ORIGINAL RESEARCH

Evaluation of the Antioxidant Capacity and Protective Effects of a Comprehensive Topical Antioxidant Containing Water-soluble, Enzymatic, and Lipid-soluble Antioxidants

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ABSTRACT

Objectives: Investigators sought to evaluate the antioxidant capacity of a comprehensive topical antioxidant (WEL-DS), its ability to protect skin against the oxidizing effects of UVA/UVB radiation, and to assess the effectiveness and tolerability of WEL-DS for visible improvements in facial photodamage. **Study Designs:** *In-vitro* testing utilized a hydrogen peroxide assay to detect activity in human skin explants following application with WEL-DS, a leading antioxidant serum (L-AOX), and a saline control. Clinical studies included a minimal erythema dose (MED) trial in female subjects, aged 35 to 60 years. Skin was initially irradiated to determine each subject's MED. WEL-DS was applied for four days to one site on the lower back of subjects; the other site remained untreated. Both sites were irradiated with 1X, 2X and 3X each subject's MED, digital images were obtained, and punch biopsies were collected from the 3X MED irradiated areas for histological analysis. A second clinical study evaluated efficacy and tolerability of twice daily application of WEL-DS in female subjects, aged 25 to 65 years with mild-to-moderate photodamage. Changes in fine lines/wrinkles, dyschromia, erythema, skin tone, pores, and tolerability were assessed at baseline and Weeks 4, 8, and 12. A subset of subjects were evaluated through Week 16. **Results:** Skin treated with WEL-DS neutralized up to 53 percent more oxidative stress relative to L-AOX. WEL-DS-treated skin demonstrated significantly less UV-induced erythema at 1X, 2X, and 3X MED and demonstrated cellular protective effects versus untreated irradiated skin (N=5). WEL-DS demonstrated average improvements from baseline of 37 percent, fine lines/wrinkles; 17 percent, skin tone; 13 percent, dyschromia; 18 percent, erythema; and four percent, pores (N=21; Week 12). Continued improvements were demonstrated in all parameters in an extension study (n=14; week 16). WEL-DS was well-tolerated. **Conclusion:** These studies demonstrate WEL-DS's innate ability to quench free radicals, protect skin from the oxidizing effects of UV radiation, and reduce the visible effects of facial photodamage.

KEYWORDS: Antioxidants, oxidative stress, UV-induced erythema, MED, photoprotection, facial aging

Skin aging is a complex process influenced by intrinsic and extrinsic factors that lead to cumulative and structural changes affecting the appearance of facial skin.[1] Three percent of the factors associated with the skin aging process are genetic or physiological in nature, whereas 97 percent are extrinsic in nature and trigger the generation of reactive oxygen species (ROS) or free radicals.[1,2] Free radicals are unstable molecules that take electrons from molecules, rendering them nonfunctional or dysfunctional, which results in cumulative damage to skin cells.[3] In addition to the natural formation of free radicals through normal metabolic processes, exogenous atmospheric factors, such as ultraviolet (UV) light, and environmental factors, such as irritants, pollution, and smoke, can trigger the production of free radicals.[3–5] Eighty percent of free radical damage is thought to be caused by UV-A and -B light exposure to the skin, and the damaging effects of UV light and infrared radiation (IR) to the skin are well documented.[3,4,6]

Skin has the ability to protect itself against the harmful effects of UV radiation and other environmental factors through an elaborate antioxidant defense system.[3,4,7–11] However, as human skin ages, the generation of free radicals increases while the natural endogenous defenses of the skin decrease in efficacy.[4,11] The inability of skin to counteract or repair the cumulative effects of free radical damage leads to oxidative stress.[12] Coupled with everyday environmental exposure and the bombardment of free radicals, internal defenses can become overwhelmed and lose the ability to function efficiently, which can lead to accelerated skin aging.[4] The resulting cumulative and structural changes to the skin manifest in the development of fine lines/wrinkles, dyschromia, sallowness, dehydration, and dryness.[11,13,14]

Supplementing skin with topical antioxidants can replenish depleted antioxidant levels,[15] which can enhance the skin's natural antioxidant defenses. In contrast to sunscreens, which work on the top layer of skin, topical antioxidants

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penetrate the skin to stabilize or deactivate free radicals before they damage cells.[16–18] Topical antioxidants counteract free radical damage caused by UV light (290–400nm), visible light (400–700nm), and IR radiation (>800nm) as well as other environmental insults (e.g., smog, ozone, particulate matter) that sunscreens are unable to neutralize.[5,19] Topical antioxidants are instrumental in skin protection and repair and provide multiple skin health benefits.[19]

Topical antioxidants are derived from numerous sources and possess unique properties that are thought to benefit the skin and provide varying levels of support in combating free radicals.[15,20] Hydrophilic antioxidants, such as vitamin C, protect the water-containing portions of cells, interior cell structures, and interstitial fluid.[15,20] Enzymatic antioxidants, such as superoxide dismutase and ubiquinone, support the body's internal defense system and protect mitochondria. Hydrophobic antioxidants, such as vitamin E, protect the lipid-rich cell components, such as the cell membrane.[15,20] Comprehensive skin protection can be achieved by using combinations of antioxidants to facilitate their synergistic interaction and provide broad-based protection from different types of ROS at all cellular levels of the skin.[6,18,21]

Alto Defense Serum™ (WEL-DS; skinbetter science, Phoenix, Arizona) comprises a balanced ratio of 19 water-soluble, enzymatic, and/or lipid-soluble antioxidants selected with the aim of providing the skin synergistic, comprehensive cellular protection against a broad range of free radicals. As part of a research program evaluating the efficacy and tolerability of WEL-DS, we first compared WEL-DS's innate antioxidant capacity with that of a well-known antioxidant serum (C E Ferulic®, SkinCeuticals, Dallas, Texas) comprising 15% L-ascorbic acid, 1% vitamin E [alpha tocopherol], and 0.5% ferulic acid [L-AOX]), and a saline control in human skin explants.[22] Testing was performed on replicates of mid-dermal grafts from excised human abdominal skin from a single female donor. Two identical, independent experiments were conducted, each involving three test groups: WEL-DS (n=9 skin grafts), L-AOX (n=9 skin grafts), and a saline control (n=4 skin grafts). Grafts were mounted onto a transcutaneous flux apparatus, and test samples and saline were applied to the grafts and left on donor surfaces for up to 20

TABLE 1. Average performance of WEL-DS, L-AOX, and saline: Tests 1 and 2*

TEST		WEL-DS	L-AOX	SALINE
Test 1	Average**	0.088	0.135	0.314
	t-test vs. saline	p=0.0003	p=0.0012	N/A
	Oxidative stress vs. WEL-DS	100%	153%	363%
Test 2	Average**	0.130	0.180	0.33
	t-test vs. saline	p=0.0029	p=0.0316	N/A
	Oxidative stress vs. WEL-DS	100%	141%	258%

*Higher values denote higher levels of oxidative stress and proportionally lower antioxidant capacity.
**Average is based on 8 time points for WEL-DS and L-AOX and 4 time points for saline control.
WEL-DS: Alto Defense Serum™; L-AOX: 15% l-ascorbic acid, 1% vitamin E, 0.5% ferulic acid; N/A: Not applicable

TABLE 2. Erythema reduction in irradiated skin treated with WEL-DS versus irradiated untreated skin

MED LEVEL	COMPARISON	ESTIMATED DIFFERENCE (SE)	*P*-VALUE*
1X MED	WEL-DS vs. Untreated	-3.55 (1.02)	0.025
2X MED	WEL-DS vs. Untreated	-6.71 (0.77)	<0.001
3X MED	WEL-DS vs. Untreated	-5.19 (0.87)	0.004

*Calculated from paired t-test. Testing hypothesis based on mean measurement being equal between treatments
WEL-DS: Alto Defense Serum™; MED: Minimal erythema dose

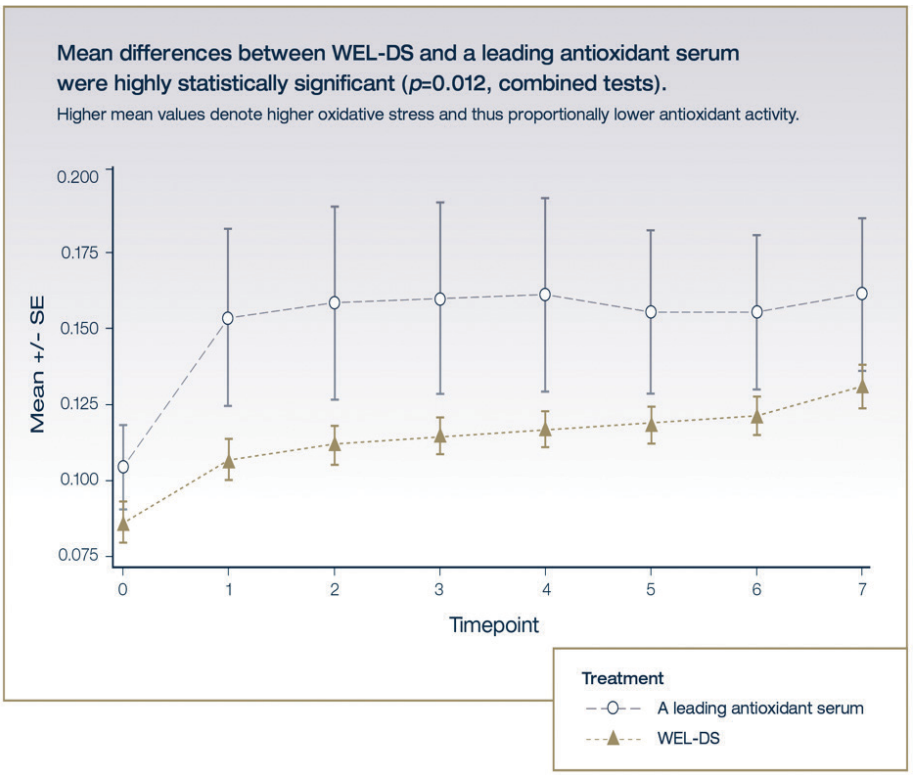

FIGURE 1. Mean variable stress over time

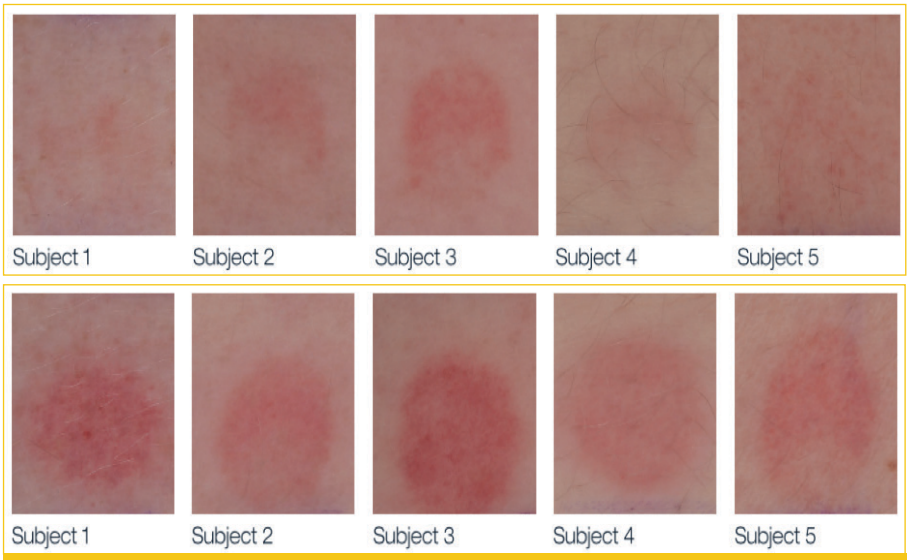

FIGURE 2. Top: erythema in irradiated skin treated with WEL-DS (2× MED); bottom: erythema in irradiated untreated skin (2× MED)

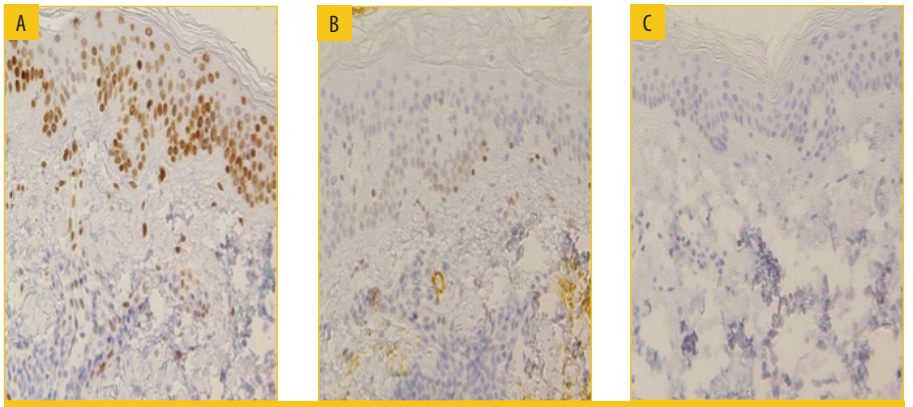

FIGURE 3. Photoprotective effect of WEL-DS on thymine dimers (3× MED)—A) irradiated untreated, B) irradiated WEL-DS, and 3) unirradiated

hours. A standardized hydrogen peroxide/peroxidase assay (20µL of 01mM) was used to assess oxidative stress and peroxide activity in washed, homogenized skin tissue over time. Absorbance was measured at baseline (pre-spike), immediately after spike (Time 0), and at one minute (Time 1), two minutes (Time 2), three minutes (Time 3), four minutes (Time 4), five minutes (Time 5), 10 minutes (Time 6), and 15 minutes (Time 7) after spike. Reductions in oxidative stress in WEL-DS, L-AOX, and saline were compared. Repetition of the assay was performed (Test 2) to validate results and ensure reproducibility.

Using a fixed-timepoint analysis, both WEL-DS and L-AOX demonstrated significant antioxidant capacity in quenching peroxide versus the saline control (WEL-DS: p=0.0003 and p=0.003 for Tests 1 and 2, respectively; L-AOX: p=0.001 and p=0.03 for Tests 1 and 2, respectively) (Table 1). Skin treated with WEL-DS neutralized 53 percent and 41 percent more oxidative stress relative to L-AOX in Tests 1 and 2, respectively. The difference between WEL-DS and L-AOX was statistically significant in each test (p=0.0106 and p=0.0051 for Tests 1 and 2, respectively) and for both tests combined (p=0.0001) (Figure 1). Differences in treatment effect within each test and when the tests were combined were significant, with WEL-DS demonstrating greater ability to neutralize peroxide in comparison with L-AOX.

Once the antioxidant capacity of WEL-DS was established, we sought to assess, in two clinical studies, 1) the ability of WEL-DS to protect skin against the oxidizing effects of UVA-UVB radiation (Minimal Erythema Dose [MED] study) and 2) its effectiveness in improving the appearance of photodamaged facial skin (Facial photodamage study).

DESIGN AND METHODS

Study ethics. These studies were conducted in accordance with all applicable guidelines for the protection of human subjects for research as outlined in 21 CFR 50, the accepted standards for Good clinical Practice (GCP), and approved by IntegReview IRB, Austin, Texas (MED study) and Chesapeake IRB, Columbia, Maryland (facial photodamage study).

MED study. This five-day, single-center, randomized, controlled trial enrolled healthy women, 35 to 60 years of age, with Fitzpatrick Skin Types II to III. Eligible subjects were enrolled in the study if they were generally in good health, nonsmokers, and willing to adhere to the requirements of the study and provide informed consent. Subjects were excluded from the study if they had known allergies to skincare products; were pregnant, nursing, or planned on becoming pregnant during the study; had a history of skin cancer or a health or dermatologic condition on their back; had used oral retinoids or steroids during the prior six months; were using anti-inflammatory medication or medication with photo-sensitizing potential; had a dermatologic condition that, in the opinion of the investigator, that might influence test results; or individuals with known abnormal responses to sunlight or artificial light, known sensitivity to sunscreens, or who had been instructed by a healthcare professional to avoid sunlight as a result of a medical condition.

Treatment with WEL-DS was randomly applied for four consecutive days to one of two sites (Site 1 or Site 2) on the lower back of each subject; the other site remained untreated (control). In an effort to establish each subject's MED, a single-port solar simulator irradiated an untreated area of skin. Treated and untreated sites were then irradiated with 1×, 2×, and 3× each subject's MED. On Day 5, individual sites were digitally photographed using a Canfield Twinflash System (Canfield Scientific, Fairfield, New Jersey) and analyzed based on erythema reduction values (a*) and the amount of visible erythema and/or edema for both treated and untreated irradiated

sites. Additionally, 3mm punch biopsies were collected from three different sites on the lower back of each subject: the treated irradiated (3× MED) site, the untreated irradiated (3× MED) site, and the untreated unirradiated site. Analysis of biomarkers indicative of skin damage were histologically evaluated using thymine dimers, matrix metalloproteinase 9 (MMP-9), cluster of differentiation (CD)1a Langerhans cells, sunburn cells, and p53 as measures.

Facial photodamage study. This 12-week, single-center, clinical study evaluated the efficacy and tolerability of twice-daily application of WEL-DS in female subjects, 25 to 65 years of age, with mild-to-moderate facial photoaging and no known medical conditions that, in the investigator's opinion, might interfere with study participation. In addition to providing written informed consent (including photoconsent), subjects had to agree to practice sun avoidance and daily use of sunscreen. Subjects were excluded if they were pregnant, breast feeding, or planning to become pregnant during the study; had any previous hypersensitivity reaction to any of the ingredients in the study product(s); or were currently using or had continuously used for more than two weeks during the previous six months any cosmetic products containing alpha hydroxy acids, retinoids, peptides, growth factors, and/or potent antioxidants.

Enrolled subjects were instructed to apply the study product to clean facial skin twice daily (AM and PM) for 12 weeks. Subjects followed the application of the study product with a supplied moisturizer (AM and PM) and sunscreen (AM), followed by application of their routine makeup products, if applicable. To ensure adherence to protocol and application instructions, participants were instructed to bring the study product with them to each clinic visit to be weighed.

Expert-graded assessments of facial photodamage, including changes in fine lines/wrinkles, dyschromia, erythema, skin tone, and pore size, were based on a six-point scale, where 0=none and 5=severe, using digital photography (Canfield Olé system; Canfield Scientific, Fairfield, New Jersey). Expert or physician evaluations also included global improvement (5-point grading scale [0=none to 4=severe]), and subjects completed a self-assessment questionnaire comprising 21 questions in which they agreed or disagreed to statements regarding perceived changes in the appearance of redness, pigmentation, lines and wrinkles, and skin brightness and texture, as well as their impressions regarding the feel and texture of the study product. Adverse events (AEs) were monitored and recorded throughout the study period. A subset of subjects (n=14) were evaluated in an extension study and continued using the study product through Week 16.

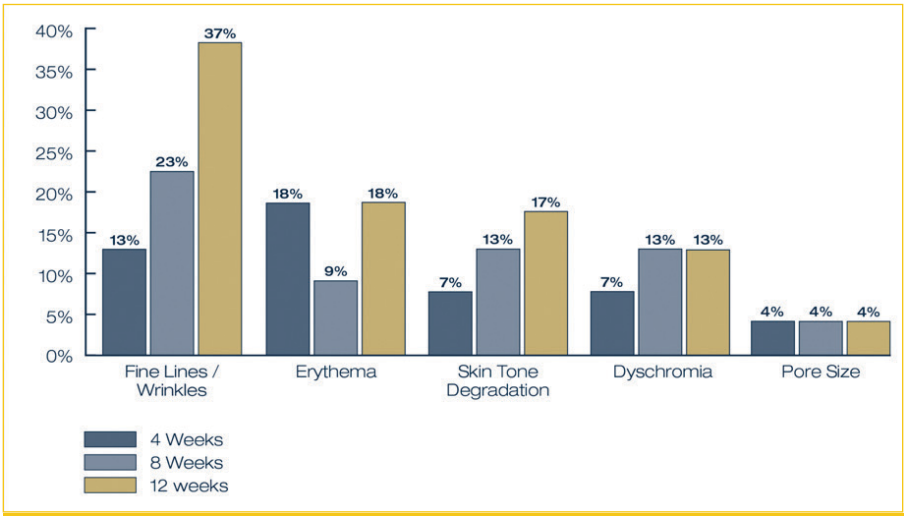

FIGURE 4. Average percent improvement in appearance of facial photodamage from baseline to Week 12 based on expert assessment

RESULTS

MED study. Six female subjects were enrolled and five subjects completed the MED study. One subject had insufficient erythema for MED determination. The mean age of the subjects was 42.6 years, and all were Fitzpatrick Skin Types II or III. No adverse events (AEs) were observed or reported during the study.

Digital photographs of test areas were evaluated for changes in erythema, as described previously. Treatment with WEL-DS demonstrated significantly less UV-induced erythema at 1×, 2×, and 3× MED exposures compared with untreated irradiated skin (p=0.025, p<0.001, and p=0.004, respectively) (Table 2 and Figure 2).

Biopsies obtained from subjects at 3× MED-irradiated treated sites revealed reductions in thymine dimers (p<0.02), MMP-9 (p<0.005), p53, and sunburn cells, as well as a lack of reduction in Langerhans cells (p<0.008), compared with untreated sites, suggesting the protective ability of WEL-DS on a cellular level against sun damage to the skin (Figure 3).[23] In addition, Langerhans cells from WEL-DS-treated irradiated sites exhibited markedly less morphological changes compared to untreated irradiated sites, in which cells were atypically less dendritic and appeared ovoid in shape.

Facial photodamage study. Twenty-two female subjects with an average age of 56 years and predominantly Fitzpatrick Skin Type II were enrolled in this study. Twenty-one subjects completed the study through Week 12. Due to possible sun exposure, one subject was not evaluated for erythema, skin tone, or dyschromia. A subset of subjects (n=14) continued in the four-week extension study, for a total of 16 weeks of treatment.

Expert-graded assessments of facial photodamage (6-point scale [0=none to 5=severe]) reported average visible improvements from baseline to Week 12 in fine lines/wrinkles (37%), erythema (18%), skin tone (17%), and dyschromia (13%) (Figures 4 and 5). Improvement in the appearance of pore size remained relatively stable, with an average four-percent reduction in the appearance of pores from baseline to Week 12.

Expert-graded assessments of facial photodamage reported progressive improvement in fine lines/wrinkles over the 12-week study period, with average improvements of 13 percent at Week 4, 23 percent at Week 8, and 37 percent at Week 12. Eighty-six percent (86%) of subjects demonstrated at least a 1-grade improvement in the appearance of fine lines/wrinkles relative to baseline severity. Forty percent (40%) of subjects demonstrated at least a 1-grade improvement in the appearance of erythema from baseline severity. Skin tone

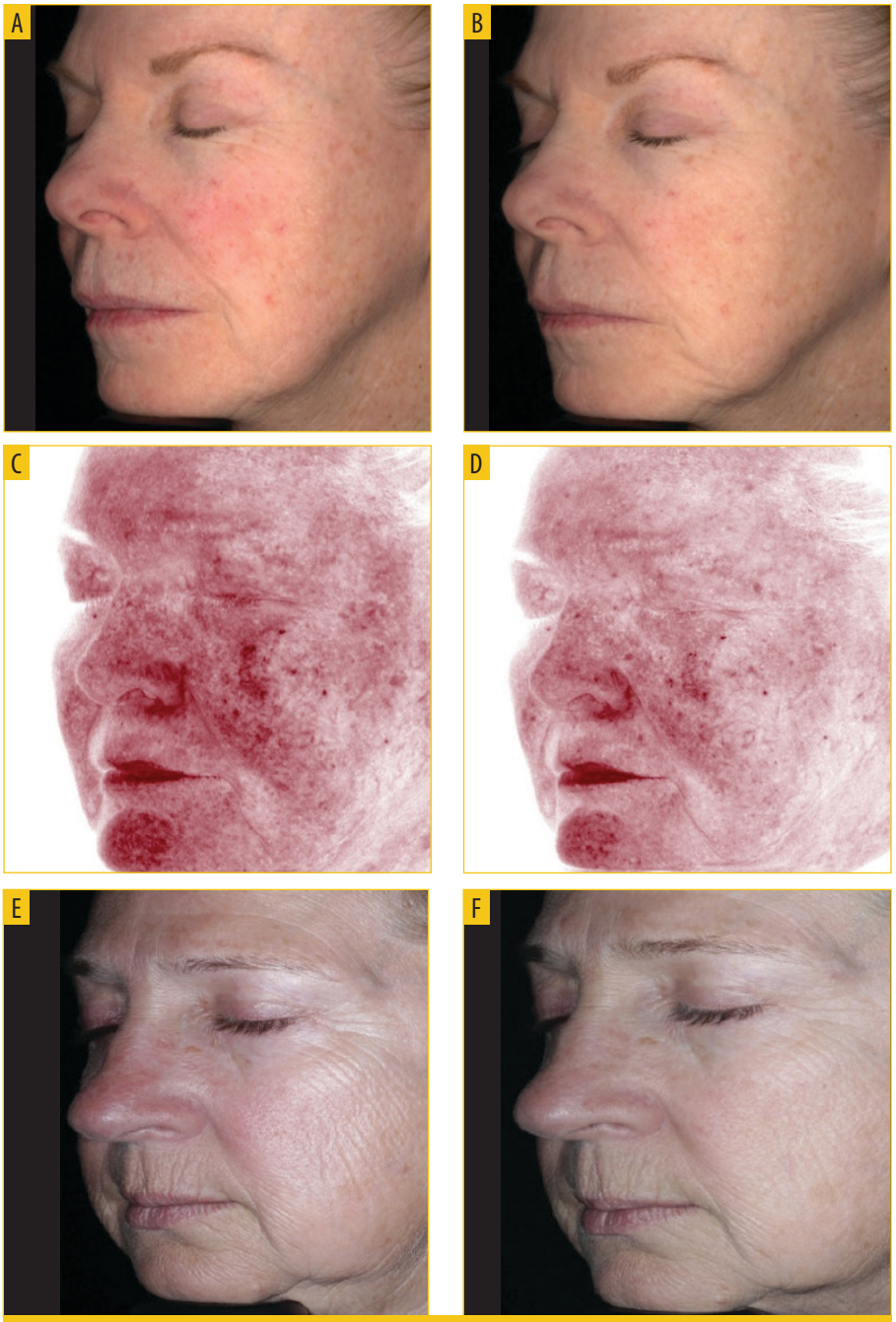

FIGURE 5. Improvement in the appearance of erythema and fine lines and wrinkles—A) baseline to B) Week 4, C) baseline to D) Week 12, and E) baseline to F) 16 weeks

showed continued, progressive improvement from baseline with seven percent, 13 percent, and 17 percent average improvement findings from baseline to Week 12. Fifty percent (50%) of subjects demonstrated at least a 1-grade improvement in the appearance of skin tone relative to baseline severity. An average visible improvement in dyschromia of 13 percent was observed at Week 8 and was maintained through Week 12, with 45 percent of subjects demonstrating at least a 1-grade improvement in the appearance of dyschromia from baseline. Ninety-five percent (95%) of subjects demonstrated at least a 1-grade increase in global improvement at Week 12.

Based on expert-graded assessments of facial photodamage, as described previously, subjects evaluated through Week 16 (n=14) demonstrated progressive average visible improvements of 39 percent in fine lines/wrinkles, 32 percent in erythema, 27 percent in skin tone and dyschromia, and 21 percent in pore size. All subjects demonstrated a minimum 1-grade increase in global improvement at the end of the 16-week study period.

All subjects reported that the study product had a light texture and feel and was absorbed quickly into the skin. WEL-DS was well-tolerated, with subjects reporting only mild, transient AEs that were deemed possibly related to study products (n=9; dryness and one blemish). No subject discontinued the study due to an AE.

DISCUSSION

The need for comprehensive protection against the cumulative effects of sun exposure is well-documented.[24] Sunscreens differ mechanistically from topical antioxidants in that they scatter, absorb, or block UV radiation before free radicals are formed in the skin, whereas topical antioxidants work by neutralizing free radicals and inhibiting their capacity to cause cellular damage.[19] While broad-spectrum sunscreens offer protection against both UVA and UVB light, to achieve IR photoprotection, sunscreens need to be supplemented with specific antioxidants.[6] Topical antioxidants play a complementary role to sunscreens by neutralizing free radicals and inhibiting their capacity to cause cellular damage.[16,18,19]

Our results from the MED study suggest WEL-DS is effective in protecting skin against the oxidizing effects of UV radiation. Skin treated with WEL-DS exhibited significantly less UV-induced erythema at all MED levels tested (1×, 2×, and 3×) in comparison with untreated irradiated skin. Histology of irradiated skin treated with WEL-DS correlated with clinical observations, demonstrating broad cellular protection, which further supports evidence of the effective percutaneous absorption and bioavailability capability of WEL-DS.

Irradiated skin treated with WEL-DS demonstrated significant reductions in thymine dimer formation and the upregulation of MMP-9 at 3× MED. Thymine dimer mutations occur due to direct UVB absorption and UVA irradiation and have been associated with nonmelanoma skin cancer.[28,29] MMP-9, a Type IV collagenase, is upregulated following UV irradiation of the skin, leading to increased

breakdown of collagen and elastin. The destruction of the extracellular matrix following UV irradiation is thought to be responsible for photoaging and induction of MMP-9, which degrades basement membranes.[30,31] WEL-DS also appeared to protect the skin against UV-stimulated sunburn cells compared to untreated irradiated skin, suggesting its ability to protect skin from UV damage and inhibit cellular apoptosis. WEL-DS also appeared to provide protective effects related to Langerhans cells and p53. Specifically, treatment with WEL-DS appeared to prevent UV-induced reductions in CD1a (Langerhans cells). Langerhans cells are epidermal antigen-presenting cells that initiate an immune response. Sites treated with WEL-DS had lower (improved) mean values of p53, a cellular protein induced by UV irradiation in response to deoxyribonucleic acid (DNA) damage and oxidative stress.[32,33] p53 slows the cell cycle for DNA repair and can induce cellular apoptosis if the damage is significant. These findings suggest WEL-DS offers varied modes of cellular protection against the damaging consequences of UV-exposure to the skin.

Correlation of both objective and subjective measures (biomarker and erythema evaluation, respectively) of UV-induced damage demonstrate the potential strength and consistency of WEL-DS in counteracting UVA/UVB-generated ROS in skin.

Prior studies have tested the ability of vitamin C-based mixtures to protect human skin against UV radiation damage.[16,34] In one study, nine subjects were treated with a combination of 15% L-ascorbic acid, 1% alpha tocopherol, and 0.5% ferulic acid (CEFer) and exposed to up to 10× MED. Significant protective benefits were first observed at 8× and 10× MED for erythema and at 6× MED for sunburn cells.[34] Another study examined the protective effects of a mixture that combined 10% L-ascorbic acid, 0.5% ferulic acid, and 2% phloretin (CFerPhlor).[16] In this study, 10 subjects were evaluated over the course of four days at up to 5× MED and biopsies were obtained from the 5× MED site. The CFerPhlor mixture showed a protective effect at 5× MED.[16]

Although our study included a small sample size (five subjects) and only tested up to 3× MED, significant and noteworthy results were observed, suggesting the potential antioxidative potency of the WEL-DS formulation in counteracting free radical damage as a result of UV exposure.

The skin's innate system of antioxidants generally provides protection from oxidant stress generated by both intrinsic and extrinsic factors. However, as the skin ages, its natural defenses, including production of protective antioxidants, decline, which can lead to significant oxidative stress; thus, when the skin is exposed to UV light or other environmental stressors, accelerated aging can occur.[12,35]

Due to the inherent sensitivity of antioxidants, developing an antioxidant formulation that remains stable over time has been challenging.[4] Historically, formulations have narrowly focused on a few specific ingredients such as vitamin C. The water-soluble form of vitamin C, L-ascorbic acid, is often used, due to its known cutaneous benefits of promotion of collagen synthesis, photoprotective capabilities against UVA/UVB exposure, and skin brightening capabilities.[59] However, L-ascorbic acid is highly unstable and must be formulated at specific concentrations and pH to ensure stability and adequate skin penetration.[35,60,61] Over the last two decades, our understanding of other potent antioxidants, their benefits, and the roles they play in defending the skin against oxidative stress has

TABLE 3. WEL-DS antioxidants

ANTIOXIDANT	ANTIOXIDANT PROPERTIES
Chlorogenic acids	Protects against UV-induced oxidative damage; reduces level of free radicals; enhances superoxide dismutase[36–38]
Coffee arabica leaf extract	Protects against skin damage as a result of sunburn cell formation and DNA degradation[39]
Theobroma cacao seed extract (cocoa)	Inhibits lipid peroxidation, glutathione oxidation, chelate redox active metals, and enzymes involved in ROS production; supports the Nrf2 signaling pathway[38,40,41]
Ergothioneine	Protects DNA and protein from oxidative damage; works synergistically with tetrahexyldecyl ascorbate[42]
Curcuma longa root extract (turmeric)	Protects against hydroxyl radicals, glycosylation, and lipid peroxidation; scavenges superoxide anion[43,44]
Euterpe oleracea fruit extract (acai)	Protects against free radical damage to the skin during the inflammatory process[43,45,46]
Vitis vinifera seed extract (grape)	Reduces lipid peroxidation and inhibits metals from reacting and forming hydroxyl radicals[4,45]
Buddleja officinalis flower extract	Free radical scavenger; protects against harmful effects of UV, blue light and IR wavelengths[47]
Camellia sinensis leaf extract (green tea)	Reduces hydrogen peroxide formation, nitric oxide, and copper; scavenges superoxide[4,43,48–51]
Carnosine	Helps quench hydroxyl radicals and provides IR protection[52]
Crocus sativus leaf extract (saffron)	Protects against free radical damage[53]
Olea europaea fruit extract (olive)	Protects against UV exposure and DNA oxidation[45]
Tetrahexyldecyl ascorbate	Inhibits lipid peroxidation and mitigates damaging effects of UV exposure[4,48]
Tocopheryl acetate	Reduces formation of free radicals from UV exposure[48]
Tocopherol	Prevents production of free radicals and protects skin from free radicals due to UV exposure[4,48,54]
Glycyrrhiza glabra root extract (licorice)	Inhibits the amount of oxidative stress; anti-inflammatory properties[43,45,55]
Superoxide dismutase (SOD)	Protects cell from superoxide toxicity[56]
Ubiquinone (CoQ10)	Effective against UVA-mediated oxidative stress[4,48,57]
Arabidopsis thaliana extract	Supports the transport of antioxidants into skin; promotes DNA repair[58]

IR: infrared; TEWL: transepidermal water loss; UV: ultraviolet; DNA: deoxyribonucleic acid; ROS: reactive oxygen species; Nrf2: nuclear factor erythroid 2-related factor 2

substantially expanded.[12] Broad antioxidant protection is essential in counteracting different types of ROS or free radicals at all cellular compartments of the skin. WEL-DS combines a selection of 19 active antioxidants—a balanced ratio of water-soluble, enzymatic, and lipid-soluble substances—to create a stable formulation designed to offer the skin broad-range protection from free radicals triggered by various extrinsic factors. Many of the antioxidants included in WEL-DS are thought to have additional benefits, such as reducing inflammation and erythema, brightening the skin, and facilitating visible improvements in fine lines and wrinkles (Table 3).[4,36–58]

In this clinical study, based on expert-graded assessments, subjects in the WEL-DS group demonstrated improvements in the appearance of fine lines/wrinkles (37%), erythema (18%), skin tone (17%), dyschromia (13%), and pore size (4%) from baseline to Week 12. Progressive visible improvements from baseline were demonstrated in all categories at Week 12 with the exception of pore size, which remained relatively stable throughout the 12-week study period. Expert-graded evaluations demonstrated that nearly all subjects (95%) achieved at least a 1-grade increase in global improvement at 12 weeks.

Achieving early visible changes to photodamaged skin with the use of topical antioxidants is meaningful and might help foster routine and consistent use by patients. Perception regarding the look, feel, and smell of a topical product is also critical in reinforcing consistent use. Among the subjects in our study, 100 percent reported that WEL-DS had a light texture and feel.

Progressive, substantial improvements in the appearance of fine lines and wrinkles (39%), erythema (32%), skin tone (27%), dyschromia (27%), and pore size (21%) were observed from baseline to Week 16 (n=14).

WEL-DS was well tolerated, with no reports of stinging or burning. Reports of dryness among our patient population could possibly be attributed to the time of year in which the study took place (winter months).

Limitations. This study involved a small number of subjects with predominantly light skin. Additional research in a larger and more diverse population would be beneficial in understanding efficacy and tolerability across different skin types. In addition, future studies examining the effects of use beyond 16 weeks in a larger patient sample would be of value, as longer durations of use will provide additional information regarding safety and efficacy.

CONCLUSIONS

In previous research, WEL-DS appeared to elicit significant antioxidant effects, compared to a saline control, by neutralizing hydrogen peroxide in a human skin model. Additionally, skin treated with WEL-DS neutralized 53 percent and 41 percent more oxidative stress (Tests 1 and 2, respectively) compared to a leading antioxidant serum. In our current two-part study, skin treated with WEL-DS demonstrated significantly less UV-induced erythema, compared to untreated irradiated skin, suggesting it provides substantial cellular protection against sun damage. Additionally, treatment with WEL-DS demonstrated early, progressive improvements in the appearance of facial aging, supporting its use as a treatment for reducing free radical damage to the skin. Together, these studies provide strong evidence supporting the use of WEL-DS as a safe and effective method of skin protection from photodamage as well as a treatment for the improving the appearance of UV-damaged facial skin.

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