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 ORIGINAL ARTICLE

Long-Term Benefits of Daily Photo-Protection With a Broad-Spectrum Sunscreen in United States Hispanic Female Population

Pearl Grimes MD,[a] Rebat Halder MD,[b] Michele Verschoore MD,[c] Janet Wangari-Talbot PhD,[d] Kumar Pillai PhD,[d] Peter Foltis MS,[d] Charbel Bouez PhD,[d] Angelike Galdi PhD,[d] Deena Abdelhalim BA,[d] I-Chien Liao PhD,[d] Qian Zheng MD PhD[d]

[a]The Vitiligo and Pigmentation Institute of Southern California, Los Angeles, CA
[b]Department of Dermatology, Howard University, Washington, DC
[c]L'Oreal Research and Innovation, Paris, France
[d]L'Oreal Research and Innovation, Clark, NJ

ABSTRACT

The skin of color population has been growing significantly in the United states and globally. This requires specific dermatological attention and patient care strategies due to unique physiological conditions and clinical manifestations regarding skin of color. Concerning photoaging, although people with higher Fitzpatrick phototypes (III and above) in general have fewer visible signs of aging such as lines and wrinkles, they are more susceptible to certain pigmentary-related conditions including uneven skin tone, ashy skin and blotchiness, post-inflammatory hyper- and hypo-pigmentation, Melasma, and seborrheic keratosis.

Effective photoprotection against harmful UVA and UVB radiation has been successful in skin cancer prevention as well as protection against solar damage. However, in skin of color communities, there are high levels of sun seeking behaviors and a lack of photoprotection with sunscreen, as a result, photoaging with dyschromia is common and certain cancer risks are growing. Historically, majority of clinical evidence for photoprotection was collected based on studies with lower skin phototypes. There is in general a lack of knowledge on the long-term impact of daily photoprotection on skin of color. In this current study, we investigated the skin benefits of daily sunscreen use with SPF 30/PPD 20 (Persistent Pigmentation Darkening rating = UVA protection) for 12 months, in phototype IV and V Hispanic females in the US, versus a real life population of the same age and phototypes without daily sunscreen in their routine. This study is to our knowledge the first one to demonstrate the benefits of long-term daily use of sunscreen on signs of aging and pigmentary concerns in patients with higher phototypes.

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INTRODUCTION

The demographics of the United states are evolving with a large increase in racial and ethnic diversity driven by international migration of Hispanic, African, and Asian populations leading to a minority-majority shift in ~2050 towards persons of color (Fitzpatrick III, IV, V, and VI).[1] Specifically, the Hispanic population is projected to be among the fastest growing population in the US, projected to increase from 55 million in 2014 to 119 million in 2060, a change of +115%.[1]

Subjects with skin of color are heterogeneous with multiple shades and tones and different reactions to intrinsic and extrinsic aging factors due to structural and physiologic differences.[2,3] Skin of color individuals have fewer visible signs of aging (deep wrinkles, fine lines, rough surface texture, and sun spots). However, darker skin tones are more susceptible to certain skin conditions including post-inflammatory hyperpigmentation (may occur after acne, eczema, injury, laceration, melasma, post-inflammatory hypopigmentation, pityriasis alba (round, light patches covered with fine scales), dry or "ashy" skin, dermatosis papulosa nigra, and/or greater risk of keloid development.[2,3] The incidence of skin cancer among US Hispanics has also increased 1.3% annually from 1992 to 2008.[4]

Photodamage is characterized histologically by degeneration of the connective tissue and abnormalities in keratinocytes and melanocytes. Clinically, it manifests primarily with wrinkles, dyschromia, texture changes, and, in more severe cases skin cancer.[5] Formulations containing broad spectrum sunscreens against both UVA and UVB play an essential role in the prevention of photodamage and UV-induced skin cancers.[6,7,8] However, the majority of clinical research on photoprotection has been conducted on subjects with Fitzpatrick types I to III skin and have reported improvements in signs associated with skin aging and texture.[9,10] Verschoore et al was the first to conduct a short-term

clinical study in India with Phototype IV and VI subjects, and provided first evidence on the effectiveness of daily sunscreen use on skin tone and radiance.[11] Similar benefits were observed in an 8-week study in US.[12]

Although sun protection is highly recommended by dermatologists for skin cancer risk-reduction and the prevention of premature aging or pigmentary disorders, adherence to the recommendations is not commonly observed among US Hispanics.[13] Moreover, a large number of US Hispanics reside in areas with high UV index with a high degree of sun seeking behavior. Among Hispanic adults who report engaging in sun protection, they do so mostly by staying in the shade (53.7%) rather than use of sunscreen (32.3%) or wearing sun protective clothes (18.1%); while 36.7% of the subjects surveyed indicated that they never use sunscreen.[14,15] There are sociodemographic factors that contribute to the adherence to safe sun behaviour such as education, age, and gender, etc, therefore there is a need to raise awareness of skin cancer risks, advocate for preventive measures and educate on benefits of sunscreen and sun protection among US Hispanics.[16]

The benefits of topical agents for reversal of sun damage has been well established. Use of retinoic acid and its derivatives or other drugs to reverse and improve sun damaged skin has been demonstrated in many studies.[17,18] Long-term sunscreen-use along with other topical agents have also been shown to prevent photodamage and hyperpigmentation in fair-skinned subjects.[19] For effective photoprotection, sunscreen products containing both SPF and PPD are essential to battle the harmful UVB (skin cancer risks) and UVA (photo-aging risks).[20] Daily use of a broad-spectrum sunscreen (SPF 30) over a one-year period has also been demonstrated to improve clinical parameters of photodamage in phototype I-III subjects.[10] However, a comprehensive long-term sunscreen use study in skin of color is lacking. Therefore, this study was designed to assess the benefits of sunscreen of SPF30/PPD 20 in Hispanic women of Fitzpatrick skin types IV and V over 12 months in comparison to a real-life observational group with subjects who did not use sunscreen regularly.

MATERIALS AND METHODS

Clinical Study Design

The investigation was approved by an independent institutional review board, and it was conducted in accordance with the principles of the 1975 Declaration of Helsinki; written informed consent was obtained from all study subjects before enrollment. The study was performed in 2 study centers, one in Los Angeles, CA, the other in Washington DC, to observe geographic and climate variation.

Healthy female Hispanic subjects between the ages of 45-65 with Fitzpatrick phototype IV and V, with mild to moderate signs of photoaging and pigmentary concerns (fine lines, wrinkles, rough texture, uneven skin tone, hyperpigmented spots, and sun-induced dyschromia) were recruited. Subjects were recruited on a rolling admission basis and received a SPF 30/PPD 20 formula to add to their daily skin care routine. The Washington, DC study was conducted from May 2016 to August 2017, while the Los Angeles (LA) study was conducted from March 2016 to May 2018. 30 subjects were enrolled in Washington, DC while 22 were enrolled in Los Angeles. The subjects were evaluated at 3, 6, 9, and 12 months at each center for signs of aging and dyschromia with clinical grading and instrumental measurements. In addition, a real-life observation was conducted at the same centers during the same time, with age- and photo-type matched subjects of similar skin conditions (n=30 in Washington DC and n=22 in LA enrolled) who were not regular sunscreen users and maintained their normal routine.

At the end of 12 months, 24 subjects in the sunscreen study and 16 subjects in the real-life observation study completed all evaluations.

Investigational product

A broad spectrum, photo-stable sunscreen with SPF 30/PPD 20 was applied daily in the morning to the entire face, both hands, and forearms for 12 months. Re-application every 2-3 hours was recommended during sun exposure. The composition of active ingredients in the sunscreen formulation was Avobenzone (3%), Homosalate (12%), Octisalate (5%), Octocrylene (1.7%), and Oxybenzone (3%). The use of the study formulation was monitored, by weighing the product to insure adherence to the daily use of the formulation across the one-year study. All subjects were allowed to use a simple moisturizer, without known antiaging actives, as and when required. Subjects were advised to avoid excessive sun exposure during the study and were recommended to apply the sunscreen every 2-3 hours and take shelter/wear protective clothing when sun exposure was unavoidable.

Clinical evaluations

Clinical evaluations by the dermatologist were carried out at baseline, 3, 6, 9, and 12-month time points. The assessment was performed *in situ* for efficacy parameters using modified Griffith's scale. Dermatologist grading was conducted by a single physician using a scale of 0 (none) to 9 (most severe) and evaluated the following signs of skin quality and photodamage: texture, skin tone evenness, overall hyperpigmentation, dark spots (intensity and number), overall skin quality (smoothness, radiance, overall imperfections), loss of elasticity, fine lines, coarse wrinkles, and skin blotchiness. These parameters were evaluated on the face on the following locations: forehead, temple, crow's feet area, under eye, nose, cheeks, and chin; as well as on the neck and both hands.

Instrumental measurements

Instrumental measurements were performed with the Minolta CR-400/410, a reflectance spectrophotometer (chromameter) for

L*, a* b* measurement for skin brightness and erythema, and a Mexameter® MX 16 for melanin content and hemoglobin (erythema). The instrumental measurements were performed on mid-forehead, both cheeks, neck, and on both dorsal forearms. Digital photographs were captured at baseline, 3, 6, 9, and 12 months with Canfield Scientific's VISIA CR 2.2 booth system (Washington, DC) or VISIA CR (Los Angeles, CA) with eyes closed using standard, cross-polarized and UV fluorescence lightening modes.

Immunohistochemistry and image analysis

2 mm diameter skin biopsies were collected from a small subset of study subjects from the cheek at baseline and 12 months. At the end of 12 months, n=3 from real life study and n=6 from sunscreen study were obtained. Biopsy samples were fixed in 10% formalin, prepared into tissue sections and stained for Hematoxylin and eosin (H&E), Masson's Trichrome, Fontana Masson, and Toluidine Blue. Presence of macrophages were immunostained using CD68 antibody (pre-diluted concentration, PM033A RTU, Biocare Medical, Pacheco, CA) followed by DAB staining (DAB peroxidase substrate kit, Abcam, Cambridge, MA). Digital images were captured (DMi8 Fluorescent Microscope, Leica, Buffalo Grove, IL) and image analysis was performed blindly by two individual assessors using Image J Analysis software.

Data analysis

All statistical analyses were carried out using paired t-test to determine whether there was a change from baseline to 12 months. Wilcoxon signed-rank test was used for Investigator's expert assessments, clinical grading of the efficacy parameters and tolerance parameters, as well as the parameters from image analysis results. The average change from baseline was calculated at each post-baseline evaluation visit. All differences were considered to be statistically significant at $P<0.05$ level.

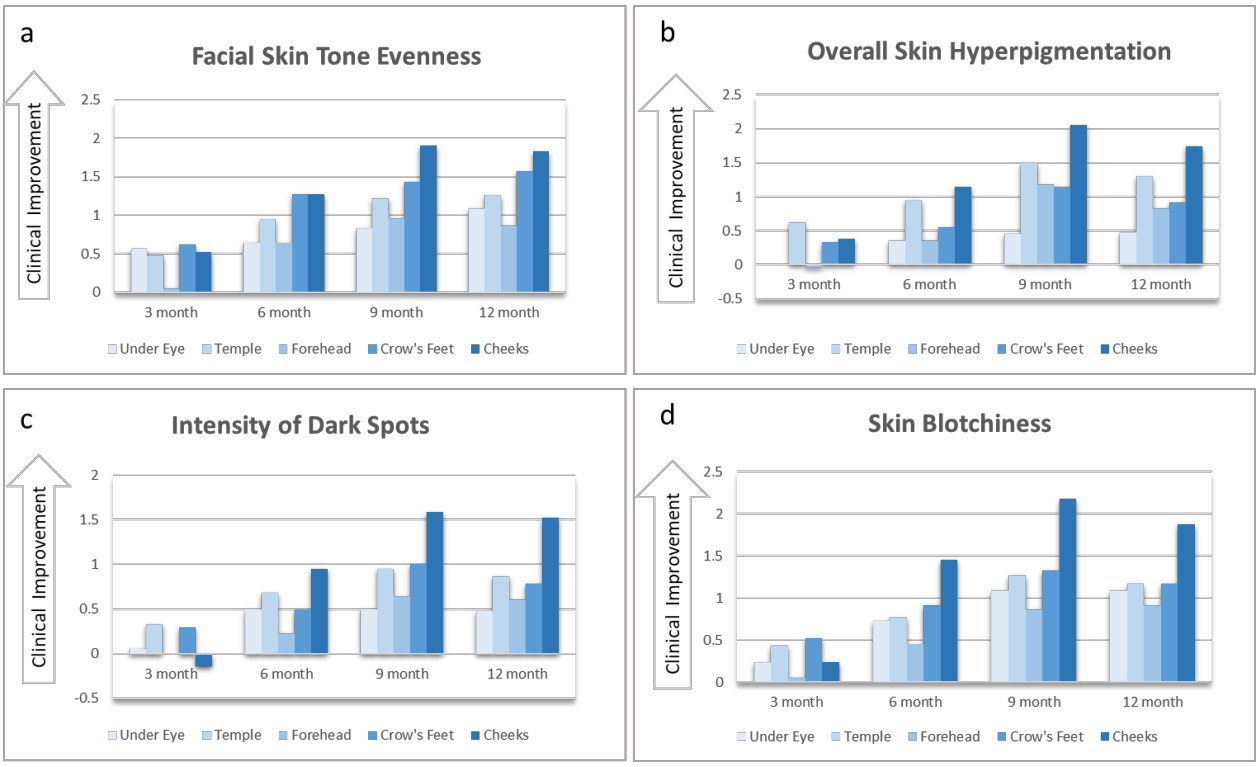
L* values, ITA values (Chromameter) and melanin values (Mexameter) were calculated for each parameter for sunscreen group and real life group as mean +/-SD for 3, 6, 9, and 12 months. Change from baseline and comparison between the two groups were calculated and expressed as mean difference and the p values were calculated.

RESULTS

Improvement on Photoaging and Dyschromia Conditions With 12-Month Daily Application Of SPF20/PPD20

Skin conditions especially skin tone and texture tend to vary based on seasonality and outdoor activities. We observed that in the real life group, a shift of color and hyperpigmented lesions towards worsening occurs in the summer with partial recovery

FIGURE 1. Improvement on pigmentary-related clinical parameters with daily application of SPF30/PPD20 over time.

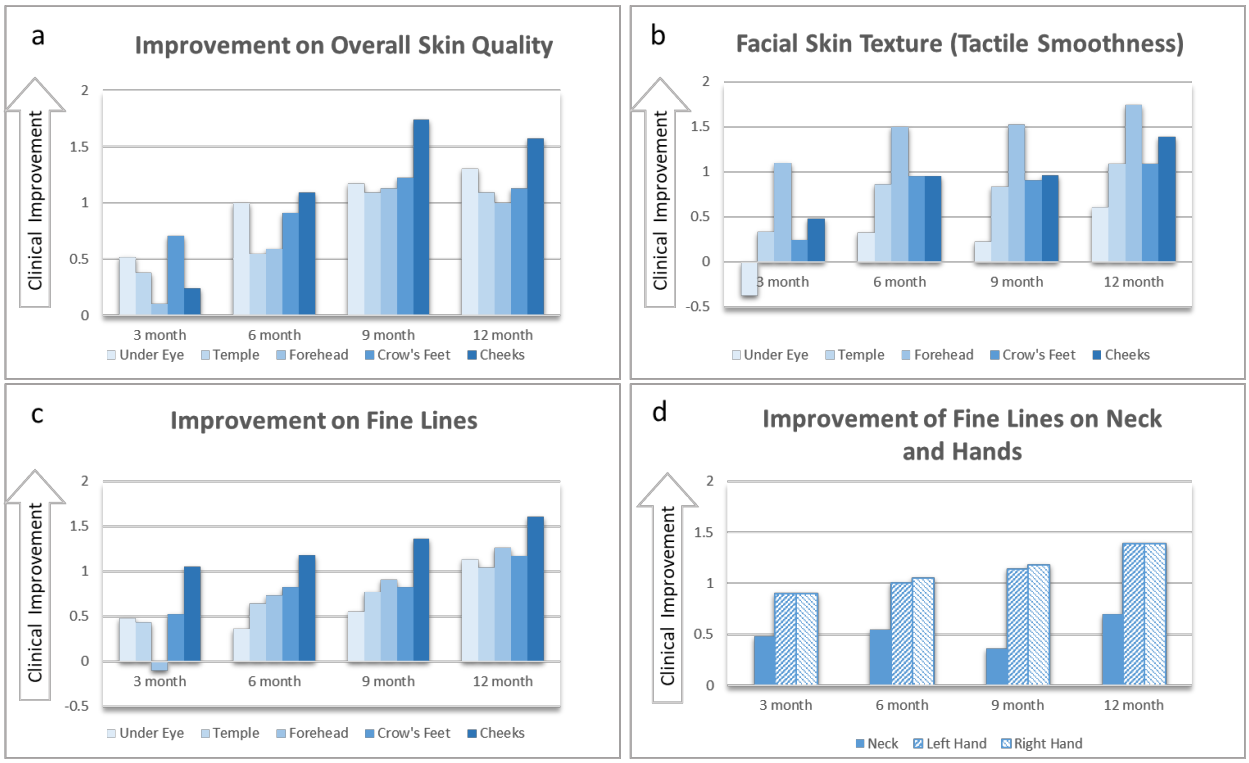


(a) Clinical grading on improvement of facial skin tone evenness at 3, 6, 9, and 12 months compared to baseline; (b) Clinical grading on improvement of overall skin hyperpigmentation on different facial areas at 3, 6, 9, and 12 months compared to baseline; (c) Clinical improvement of dark spots on different facial areas at 3, 6, 9, and 12 months compared to baseline; (d) Clinical improvement of skin blotchiness on different facial areas at 3, 6, 9, and 12 months compared to baseline.

during the winter, in agreement with previous findings.[20] With daily application of sunscreen (SPF 30/PPD 20), significant clinical improvements on skin dyschromia-related parameters (skin tone, hyperpigmentation, dark spots) were observed over time at 3, 6, 9, and 12 months compared to baseline (Figure 1), on multiple areas on the face (forehead, temple, crow's feet, under eye, cheeks). Similar improvements were seen on both hands and neck area (data not shown). Although there is still minor seasonal variation, especially during the first few month of product usage, the overall benefits of sunscreen overcome seasonal effect with a strong and progressive global improvement.

In addition to the improvements on skin tone and hyperpigmented areas, significant benefits on skin aging parameters were demonstrated in the sunscreen group, including fine lines, texture smoothness, and overall skin quality (Figure 2) for face, neck, and hands. The improvements were incremental and perceivable. There was minimal improvement on coarse wrinkling an aging sign that requires deeper acting interventions such as retinoids to address. The demonstrated improvement by daily SPF 30/PPD 20 is summarized in Table 1.

FIGURE 2. Improvement on skin aging parameters with daily application of SPF 30/PPD 20 over time.



Overall skin quality, skin texture (tactile smoothness), fine lines were improved significantly over time after daily sun screen use (3, 6, 9, and 12 months) compared to baseline. Strong improvements were also observed on the neck and hands.

TABLE 1.

Significant Improvement on Clinical Daily Application of SPF 30/PPD 20				
Attributes	Evaluation Time Points			
	3 Month	6 Month	9 Month	12 Month
Overall Skin Quality	--	Face	Face & Eye Area	Face
Skin Tone Evenness and Hyper-pigmentation	Eye area	Face & Neck	Face & Eye area; Neck, Hand	Face & Eye area; Neck, Hand
Blotchiness	--	Face	Face & Hand	Hand
Tactile Smoothness	Face	--	Face & Hand	Face & Hand
Fine lines	--	Face	Face	Face

All listed facial/body areas demonstrated significant improvement vs real life group ($P<0.05$) after daily SPF 30/PPD 20 application for indicated duration (3, 6, 9, and 12 month).

Instrumental Evaluation of Skin Color and Melanin Index over 12 Months

Objective measurement of color and melanin levels in long-term clinical studies is challenging, due to many factors including skin color and undertone variability, seasonality impact on skin, and external light conditions. Skin of color patients tend to have higher heterogeneity on facial skin thus increase the complexity of accurately measurement. Del Bino and Bernard reported on the effectiveness of using Individual Typology Angle measurements based on Chromameter L*a*b values and the melanin index recorded with a Mexameter, and good correlation between these two instruments.21

In the current study, both Chromameter ITA/L* and Mexameter melanin index were investigated at baseline, 3, 6, 9, and 12 months. Both instruments gave similar measurement trends as observed in previous studies. Seasonal impact on skin color and high variability among individuals were observed, as expected. An increase of skin brightness and reduction of melanin content in skin were observed over time with daily sunscreen when compared to the real life group. The effect was most apparent at 12 months (Table 2). These findings support the clinical grading results of positive impact by daily application of sunscreen.

TABLE 2.

Changes in ITA and Melanin Index for Sunscreen Group

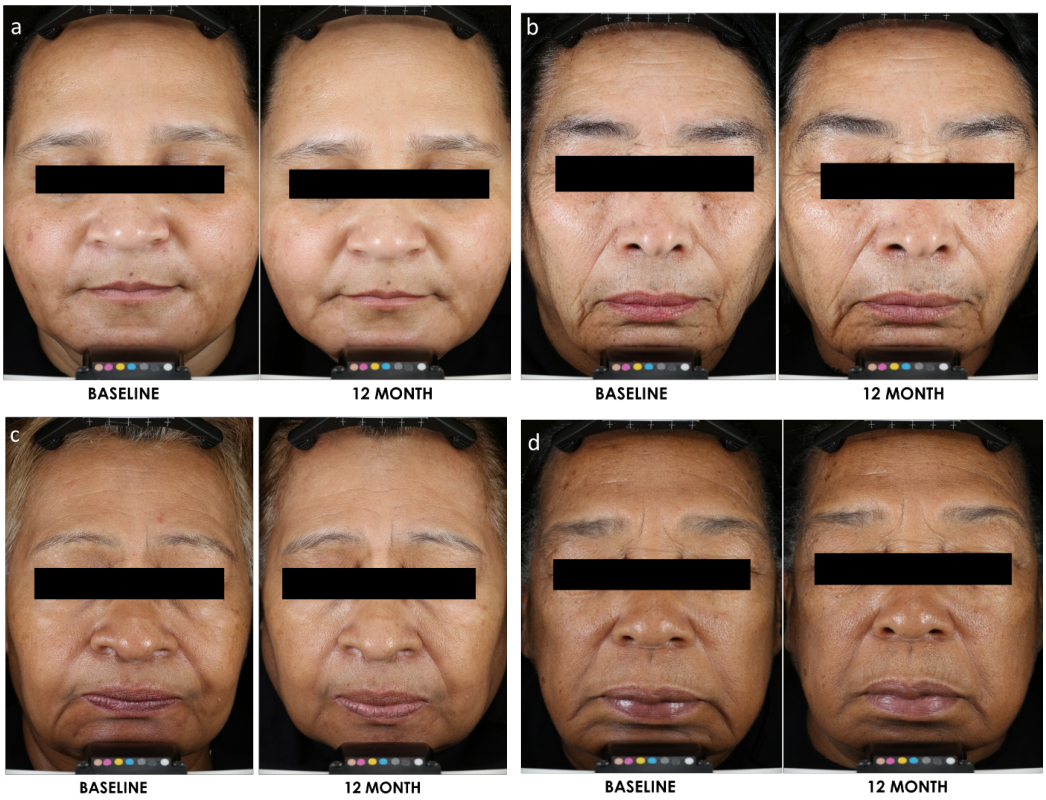
Area of Evaluation	Parameter	3 Month	6 Month	9 Month	12 Month
Face	ITA/L*		*		*
	Mel Index		*	*	*
Neck	ITA/L*	*			*
	Mel Index	*			*
Hand	ITA/L*	*		*	*
	Mel Index				*

*Indicates Sunscreen group showed improvement compared to Real Life group (P<0.1)

Biopsy Analysis

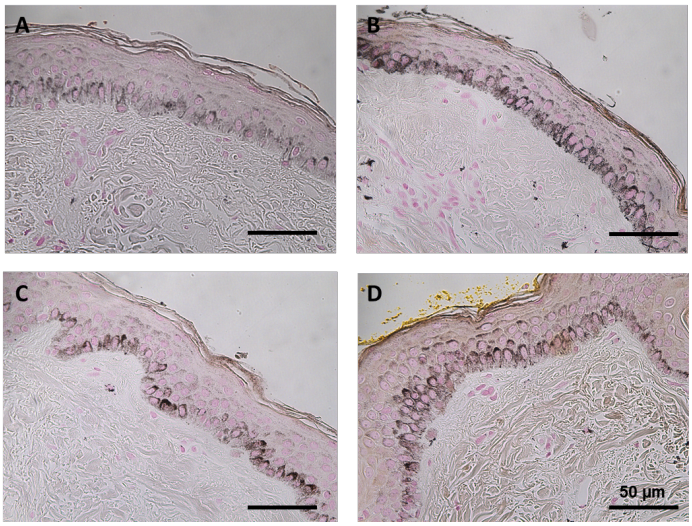
The biopsy samples were evaluated for potential histological changes between the sunscreen and real-life groups at the initiation and the conclusion of the 12-month study. Fontana-Masson staining was used to visualize melanin content of skin (Figure 4), and CD68 was used as a biomarker for Macrophage infiltration (Figure 5). The real-life samples at the 12-month time-point showed a tendency for higher levels of pigmentation incontinence compared to the sunscreen group with visibly increase dermal melanin (Figure 4a-d, P=0.086). Indeed, when

FIGURE 3. Representative VISIA images demonstrating the benefits of daily sunscreen application over 12 months.



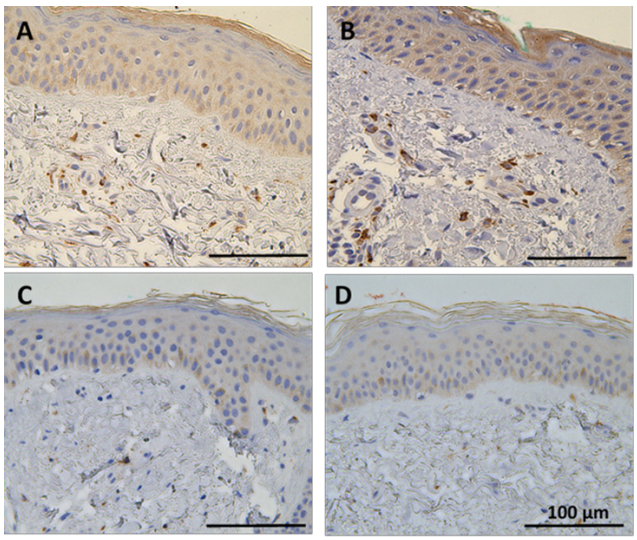
Example of overall skin quality improvement after 12-month daily use of sun screen in phototype-IV (a) and phototype-V (c) patients: significant skin tone evenness, brightening, texture roughness reduction, reduction of mottled pigmentation, increase of clarity, and reduction of fine lines were observed. In phototype-matched real-life group, a slight worsening of skin tone, perioral fine lines, and forehead wrinkles were observed (b and d).

FIGURE 4. Fontana – Masson Staining and Pigmentation incontinence.



Fontana Masson staining (A-D) of the biopsy samples taken in this study. This panel compares the changes between real life group at baseline (A) and 12 month(B) to the changes observed in the sunscreen group at baseline (C) and 12 month (D). Scale bar: 100 µm.

FIGURE 5. CD68 immunostaining for macrophage infiltration.



CD68 (A-D) immunostaining of the biopsy samples taken in this study. This panel compares the changes between real life group at baseline (A) and 12 month(B) to the changes observed in the sunscreen group at baseline (C) and 12 month (D). Scale bar: 100 µm.

we examined the corresponding chromameter measurements of the representative subjects, we noted an improvement in the L*values of the sunscreen panelist and a decrease in the L* Value of the real-life control subject on the cheeks indicating a lightning and darkening respectively. In the dermis, 2 out of 3 of the real-life samples showed an increase in CD68 positive macrophage cells (Figure 5b) when compared to baseline (Figure 5a), while such changes were not observed in the biopsies from the sunscreen group (Figure 5c, 5d). Between the real life and the sunscreen groups, there were no observable differences in the number of sunburn cells, epidermal hyperplasia and changes to the dermal matrix (data not shown).

DISCUSSIONS AND CONCLUSIONS

Effective photoprotection is critical for healthy skin, in preventing skin cancers, reducing photodamage, and improving aesthetic appearance. A broad spectrum sunscreen protecting against both UVA and UVB irradiation is essential. Protecting against the UVA spectrum needs special attention, especially under daily diffused exposure, as UVA is more penetrating and less affected by seasonality and impacts photoaging and skin oxidative stress.[22] It has been reported that in order to receive effective photoprotection on skin, a PPD value of 18 is desired.[20] In this study, the investigational product with SPF 30/PPD 20 is considered sufficient for daily activity without prolonged direct sun exposure when applied properly. Concerning skin of color population, the use of sunscreen is lower than in Caucasians despite high prevalence of sun-related pigmentary disorders and rising rates of cutaneous cancers.[4] This study provides strong evidence to educate and advocate for daily use of a proper sunscreen product for populations with high phototype skin.

The clinical evaluation demonstrated significant visible improvement in sunscreen group starting from 3 months and progressive increased over time. Benefits on multiple facial areas and body sites were visible (upper, mid- and lower face, neck, and hands), not only on pigmentary-related concerns (skin tone evenness, overall hyperpigmentation, dark spots, and blotchiness), but also on aging parameters such as fine lines, skin texture, and overall skin quality. This suggests that beyond the preventative benefits, long-term persistent use of a proper sunscreen may also allow the photodamaged skin to self-heal and repair over time.

Histological observations further supported the clinical findings. The observation that the real-life group had higher tendency for pigmentation incontinence is of strong research interest. It has been reported that UV irradiation can destabilize and damage the dermal-epidermal junction (DEJ), which facilitates the entrapment of melanin in the dermis.[23] The dermal melanin is extremely difficult to remove, often resulting in stubborn hyperpigmentation.[24] This is especially important for skin of color population in whom dermal hyperpigmentation lesions are common and can be worsened with excessive sun exposure. This study provides the first evidence that effective daily photoprotection can be a strategy to prevent dermal melanin formation by protecting the DEJ. A larger sample size study with DEJ biomarkers will help to further elucidate this hypothesis.
Infiltration of CD68-positive Macrophages is a hallmark of the inflammatory response after UV irradiation. In the dermis, 2 out of 3 of the real-life biopsy samples showed significant increase in CD68 positive macrophage cells at 12 months compared to baseline, while such change was not observed in the sunscreen group. This suggests the potential preventative benefits of sunscreen in subclinical skin inflammation induced by chronic exposure to UV. In all of the histological evaluations, the

geographical location in which the study was conducted (Los Angeles versus Washington, DC) was not a strong contributing factor to any of the observed differences. However, the histological findings in this study are limited by the small number of biopsies obtained.

In summary, this 12-month study on long-term persistent use of an SPF30/PPD20 sunscreen on phototype IV and V subjects demonstrated significant improvement in skin quality and improvement in skin color and photoaging parameters. To our knowledge, this is the first study of this kind in skin of color and Hispanic population. This study confirms that effective sunscreen use is not only protective and beneficial for light skin population but is also critical in improving skin condition for skin of color patients. Overall, the study demonstrates that daily use of sunscreen can protect skin from photo related damage and even reverse some of the photo-damage that has already occurred in skin. In addition to previous studies that demonstrated the photo-protective properties of sunscreen use in normal and diseased skin states[7,8,9,10] and in view of the fact that good photoprotection behaviors are not common among Hispanics,[14,15,16] studies of this type can help educate and stress the importance of daily use of sunscreen and other sun protection behaviors in Hispanic and other skin of color populations.

DISCLOSURES

The authors state that there is no conflict of interest. This research is sponsored by L'Oreal Research & Innovation.

REFERENCES

1. Colby SL, Ortman JM. Projections of the Size and Composition of the U.S. Population: 2014 to 2060. March, 2015. https://www.census.gov/content/dam/Census/library/publications/2015/demo/p25-1143.pdf.
2. Grimes P, Boyd C, Alexis A, Downie J, Kolodziejczyk J, Gallagher C. Self-reported characteristics associated with the signs of facial aging by race/ethnic group and Fitzpatrick skin type among a diverse, multinational sample. *74th Annual Meeting of the American Academy of Dermatology.* 2016.
3. Alexis AF, Obioha O. Ethnicity and Aging skin, *J Drugs in Dermatol.* 2017;16: s77–80.
4. Perez MI. Skin cancer in Hispanics in the United States. *J Drugs Dermatol.* 2019;18: s117-120.
5. Gilchrest BA. Skin aging and photoaging: an overview. *J Am Acad Dermatol.* 1989;21: 610–613.
6. Sambandan DR, Ratner D. Sunscreens: an overview and update. *J Am Acad Dermatol.* 2011;64: 748–58.
7. Boyd AS, Naylor M, Cameron GS, Pearse AD, Gaskell SA, Neldner KH. The effects of chronic sunscreen use on the histologic changes of dermatoheliosis. *J Am Acad Dermatol.* 1995;33: 941–946.
8. Naylor MF, Boyd A, Smith DW, Cameron GS, Hubbard D, Neldner KH. High sun protection factor sunscreens in the suppression of actinic neoplasia. *Arch Dermatol.* 1995;131: 170–175.
9. Kligman LH, Akin FJ, Kligman AM. Sunscreens promote repair of ultraviolet radiation-induced dermal damage. *J Invest Dermatol.* 1983; 81:98–102.
10. Randhawa M, Wang S, Leyden JJ, Cula GO, Pagnoni A, Southall MD. Daily use of a facial broad spectrum sunscreen over one-year significantly improves clinical evaluation of photoaging. *Dermatol Surg.* 2016; 42: 1354-1361.
11. Sarkar R, Garg VK, Jain A, Agarwal D, Wagle A, Flament F, Verschoore M. A randomized study to evaluate the efficacy and effectiveness of two sunscreen formulations on Indian skin types IV and V with pigmentation irregularities. *Ind. J. Dematol. Venerol. Leprol.* 2019; 85: 160-164.
12. Halder R, Rodney I, Munhutu M, Foltis P, Battie C, Verschoore M, Oresajo C. Evaluation and effectiveness of a photoprotection composition on subjects of skin of color. *J Am Acad Dermatol.* 2015; 72: AB215.
13. Andreeva VA, Unger JB, Yaroch AL, Cockburn MG, Baezconde-Garbanati L, Reynolds KD. Acculturation and sun-safe behaviors among US latinos: findings from the 2005 health information national trends survey. *Am J Public Health.* 2009; 99:734–741.
14. Coups EJ, Stapleton JL, Hudson SV, Medina-Forrester A, Natale-Pereira A, Goydos JS. Sun protection and exposure behaviors among Hispanic adults in the United States: Differences according to acculturation and among Hispanic subgroups. *BMC Public Health.* 2012; 12, 985-993.
15. Coups EJ, Stapleton JL, Hudson SV, Medina-Forrester A, Rosenberg SA, Gordon M. Linguistic acculturation and skin cancer-related behaviors among Hispanics in the southern and western United States. *JAMA Dermatol.* 2013; 149: 679–686.
16. Coups EJ, Stapleton J, Manne SL, Hudson SV, Medina-Forrester A, Rosenberg S. Gordon M, Tatum KS, Robinson JK, Natale-Pereira A, Goydos JS. Psychosocial correlates of sun protection behaviors among U.S. Hispanic adults. *J Behav Med.* 2014; 37:1082-1090.
17. Maddin S, Lauharanta J, Agache P, Burrows L. Isotretinoin improves the appearance of photodamaged skin: results of a 36-week, multicenter, double-blind, placebo-controlled trial. *J Am Acad Dermatol.* 2000; 42: 56–63.
18. Kang S, Krueger GG, Tanghetti EA, Lew-Kaya D, et al. A multicenter, randomized, double-blind trial of tazarotene 0.1% cream in the treatment of photodamage. *J Am Acad Dermatol.* 2005; 52: 268–274.
19. Herndon JH, Makino ET, Jiang LI, Stephens TJ, Mehta RC. Long term, multiproduct facial regimen in subjects with moderate to severe photodamage and hyperpigmentation. *Clinical Aesthetic Dermatol.* 2015; 8: 16-21.
20. Flament F, Qiu H. Effects of seasonality and a daily photo-protection upon some facial signs of Chinese women. *Int J Cosmet Sci.* 2017; 39: 256-268.
21. Del Bino S, Bernerd F. Variations in skin colour and the biological consequences of UV radiation exposure. B*r J Dermatol.* 2013; 169: 33-40.
22. Battie C, Jitsukawa S, Bernerd F, del Bino S, Marionnet C, Verschoore M. New insights in photoaging, UV induced damage and skin types. *Exp. Dermatol.* 2014; 23: 7-12.
23. Brenner M, Hearing VJ. The protective role of melanin against UV damage in human skin. *Photochem. Photobiol.* 2008; 84: 539-549.
24. Silpa-Archa N, Kohli I, Chaowattanapanit S, Lim HW, Hamzavi I. Proinflammatory hyperpigmentation: A comprehensive overview epidemology, pathogenesis, chinical presentation and non-invasive assessment techniques. *J Am Acad Dermatol.* 2017; 77: 591-605.

AUTHOR CORRESPONDENCE

Qian Zheng MD PhD
E-mail:..... qian.zheng@rd.loreal.com