance of the depth distribution of melanin in skin for DNA protection and other photobiological processes. J Photochem Photobiol B. 2006;82(3):194-198.
50. Rijken F, Bruijnzeel PL, van Weelden H, Kiekens RC. Responses of black and white skin to solar-simulating radiation: differences in DNA photodamage, infiltrating neutrophils, proteolytic enzymes induced, keratinocyte activation, and IL-10 expression. J Invest Dermatol. 2004;122(6):1448-1455.

51. El-Abaseri TB, Hammiller B, Repertinger SK, Hansen LA. The Epidermal Growth Factor Receptor Increases Cytokine Production and Cutaneous Inflammation in Response to Ultraviolet Irradiation. ISRN Dermatol. 2013;2013:848705.
52. Del Bino S, Duval C, Bernerd F. Clinical and Biological Characterization of Skin Pigmentation Diversity and Its Consequences on UV Impact. Int J Mol Sci. 2018;19(9):2668.

Tables

Table 1. Characteristics of study participants

Characteristic	**Total N=63**	**Chinese subgroup N=53**	**Caucasian subgroup N=10**
Age, years, mean (min-max)	30 (21-45)	30 (21-45)	30 (25-45)
Sex			
Male	32 (51%)	31 (58%)	1 (10%)
Female	31 (49%)	22 (42%)	9 (90%)
Skin color category (ITA)			
ITA 42-55 “light”	26 (41%)	24 (45%)	2 (20%)
ITA 29-41 “intermediate”	26 (41%)	22 (42%)	4 (40%)
ITA 20-28 “tan”*	11 (17%)	7 (13%)	4 (40%)
ITA, mean±SD (min-max)			
Total group	38±9 (21-53)	39±8 (21-53)	32±8 (22-46)

* The cutoff for this skin color category would be 11-28; however, this study used a lower cutoff of ITA 20 for inclusion in the analysis.

Figures

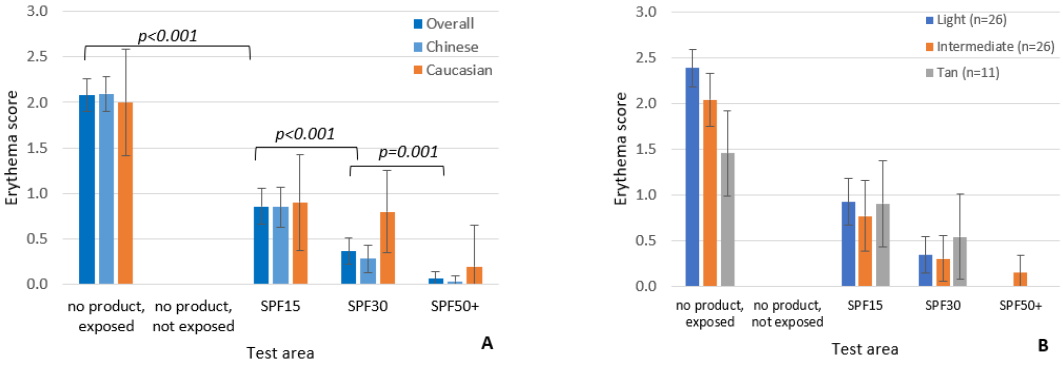

Figure 1. Clinical erythema scores at 24 hours. **A**. Overall and Chinese and Caucasian subgroups; **B.** By skin color category. Light: 41<ITA°≤55; intermediate: 28<ITA°≤41, tan: ITA 10<ITA°≤28. The height of the bars are the means and error bars indicate 95% confidence intervals (CI). Note: subjects with light skin had a shorter exposure time to minimize sunburn.

Statistical test: Wilcoxon Signed Rank test with Bonferroni's adjustment

Abbreviations: SPF, sun protection factor

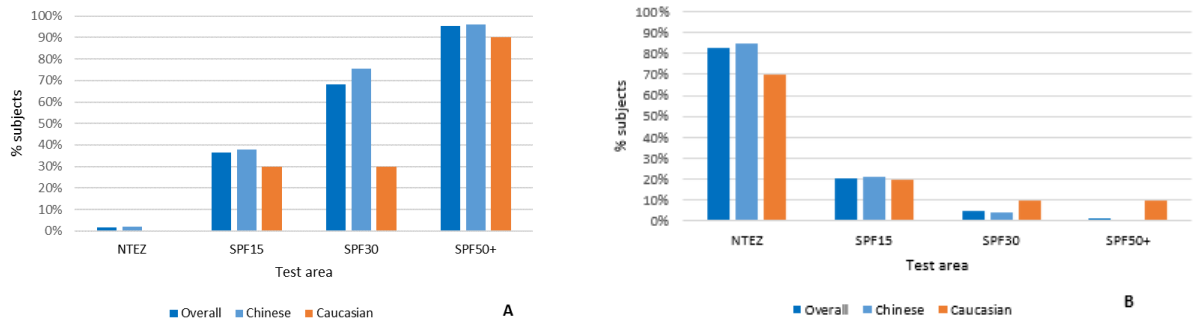

Figure 2. **A**, Percentage of subjects with no evidence of sunburn (erythema score 0) at 24 hours; **B**, Percentage subjects with failure of photoprotection (score ≥2, unequivocal erythema) at 24 hours.

Abbreviations: NTEZ, non-treated exposed zone

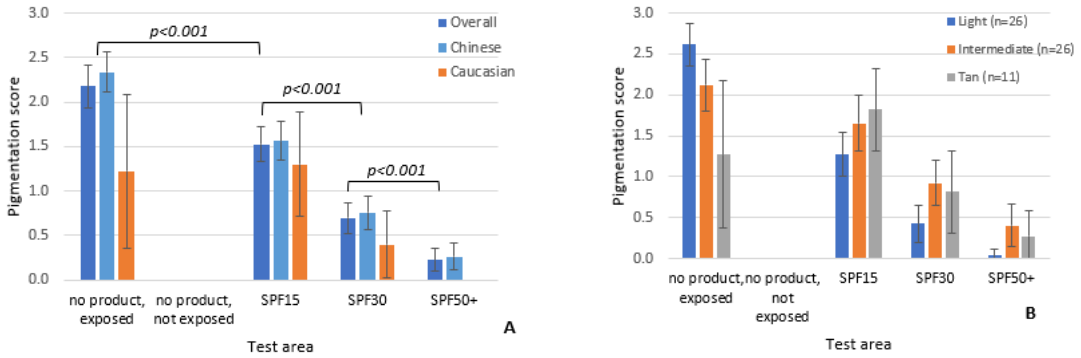

Figure 3. Clinical pigmentation scores at 1 week. **A**. Overall and by Chinese and Caucasian subgroups; **B** By skin color category. Light: 41<ITA°≤55; intermediate: 28<ITA°≤41, tan: ITA 10<ITA°≤28. The height of the bars are the means and error bars indicate 95% CI. Note: subjects with light skin had a shorter exposure time to minimize sunburn.

Statistical test: Wilcoxon signed rank test followed by Bonferroni's adjustment

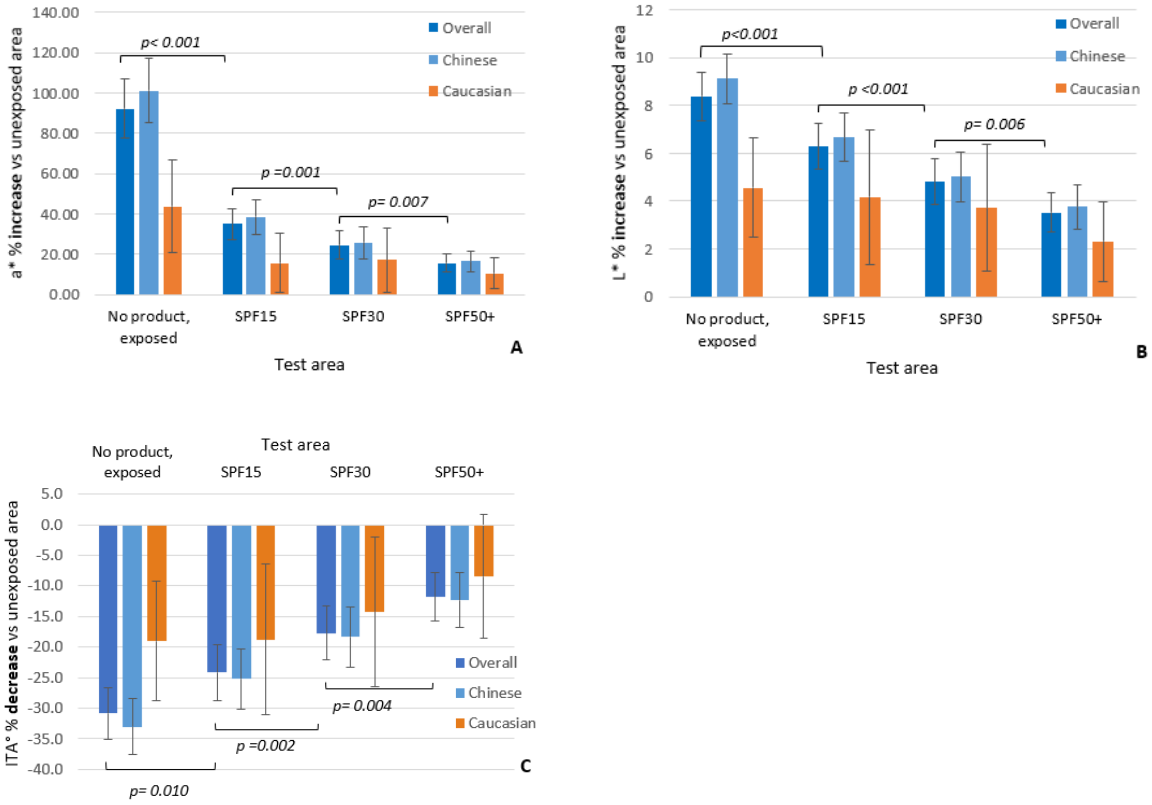

Figure 4. Colorimetry at 24 hours, expressed as percentage with respect to unexposed skin. Significant differences between adjacent protection levels for all parameters. **A:** a*parameter, higher values denote more erythematous skin; **B**: L*, lower values denote more pigmented skin.; **C:** ITA°, lower values denote darker skin.

Statistical test: Paired samples *t*-test followed by Bonferroni's adjustment

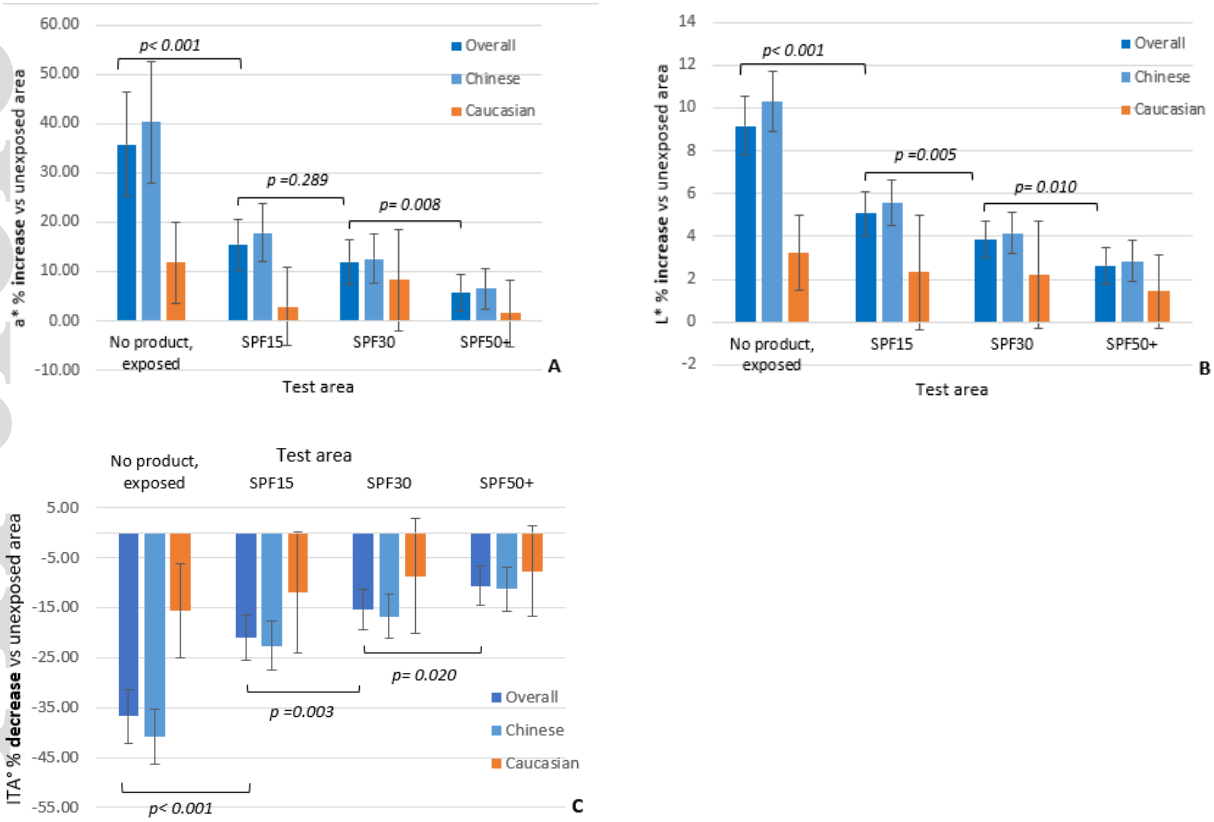

Figure 5. Colorimetry at 1 week, percentage difference vs unexposed skin. **A:** a*parameter, higher values denote more erythematous skin; **B**: L*, lower values denote more pigmented skin.; **C:** ITA°, lower values denote darker skin.

Statistical test: Paired samples *t*-test followed by Bonferroni's adjustment