Evaluation of a Novel Inorganic Tinted Sunscreen Enriched with Five Antioxidants for Protection Against UVA1 and VL Induced Hyperpigmentation and Erythema

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Abstract

Visible light (VL, 400-700 nm) and long wavelength UVA1 (VL+UVA1, 370-700 nm) have been reported to cause erythema in light skin phototypes, Fitzpatrick skin types I-III (FST I-III), and to exacerbate pigmentary dermatologic conditions (e.g., melasma, hyperpigmentation, post-inflammatory hyperpigmentation) in individuals with dark skin phototypes (FST IV-VI). Until recently, there remained limited options for photoprotection against VL+UVA1, including tinted (containing iron oxide [Fe_2O_3]), pigmentary titanium dioxide (TiO_2), organic-based (chemical) filters, or utilization of a five antioxidant (5 AOX) enriched formulation. Zinc oxide (ZnO) and TiO_2 are often utilized in the development of mineral-based (inorganic) sunscreens as the active ingredients to protect against broad-spectrum ultraviolet (UV) radiation via their absorption properties. However, some of these products often leave a white cast, particularly on dark skin, making these products unfavorable, altering skin tone appearance, leading to concerns for sunscreen compliance. The addition of tint (Fe_2O_3) to mineral-based sunscreens aims to improve the cosmetic elegance, blendability into multiple skin tones, and overall compliance for daily sunscreen use.

This study aims to evaluate the photoprotection properties of a novel ZnO-based inorganic tinted sunscreen enriched with five antioxidants (5 AOX) against VL+UVA1 induced biologic effects (hyperpigmentation and erythema). Ten healthy adult subjects with FST IV-VI were enrolled and the effectiveness of the new ZnO/Fe_2O_3/5 AOX sunscreen, compared to several commercially available tinted and non-tinted mineral sunscreens was evaluated. The erythema and pigmentation assessment was performed by diffuse reflectance spectroscopy (DRS), polarized photography, and investigator global scoring immediately, 24 hours, and 7 days after irradiation (320 J/cm^2). DRS results demonstrated that the novel ZnO/Fe_2O_3/5 AOX can effectively reduce immediate erythema and pigmentation as well as delay pigmentation when compared with formulas containing ZnO only ($p \leq 0.05$). Not all inorganic/Fe_2O_3 formulas could significantly reduce erythema and pigmentation induced by UVA1/VL when compared with ZnO-only formula. These results highlight the enhanced effects of 5 AOX-enriched tinted mineral sunscreen to be photoprotective against VL+UVA1, with a blendable tint designed for use on skin of all color, aimed at improving patient compliance and overall sunscreen use.

Materials and Methods

Study Participants:

Ten (10) subjects with FST IV-VI were enrolled. The study was approved by Sterling Investigational Review Board and conducted at Dermico Laboratory, Broomall, PA. Written informed consent was obtained from all subjects.

VL+UVA1 Phototesting:

A single VL+UVA1 dose of 320 J/cm^2 was administered with a modified solar simulator. Solar Light LS1000 (Solar Light Company Inc, Glenside, PA), with xenon arc light and customized filters. Filtered spectral output consisted of 1.4% UVA1 (340-400 nm), 96.3% VL (400-700 nm) and 2.28% IR (700-1800 nm). Spectroradiometric assessment of the long UVA/VL sources was performed with a calibrated spectroradiometer OL-754 (Gooch and Housego, Orlando, FL).

PRODUCT APPLICATION AND VL/UVA1 EXPOSURE

On visit 1 (day 0), subjects were marked with sites on their mid-lower back. On one (1) of the sites product C was applied at 2 mg/cm^2 in a randomized fashion, and allowed to dry for 20 minutes. On visit 2 (day 1), product C was reapplied at 2 mg/cm^2 to the same site and allowed to dry for 20 minutes. On visit 3 (day 2) product C was reapplied at 2 mg/cm^2 to the same site and allowed to dry for 20 minutes. On visit 4 (day 3) product C was reapplied at 2 mg/cm^2 to the same site. Products A, E, F, G, H and I were applied to other marked sites at 2 mg/cm^2 and all products were allowed to dry for 20 minutes following which all treated sites and an untreated site U were irradiated with a VL+UVA1 dose of 320 J/cm^2 at an irradiance of 95 mW/cm^2 (~ 1 hour). Site U served as positive control because it was untreated but irradiated.

ASSESSMENTS

Assessments were done by digital cross-polarized photography, investigator global assessment (IGA) score for pigmentation, and diffuse reflectance spectroscopy (DRS). All assessments were performed for all sites immediately, 24 hours and 7 days after VL+UVA1 exposure. For DRS, the instrument consisted of a quartz halogen light source (Ocean Optics, Boca Raton, FL), a bifurcated fiber bundle (Multimode Fiber Optics, East Hanover, NJ), a BWTEK Glacier spectrometer (B&W Tek, Plainsboro, NJ), and a laptop. One leg of the fiber bundle was connected to the light source and the other to the spectrometer. Measurements were performed by placing the common end of the fiber bundle gently against the skin without perturbing blood flow. A reflectance spectrum was acquired in the range of 400-820 nm. Five (5) measurements were collected from each site at all time points after VL+UVA1 exposure. Measurements from normal untreated and non-irradiated skin were also collected for normalization. Apparent concentrations of hemoglobin and melanin, and area under the curve from 400-700 nm (AUC, relative dyschromia) were calculated from the DRS data.

DATA ANALYSIS

Primary data analysis was to compare the pooled data from all time points as well as DRS results between 24.08% zinc oxide control and each treated pooled data set using Fisher LSD Method with 95% confidence. Significance was determined for each paired data set with a p-value less than or equal to 0.05. All analyses were done using OriginPro software (OriginLab Corporation, Northampton, MA).

TABLE 1. PRODUCTS TESTED

	Formula Information
A	24.08% Zinc Oxide Control SPF 50
C	24.08% Zinc Oxide + 5 AOX + Iron Oxides SPF 35
E	5.5% TiO_2 + 10% Zinc Oxide + Iron Oxides SPF 30
F	2% TiO_2 + 15% Zinc Oxide + Iron Oxides SPF 40
G	9% Zinc Oxide + 7.5% Octinoxate + Iron Oxides SPF 46
H	11% TiO_2 + Iron Oxides SPF 50
I	21.6% Zinc Oxide SPF 50

Results

FIGURE 1. Representative cross-polarized photographs of control and treated site of a subject's back at various time points. Ten healthy adult subjects with FST IV-VI were enrolled and the effectiveness of the novel ZnO/Fe_2O_3/5 AOX sunscreen, compared to several commercially available tinted and non-tinted mineral sunscreens was evaluated. The erythema and pigmentation assessment was performed by diffuse reflectance spectroscopy (DRS), polarized photography, and investigator global scoring immediately, 24 hours, and 7 days after irradiation (320 J/cm^2).

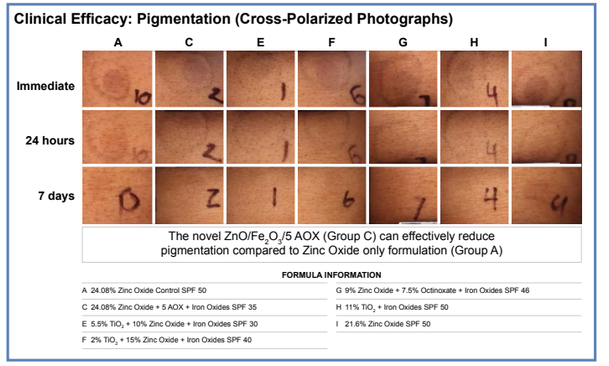

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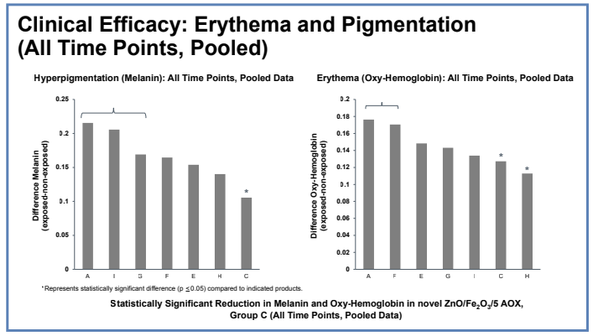
FIGURE 2. DRS measured change A) in melanin content (all time points, pooled) and B) in Oxy-Hemoglobin (delta oxy-Hb, all time points, pooled) for all sites after VL+UVA1 irradiation. *Represents statistically significant difference ($p \leq 0.05$) compared to indicated products. A. 24.08% Zinc Oxide Control SPF 50; C. 24.08% Zinc Oxide + 5 AOX + Iron Oxides SPF 35; E. 5.5% TiO_2 + 10% Zinc Oxide + Iron Oxides SPF 30; F. 2% TiO_2 + 15% Zinc Oxide + Iron Oxides SPF 40; G. 9% Zinc Oxide + 7.5% Octinoxate + Iron Oxides SPF 46; H. 11% TiO_2 + Iron Oxides SPF 50; I. 21.6% Zinc Oxide SPF 50.



Summary and Conclusions

- VL+UVA1 has been reported to cause erythema in light skin phototypes (FST I-III) and hyperpigmentation in dark skin phototypes (FST IV-VI)
- Zinc oxide (ZnO) and titanium dioxide (TiO_2) are often utilized in the development of mineral-based (inorganic) sunscreens as the active ingredients to protect against broad-spectrum ultraviolet (UV) radiation via their absorption properties. However, some of these products often leave a white cast, particularly on dark skin, making these products unfavorable, altering skin tone appearance, leading to concerns for sunscreen compliance
- This study demonstrates the photoprotective efficacy of a novel ZnO-based inorganic tinted sunscreen enriched with five antioxidants (5 AOX) against VL+UVA1 induced biologic effects (hyperpigmentation and erythema)
- DRS results demonstrated that the novel ZnO/Fe_2O_3/5 AOX can effectively reduce immediate erythema and pigmentation as well as delay pigmentation when compared with formulas containing ZnO only ($p \leq 0.05$)
- These results highlight the enhanced effects of 5 AOX-enriched tinted mineral sunscreen to be photoprotective against VL+UVA1, with a blendable tint designed for use on skin of all color aimed at improving patient compliance and overall sunscreen use

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