

Iron oxides in novel skin care formulations attenuate blue light for enhanced protection against skin damage

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Abstract

Background: Ultraviolet (UV) radiation is a main cause of aging of sun-exposed skin, but greater attention is being focused on the damaging effects of high-energy visible (HEV) light (400 and 500 nm). HEV light exposure has increased with expanding use of consumer electronics, such as smartphones, which have a peak emission in the 400-490 nm range. Sunscreens containing titanium dioxide and zinc oxide protect against UVA and UVB radiation but provide limited protection against HEV light.

Aim: Iron oxides including red iron oxide (Fe₂O₃), yellow iron oxide (Fe(OH)₃/FeOOH), and black iron oxide (Fe₃O₄) effectively block HEV light, each with a different attenuation profile. Zinc oxide, titanium dioxide, and iron oxides with patented skin care ingredients have been incorporated into several formulations to provide enhanced skin protection (Colorescience, Inc).

Methods: The percent of HEV light attenuation from 400 nm to 490 nm light was measured in vitro using a technique known as diffuse transmittance spectroscopy using a Perkin Elmer Lambda™ 750 UV/Vis/NIR Spectrophotometer equipped with a 100-mm integrating Labsphere® and PbS detector.

Results: Products formulated with zinc oxide, titanium dioxide, and iron oxides demonstrated 71.9%-85.6% attenuation across the tested wavelengths of 415-465 nm.

Conclusion: Sunscreens formulated with iron oxides provide enhanced protection against blue light, especially when combined with zinc oxide. To our knowledge, similar studies with iron oxides have not been performed.

KEYWORDS

high-energy visible light, iron oxides, photoaging of the skin, photoprotection

1 | INTRODUCTION

Sunlight is comprised of approximately 3%-7% of ultraviolet (UV) radiation (290-400 nm), 44% visible light (400-780 nm), and 53% infrared radiation (700-1440 nm).¹ UV radiation can be further divided into UVA (315-400 nm) and UVB (280-315 nm). More UVA reaches the earth's surface than UVB; however, UVB is more energetic than UVA and is far more damaging to our skin, causing sunburns. UVA

can be still further divided into UVA1 (315-340 nm) and UVA2 (340-400 nm). Visible light corresponds to the color spectrum ranging from violet (400 nm) to red (780 nm). UV radiation has long been known to be the leading cause of skin damage.² Until recently, less research had been conducted on the impact of visible light on the skin. Shorter wavelengths of solar radiation are more energetic than longer ones, so the wavelength band with the greatest effect on the skin is high-energy visible (HEV) or violet/blue light.³ HEV has a

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wavelength range between approximately 400 nm and 500 nm. As can be seen in Figure 1, the violet/blue light spectrum resides adjacent to UVA, as this is a continuum of wavelengths, one of the main distinguishing features is that we can see the visible violet/blue light but UVA is invisible. Numerous studies now indicate that HEV light contributes to various elements of photoaging, including increased wrinkles, worsening skin laxity, and especially hyperpigmentation.⁴

1.1 | Effect of blue light on skin

It has been estimated that as much as half of the free radicals produced in the skin are due to exposure to sunlight in the visible regions of the spectrum.⁵ High doses and long-term exposure can generate damaging reactive oxygen species (ROS) and reactive nitrogen species (RNS).^{6,7} These molecules contribute to the degradation of the extracellular matrix in skin, including collagen and elastin fibers.^{8,9} The contribution HEV makes toward skin aging is similar to that of UVA, such as hyperpigmentation, as mechanistically they both rely more on generation of free radical formation, in contrast with UVB which exerts its effects through DNA damage.^{10,11}

The application of antioxidants can decrease oxidative stress, reduce hyperpigmentation, and increase skin fibroblast proliferation providing further evidence of the oxidative cell damage caused by HEV.¹² Clinically, the effects of visible light include erythema, pigmentation, thermal injury, and DNA damage.^{13,14} HEV light also contributes to premature skin aging by impeding normal cellular functions. Analysis of tissue cultures exposed to HEV light revealed impaired fibroblast growth, altered cell distribution, and decreased type I procollagen secretion.¹⁵ Irradiation of human epidermis with HEV light in vitro induced production of ROS, proinflammatory cytokines, and matrix metalloproteinase expression, which was qualitatively similar to responses following exposure to UV radiation.¹⁴ A large proportion of cutaneous free radicals in sun-exposed skin are

due to light in the visible and infrared spectra.⁵ In fact, exposure of skin to HEV light stimulates melanogenesis and increased skin pigmentation.¹⁶ Several studies have described the ability of HEV light to increase skin pigmentation.^{4,11,17}

When human subjects with Fitzpatrick skin types II and IV-VI were irradiated with UVA1 (340-400 nm) and HEV light (400-700 nm),¹⁸ both wavelength ranges caused increased pigmentation; however, the pigmentation induced by HEV light was darker and more sustained than that produced by UVA. Increased pigmentation was not observed in subjects with skin type II. The longest wavelength capable of eliciting immediate pigment darkening appears to be approximately 470 nm.¹⁹ Darker and more sustained hyperpigmentation occurs following multiple exposures to HEV relative to UV exposure.²⁰ Compared with UVB, exposing subjects with skin types III and IV to blue-violet light resulted in significantly more marked hyperpigmentation that lasted up to 3 months.²¹ Others have also demonstrated persistent hyperpigmentation following exposure of sun-protected skin to visible light.²² Visible light is also synergistic with UVA1 for increasing pigmentation in darker-skinned (types IV-VI) individuals.²³ It appears that blue light stimulates melanogenesis through an alternative pathway, the OPN3 pathway, relative to UV-mediated pigmentation.

1.2 | Melanogenesis and the Impact of Blue Light via the Opsin-3 pathway

Opsins comprise a family of light-activated, G protein-coupled receptors that serve numerous visual and nonvisual functions.²⁴ Opsin-3 (OPN3) is highly expressed in human epidermal, melanin-producing melanocytes, which provide protection against UV radiation. Opsins mediate cellular responses to distinct wavelengths of visible and ultraviolet light.²⁵ OPN3 regulates melanocyte activity via melanocortin 1 receptors²⁴ and is responsible for the persistent hyperpigmentation induced by blue wavelengths of visible light.

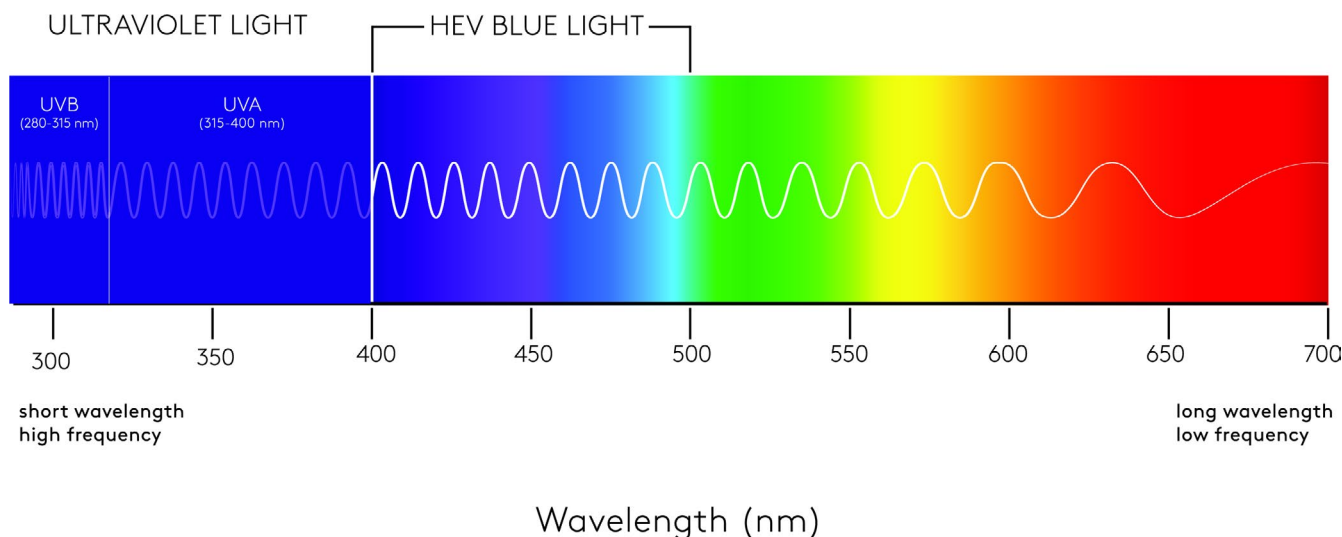


FIGURE 1 Visible light spectrum. The 400-500 HEV wavelength spectrum resides adjacent to ultraviolet A

OPN3-induced melanogenesis results from a cascade of events ultimately leading to an increase in the melanogenesis enzymes.¹⁷ Blue light induces the formation of a tyrosinase-related protein complex formed by melanogenesis enzymes primarily in dark-skinned (\geq type III) melanocytes resulting in long-lasting hyperpigmentation following blue light irradiation in this population.¹⁷

1.3 | Sources of HEV light

It has been demonstrated that up to one-half of the free radicals produced in the skin may be due to sunlight in the visible regions of the spectrum.⁵ High doses and long-term exposure can generate damaging free radicals, such as nitric oxide.⁶ While natural sunlight includes HEV light¹ and contributes to the greatest amount of skin damage, people today are being exposed to ever-increasing amounts of artificial light from fluorescent lighting and light generated from consumer electronics, such as smartphones, computers, and televisions. The widespread application of LEDs and the rapidly increasing use of smartphones, tablets, laptops, and desktop computers have led to a growing concern over the safety of these light sources, which have their peak emission in the blue region (400–490 nm).²⁶ Although white LEDs are widely used in digital camera photoflashes, their peak spectral intensity is also in the blue region.²⁶ Blue light also can have harmful effects on vision.²⁷

1.4 | Protecting against blue light

The use of sunscreens is central to the treatment of melasma and prevention of hyperpigmentation,^{28,29} especially among dark-skinned individuals.^{13,18,30} Sunscreens containing titanium dioxide (TiO₂) and zinc oxide (ZnO) help provide protection against UVA and UVB radiation but provide limited protection against visible and near-infrared radiation, especially at longer wavelengths.³¹ Zinc oxide, due to its ability to block a broad spectrum of wavelengths, especially its ability to attenuate wavelengths up through the mid-400 nanometer range, has been shown to play a role in blue light attenuation. Antioxidants are protective against injury from free radicals as a result of UV and blue light exposure,³² but cannot prevent blue light-induced melanogenesis.¹⁷ Likewise, UV-absorbing chemical ingredients such as oxybenzone, octinoxate, homosalate, avobenzone, and octocrylene have limited to no data demonstrating their ability to attenuate blue light.

Recently, iron oxides have been shown to provide effective protection against HEV. These include red iron oxide (Fe₂O₃), yellow iron oxide (Fe(OH)₃/FeOOH), and black iron oxide (Fe₃O₄). As iron oxides are used to provide color to mineral sunscreens, the use of tinted mineral sunscreens is more beneficial than nontinted products, since they protect against UV and visible light.³³ Sunscreens formulated with iron oxides have been shown to aid in the treatment of melasma and prevent hyperpigmentation in patients with melasma including dark-skinned individuals (Fitzpatrick skin types IV–VI).³⁴

Importantly, each iron oxide has a different light attenuation profile, maximally attenuating HEV in various nanometer segments of the blue light range. Yellow iron oxide provides attenuation below about 500 nm nanometers, while red iron oxides provide attenuation below about 570 nm. Black iron oxide provides attenuation across the entire visible spectrum. A combination of these iron oxides, coupled with zinc oxide that provides attenuation via scattering between 400 and 450 nanometers, may have a complimentary benefit to optimally inhibit blue light throughout the blue light spectrum and maximally attenuating light in the 400–430 nanometer range, which is most often implicated in melanogenesis. Thus, to provide broad and effective attenuation of HEV, it is relevant to utilize a constructed blend of these three iron oxides and zinc oxide. The total concentration of iron oxides can be meaningful, and there are other things to consider such as the synergy of all three shades of iron oxides, the processing that ensures even distribution of the iron oxides, the addition of other blue light-attenuating ingredients, such as zinc oxide, plus advanced antioxidants, which can provide an additive benefit.

2 | METHODS

The attenuation of HEV 400 nm to 490 nm light was measured in vitro using a technique known as diffuse transmittance spectroscopy (Perkin Elmer Lambda™ 750 UV/Vis/NIR Spectrophotometer equipped with a 100-mm integrating Labsphere® and PbS detector). A schematic drawing of the experimental design is provided in Figure 2. A unique formulation combining zinc oxide, titanium dioxide, and iron oxides with patented skin care ingredients has been incorporated into several formulations designed to provide protection and address skin concerns such as redness, hyperpigmentation, and upper and lower eyelid issues (Colorescience, Inc, Carlsbad, CA). The percent attenuation for HEV light was calculated from the percent transmittance values.

3 | RESULTS

Overall, the products formulated with zinc oxide, titanium dioxide, and iron oxides demonstrated 71.9 to 85.6% attenuation across the tested wavelengths of 415 to 465 nm. The percent HEV attenuation results are summarized in Table 1 and displayed in Figure 3. All three iron oxides provided protection against HEV light with the greatest attenuation occurring at the shorter wavelengths. As expected, the product formulated without iron oxides or zinc oxide and titanium dioxide showed no significant HEV attenuation.

4 | DISCUSSION

A group of investigators developed a new method for evaluating the effectiveness of sunscreens by determining the “Visible

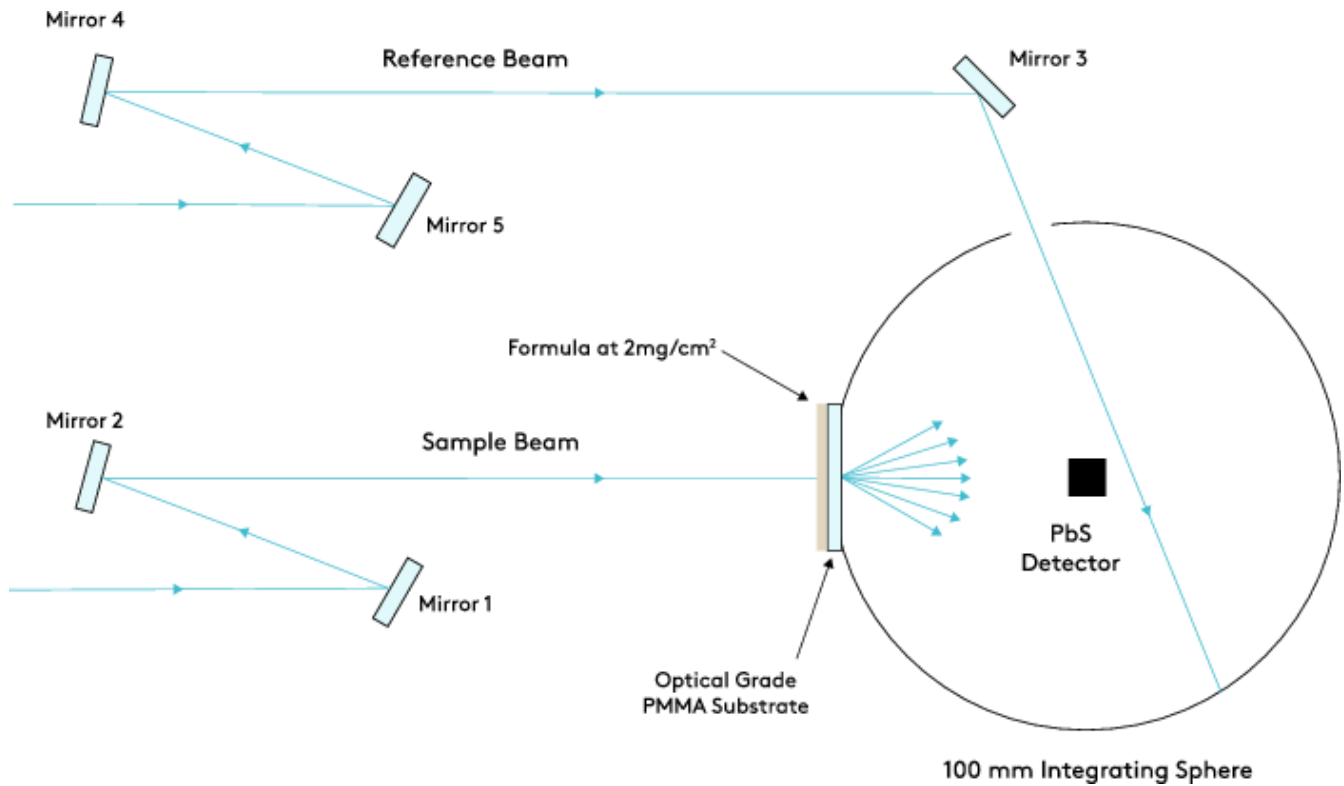


FIGURE 2 Diffuse transmittance experimental setup. The attenuation of HEV 400 nm to 490 nm light was measured in vitro using a technique known as diffuse transmittance spectroscopy

TABLE 1 Percent attenuation values for at selected HEV wavelengths

Product	% HEV attenuation		
	415 nm	440 nm	465 nm
SPF 35 (titanium dioxide 7.9%, zinc oxide 6.7%, and black (CI 77 499), yellow (CI 77 492), and red (CI 77 491) iron oxides) ^a	85.6	82.2	79.5
SPF 50 (titanium dioxide 11.6%, zinc oxide 8.6%, and black (CI 77 499), yellow (CI 77 492), and red (CI 77 491) iron oxides) ^b	83.7	78.9	74.7
SPF 50 (titanium dioxide 11.6%, zinc oxide 8.6%, and black (CI 77 499), yellow (CI 77 492), and red (CI 77 491) iron oxides) ^c	82.0	76.8	71.9
No sunscreen ^d	3.9	4.7	4.9

^aTotal Eye® 3-in-1 Renewal Therapy, SPF 35.

^bAll Calm® Clinical Redness Corrector, SPF 50.

^cEven Up® Clinical Pigment Perfector®, SPF 50.

^dPep Up® Collagen Renewal Face & Neck Treatment.

Light Protection Factor" (PF-VIS) and "Pigmentation Protection Factor" (PPF).³ They evaluated 33 commercial sunscreens of which 17 contained iron oxide and were tested using long-wavelength UVA and visible light wavelengths in the 250–450 nm range. Each product underwent spectrophotometric analysis (see original publication for measurement calculations).³ The iron oxide-containing products had PF-VIS values > 3, while those formulated without iron oxide had PF-VIS values < 2. The PPF values in products containing iron oxide were > 7,

while those formulated without iron oxide had PPF values < 5.³ Although this measurement system still requires validation, the protective effect of iron oxide on both long-wavelength UVA and blue visible light is clear.

An additional study published by the same investigators demonstrated that a series of products intended to prevent UVA and UVB skin damage that contain a combination of titanium dioxide, zinc oxide, and a blend of red, yellow, and black iron oxides attenuates 55% to 98% of blue light depending on the concentration

A Balanced Mineral Blend For Effective HEV Shielding

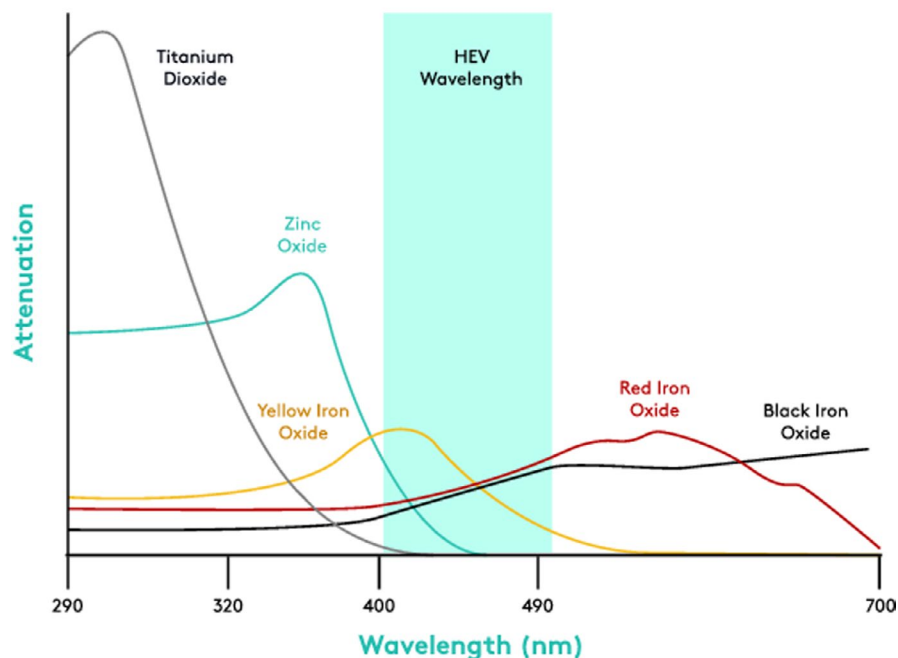


FIGURE 3 Wavelength attenuation of three iron oxides. All three iron oxides provided protection against HEV light with the greatest attenuation occurring at the shorter wavelengths

of zinc oxides and the level of iron oxides.³⁵ This analysis also utilized a similar diffuse transmittance spectroscopy approach as cited above. The powder dosage format containing 22.5% zinc oxide and 22.5% titanium dioxide and proprietary combination iron oxides resulted in the maximum blue light (400–490 nm) protection of 98.5%.³⁵

5 | CONCLUSION

The formulation of sunscreens to include iron oxides is a safe, effective, and environmentally friendly way to protect against high-energy visible blue light. This effect is especially significant when combined synergistically with zinc oxide. The iron oxide-containing products described in this paper are the result of extensive HEV testing, and to our knowledge, this is among the first reports of such testing. Formulating with iron oxides in the manner in which these products were designed has been shown to attenuate HEV and contribute to creating specific shades and colors which enhance the cosmetic appeal.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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