The Effects of GliSODin Skin Nutrients Advanced Skin Brightening and Dermal Formulae on Facial Skin Hyperpigmentation and Erythema

ABSTRACT

Background: GliSODin Skin Nutrients' (GSN) Advanced Skin Brightening Formula and Advanced Anti-Aging/Dermal Formula are nutricosmetics developed to address skin pigmentation and inflammation, respectively, in addition to other cosmetic and functional skin issues.

Objective: This study will objectively evaluate the change in facial skin erythema and pigmentation from usage of the Dermal and Skin Brightening Formulae to confirm clinical efficacy.

Method: A 90-day multicenter randomized, placebo-controlled, single-blinded clinical trial of 36 participants with a history of either facial photodamage or an inflammatory skin condition. Participants were randomized into 4 treatment groups: GSN Advanced Skin Brightening Formula (SB) group, SB placebo group, GSN Advanced Anti-Aging/Dermal Formula (DF) group, or DF placebo group. Pigmentation was assessed using VECTRA XT 3D images taken at days 0, 30 and 90 of treatment. Participant skin satisfaction was evaluated with 100 mm visual analog scale (VAS) questionnaires completed on days 0 and 90.

Results: No significant changes in total pigmentation occurred at 30 days in any of the treatment groups ($p > 0.05$). After 90 days of treatment, total redness in the DF group was reduced from 52.20 ± 12.57% to 44.96 ± 9.24% ($p = 0.008$). Total brown pigmentation was reduced from 73.77 ± 12.69% to 69.15 ± 13.56% ($p = 0.042$) in the SB group, with a decrease in total dark spots from 20.47 ± 16.57 to 13.76 ± 12.04 ($p = 0.010$). No significant changes in total redness or brown pigmentation occurred in either the DF or SB control groups ($p = 0.75$ and 0.89). At 90 days, VAS scores were significantly improved for radiance, brown spots and dryness in the DF group, with no significant changes in the placebo group. Radiance, softness and overall quality scores were significantly improved in the SB group. The SB placebo group reported significant improvements in brown spot and dryness scores.

Conclusion: This study suggests that DF and SB provide significant clinical benefits in the reduction of facial erythema and hyperpigmentation.

Introduction

Facial erythema and hyperpigmentation are common cosmetic concerns that are caused by a variety of factors, although increased production of reactive oxygen species (ROS) is a key factor for both conditions. Increasing the skin's natural antioxidant defense network may therefore help to minimize ROS production and reduce the clinical severity of both erythema and hyperpigmentation.

Erythema

One of the predominant causes of facial erythema is rosacea, a chronic inflammatory skin condition that primarily affects the central regions of face, including the cheek, nose, chin, and forehead.[1] Prevalence rates are estimated to range from as low as 1.3-2% to as high as 22%.[2-10] Rosacea often develops between the ages of 30 and 50 and is more common in women.[11,12] Rosacea has been classified into 4 subtypes based on clinical characteristics.[13] Subtype 1 (erythematotelangiectatic rosacea) is the most common and involves either flushing (transient) or persistent central facial erythema. Subtype II (papulopustular rosacea) is the second most prevalent and involves persistent erythema and transient pustules and papules in the central facial regions.[11,1] In comparison with healthy controls, skin biopsies from rosacea patients tend to have higher ROS activity.[14,15] Following treatment with the antibiotic azithromycin, skin ROS levels have been shown to decline,[14] indicating that ROS levels play a role in rosacea pathology.[16] Ultraviolet (UV) exposure may worsen the clinical symptoms of rosacea[17] by promoting ROS production and causing an acute erythemal response.

Hyperpigmentation and Aging

Solar UV exposure is responsible for up an estimated 80% of visible aging signs. Long-term UV exposure is associated with pigmentation disorders such as hyperpigmentation, as well as vascular disorders, poor skin texture, increased wrinkling and decreased firmness.[18] Skin damage caused by UV exposure, or "photoaging", is primarily caused by UVA (320 to 400 nm)-dependent ROS production.[19] UVA exposure generates ROS such as singlet oxygen ($^1O_2$), hydrogen peroxide (H_2O_2) and hydroxyl radicals (OH) that damage cells and promote skin erythema, inflammation and visible photoaging.[20]

As part of the intrinsic aging process, skin becomes thinner, dryer and begins to lose its normal moisture barrier function.[21-23] ROS levels increase significantly[19] and concentrations of key skin antioxidants such as coenzyme Q10 (CoQ_{10}) are reduced.[24] As a result of these processes, facial redness tends to be more pronounced: healthy older adults have significantly more redness than young adults, and they typically have a more heterogeneous distribution of red pigmentation across their face.[25] This uneven facial redness is associated with a greater perceived age among older women.[26]

Superoxide Dismutase

Superoxide dismutase (SOD) enzymes are a critical component of the skin's antioxidant network. SOD enzymes are responsible for converting superoxide radicals into either molecular oxygen (O_2) or hydrogen peroxide. There are three forms of SOD enzymes, each of which is expressed in separate cellular components: SOD1 (found in the cytosol and nucleus), SOD2 (located in the mitochondria) and SOD3 (in the extracellular matrix).[27] Prolonged UVA exposure impairs the skin's antioxidant defense mechanisms[20] and has been shown to decrease SOD expression in human skin fibroblasts.[28] SOD enzymes are also dependent upon adequate supply of micronutrient enzymes: SOD1 and SOD3 both require copper and zinc to function, whereas SOD2 needs magnesium.[29]

GliSODin® is a nutritional supplement containing SOD that is extracted from melon (*Cucumis melo*) and bound to gliadin biopolymers for enhanced bioavailability and resistance to gastrointestinal degradation.[30] In healthy trained athletes, GliSODin® supplementation has been shown to significantly improve erythrocyte SOD activity levels while reducing levels of inflammatory C-reactive protein.[31] When used in combination with the topical retinoid tazarotene for 90 days in healthy subjects with photodamage, GSN Advanced Anti-Aging/Dermal Formula significantly improved hyperpigmentation, photodamage, and participant satisfaction with skin quality, in comparison to treatment with tazarotene alone.[32]

GSN Advanced Skin Brightening Formula helps to maintain an even skin tone using a combination of lycopene, acerola and hesperidin; lycopene supplementation minimizes UV-induced photodamage,[33-35] and both acerola and hesperidin have been shown to reduce melanin pigment production *in vitro* via inhibition of the enzyme tyrosinase.[36,37] GSN Advanced Anti-Aging/Dermal Formula was developed to support optimal skin health in older individuals: borage oil supplementation improves skin barrier function in older adults,[38] sea buckthorn increases skin hydration,[39] and cocoa enhances skin microcirculation,[40] which typically declines with age.[41]

Materials and Methods

Participants

All participants provided written informed consent prior to their enrollment. The study was conducted at three clinic locations from September to December 2014, including the offices of Dr. Cory Goldberg and Dr. Cory Torgerson in Toronto, Ontario, and Dr. Rohan Bissoondath in Calgary, Alberta, Canada. Eligible participants were 18-65 years of age, male or female, and had either facial photodamage (fine wrinkles, sun damage, skin aging) or inflammation (rosacea, acne, or other inflammatory skin issues), as evaluated by the center clinician. Exclusion criteria included pregnancy, liver disease, renal disease, celiac disease, gluten intolerance, tomato allergy, and the prior use of GSN products.

Treatments

GSN Advanced Skin Brightening Formula and Advanced Anti-Aging/Dermal Formula both provide 500 mg per daily serving of GliSODin® enzymes, in addition to vitamins, essential minerals and plant extracts that support skin health (Table 1). Participants with facial photodamage were randomized to either the SB treatment group (*n*=13) or placebo control group (*n*=6). Participants with facial inflammation were randomized to either the DF treatment group (*n*=13) or placebo control group (*n*=4). Each participant received a 90-day supply of DF, SB or placebo capsules (270 capsules total) and was instructed to take three capsules daily with a meal. Participants were asked to maintain their current topical skin care regimen and to avoid any ablative/non-ablative skin treatments.

Table 1: Advanced Skin Brightening and Advanced Anti-Aging/Dermal Formulae Composition

GSN Advanced Skin Brightening Formula	Per Daily Serving (3 capsules):	**GSN Advanced Dermal Formula**	Per Daily Serving (3 capsules):
Borage (*Borago officinalis*) seed oil	1080 mg (standardized to 20% gamma-linolenic acid [GLA])	Borage (*Borago officinalis*) seed oil	735 mg (standardized to 20% gamma-linolenic acid [GLA])
GliSODin®	500 mg	Krill oil	600 mg
Acerola (*Malpighia punicifolia*) extract 6:1	249.9 mg, equivalent to 1499 mg of dried fruit	GliSODin®	500 mg
Hesperidin	50 mg	Sea buckthorn (*Hippophae rhamnoides*)	200 mg
Tomato (*Lyopersicon esculentum*)	40 mg (15% lycopene)	Cocoa (*Theobroma cacao*)	100 mg
Lemon balm (*Melissa officinalis*) extract 6:1	100 mg, equivalent to 600 mg of dried herb	Red clover (*Trifolium pratense*)	100 mg (20 mg AIE isoflavones)
Coenzyme Q_{10}	30 mg	Sodium hyaluronate	30 mg
Selenium	50 mcg	Zinc	10 mg
Vitamin D	15 mcg	Vitamin D	10 mcg
Vitamin E	75 IU		

Photography

Facial photographs were taken at baseline, at 30 days and at the end of the 90-day treatment period using the VECTRA XT (Canfield Scientific, Fairfield, NJ, USA) 3D imaging system. Female participants were instructed to avoid using makeup earlier in the day of each study visit. Photographs were imported into the VECTRA® 3D Analysis Module software program (Canfield Scientific, Fairfield, NJ, USA) and then opened in the integrated Face Sculptor® program. The 3D images were then processed into red and brown pigment images using the VECTRA XT's integrated RBX™ processing technology. RBX™ technology incorporates cross-polarized images captured from the VECTRA XT's camera and uses a proprietary algorithm to

determine surface and sub-surface skin pigmentation, including hemoglobin (red) and melanin (brown) pigmentation.[42] Each image was processed into separate 3D red and brown pigment images in Face Sculptor® and then exported as a lossless 2D PNG image file for subsequent analysis.

Red and Brown Pigment Analysis

The degree of red and brown pigmentation in the 2D facial images was determined using color threshold analysis conducted with ImageJ software (National Institutes of Health, version 1.48). A region of interest (ROI) was selected from the center of the forehead (400 x 200 pixels), from each cheek (200 x 200 pixels), the nose (100 x 100 pixels) and the chin (150 x 100 pixels) of each image. These ROI dimensions were selected in order to cover the majority of the facial surface area, with the exclusion of the eye and lip areas (Fig. 1).

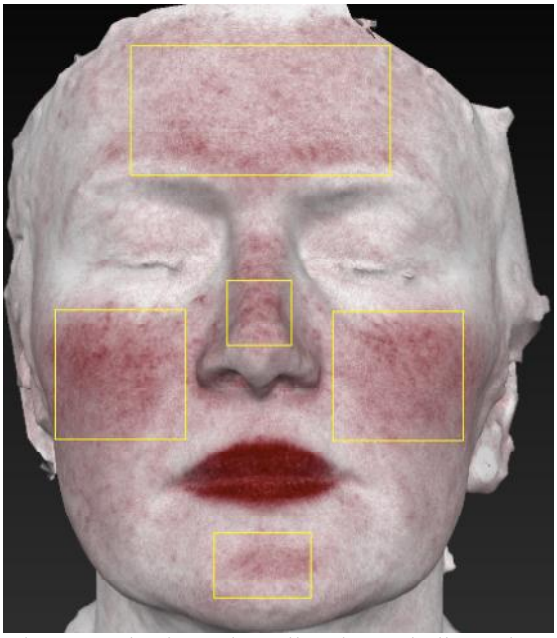
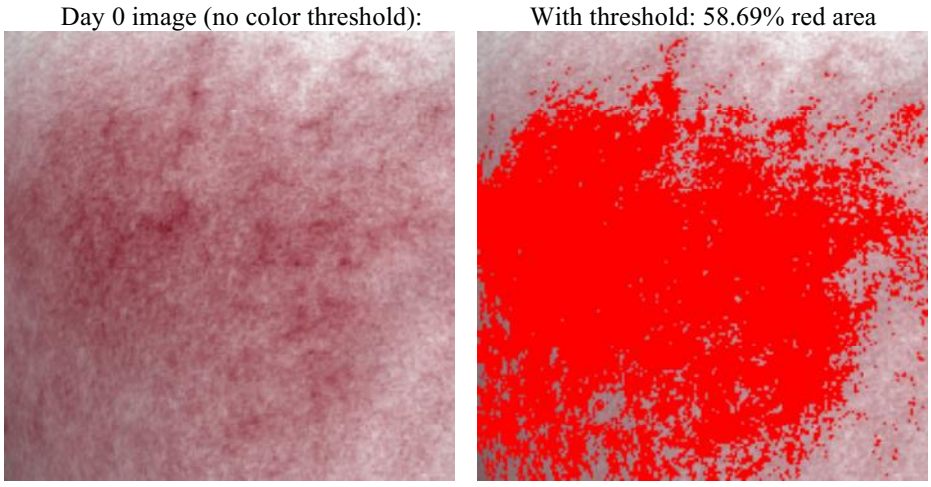


Figure 1: Sample ROI Selection. The yellow boxes indicate the ROIs analyzed.

Red Pigment Analysis

Color threshold processing was used to separate the red areas from the "non-red" areas for each ROI taken from the DF treatment arm. The red areas were identified based on their greater saturation (intensity) and decreased brightness, in comparison with the white/light pink "non-red" areas. The red area was selected with the Color Threshold tool [Image → Adjust → Color Threshold] by increasing the minimum intensity and decreasing the maximum brightness (Fig. 2). The image was then converted to 8-bit color format [Image → Type → 8-bit] and then the total percent area occupied by red pigment in each ROI was measured [Analyze → Measure].

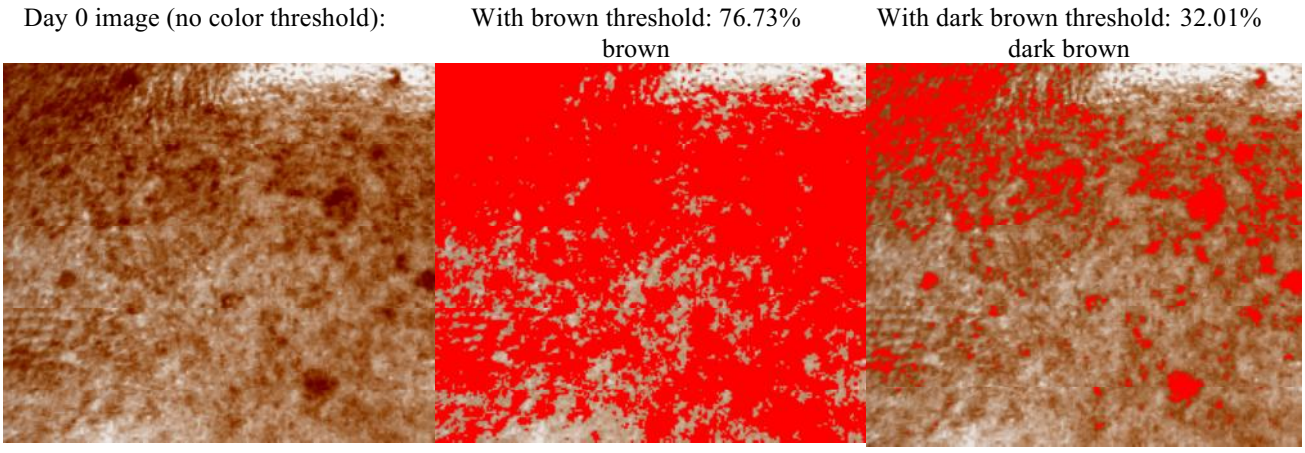
Figure 2: Red area analysis in right cheek ROI taken from DF participant on day 0 – the bright red portion indicates the selected area.



Brown Pigment Analysis

Color threshold processing of the total brown-pigmented areas (including both dark and light brown areas) in the ROI taken from the SB treatment arm was performed as above. A sub-analysis was also performed to determine the amount of dark brown areas in each ROI by selecting only the areas with maximum intensity, by setting the minimum saturation equal to the maximum saturation. The total dark brown area was then measured by adjusting the threshold until only the filtered area was selected [Image → Adjust → Threshold].

Figure 3: Comparison of total and dark brown area analysis in forehead ROI taken from SB participant on days 0 and 90 of treatment – the bright red portion indicates the selected area.



Subjective Skin Satisfaction Questionnaires

Participants evaluated their subjective skin satisfaction prior to and following 90 days of treatment by completing a set of seven 100-mm visual analog scale (VAS) questions that scored their subjective satisfaction with their skin's radiance/glow, redness, irritation, pigment/brown

spots, softness/feel, dryness, and overall quality. The VAS endpoints were "worst possible" on the left end (0 mm) and "best possible" on the right end (100 mm).

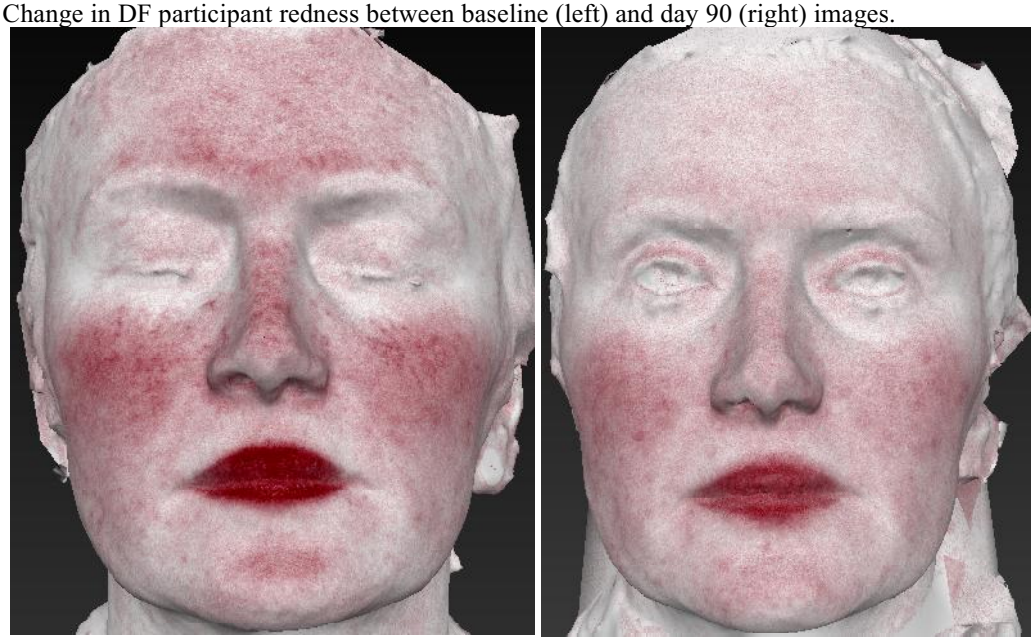
Statistical Analyses

Statistical analysis was performed using GraphPad Prism (Version 6, GraphPad Software Inc., La Jolla, CA, USA). Facial redness (DF treatment arm) and pigmentation (SB treatment arm) prior to and following 90 days of supplementation were compared with a paired two-tailed *t*-test. The active groups were compared to their respective placebo groups using an independent two-tailed *t*-test. Statistical significance was set at the 95% level ($p < 0.05$). Results were expressed as mean ± standard deviation.

Results

Erythema:

Figure 4: Change in DF participant redness between baseline (left) and day 90 (right) images.



The participant's baseline mean total facial redness prior to treatment was 57.59%. At 90 days of treatment, the facial redness score was 46.13%.

Table 2: Mean facial redness prior to and following treatment

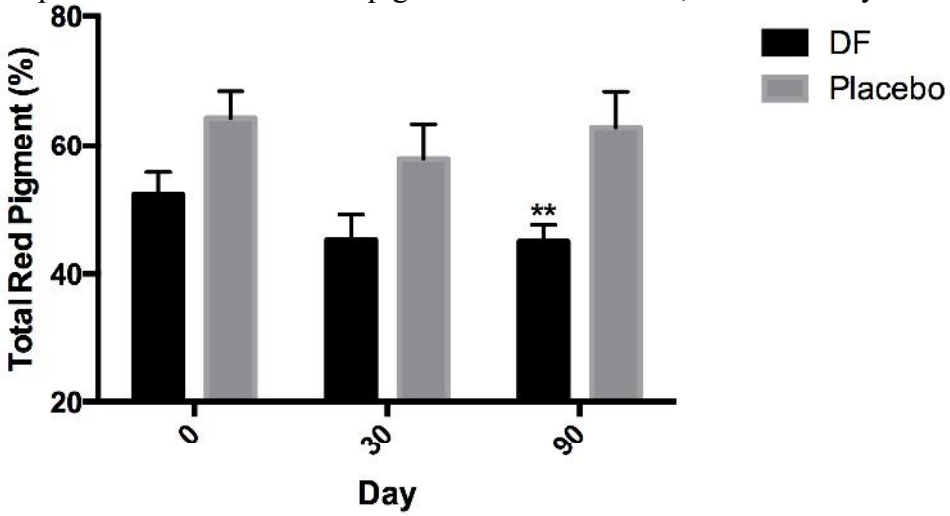
	DF Group (*n*=13)			Placebo Group (*n*=4)		
Variable	**Baseline**	**30 days**	**90 days**	**Baseline**	**30 days**	**90 days**
Left cheek (%)	53.79 ± 15.50	51.00 ± 18.57	47.06 ± 12.06	63.32 ± 14.00	56.38 ± 18.18	58.10 ± 14.86
Right cheek (%)	54.24 ± 13.42	53.11 ± 17.75	49.63 ± 10.77	64.84 ± 15.13	61.83 ± 6.55	66.77 ± 10.89
Forehead (%)	37.05 ± 18.10	32.43 ± 13.62	31.04 ± 13.73	58.69 ± 8.95	46.35 ± 21.74	57.74 ± 13.06
Chin (%)	53.69 ± 17.21	39.96* ± 15.45	43.31** ± 14.61	67.51 ± 10.68	60.29 ± 11.73	66.82 ± 14.73
Nose (%)	62.24 ± 14.43	49.58* ± 14.04	53.74* ± 11.99	66.71 ± 5.99	63.23 ± 10.94	64.44 ± 11.11
Total (%)	52.20 ± 12.57	45.22 ± 14.02	44.95** ± 9.24	64.21 ± 8.32	57.62 ± 11.29	62.77 ± 11.15

* $p < 0.05$, ** $p < 0.01$, in comparison with baseline (paired two-tailed *t*-test).

Chin and nose redness were significantly decreased in the DF treatment group at 30 days of treatment, although the decrease in total facial redness did not reach significance ($p = 0.014$, 0.010 and 0.083, respectively. Total facial redness was significantly decreased following 90 days

of treatment ($p = 0.008$), including significantly reduced redness in the chin ($p = 0.003$) and nose ($p = 0.016$) regions, but not in the left cheek ($p = 0.09$), right cheek ($p = 0.17$) or forehead ($p = 0.52$). The total redness in the DF group was not significantly different than the placebo group at baseline ($p = 0.94$), but was significantly lower at 90 days ($p = 0.0057$). Total redness scores in the placebo group did not change significantly following 30 or 90 days of treatment ($p = 0.073$ and 0.75). There were no significant changes in any of the placebo group facial regions at 90 days (left cheek $p = 0.58$, right cheek $p = 0.82$, forehead $p = 0.89$, chin $p = 0.89$, and nose $p = 0.51$).

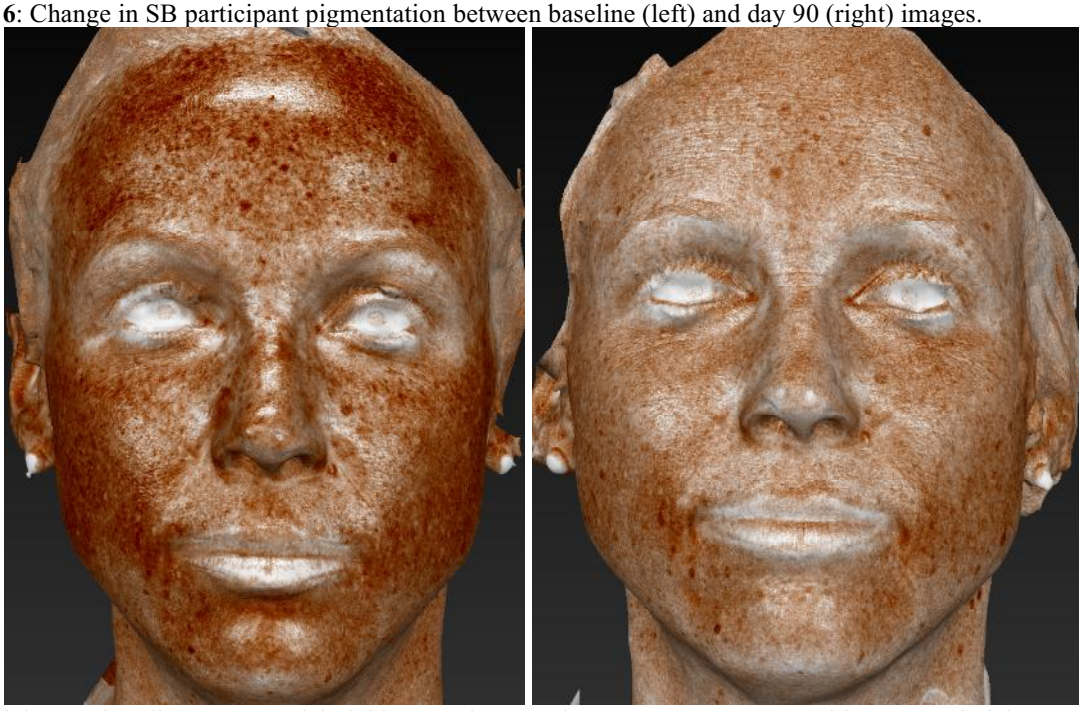
Figure 5: Comparison of total red facial pigmentation at baseline, 30 and 90 days



Mean + SEM (standard error of the mean), ** $p < 0.01$ for day 90 vs. day 0

Hyperpigmentation:

Figure 6: Change in SB participant pigmentation between baseline (left) and day 90 (right) images.



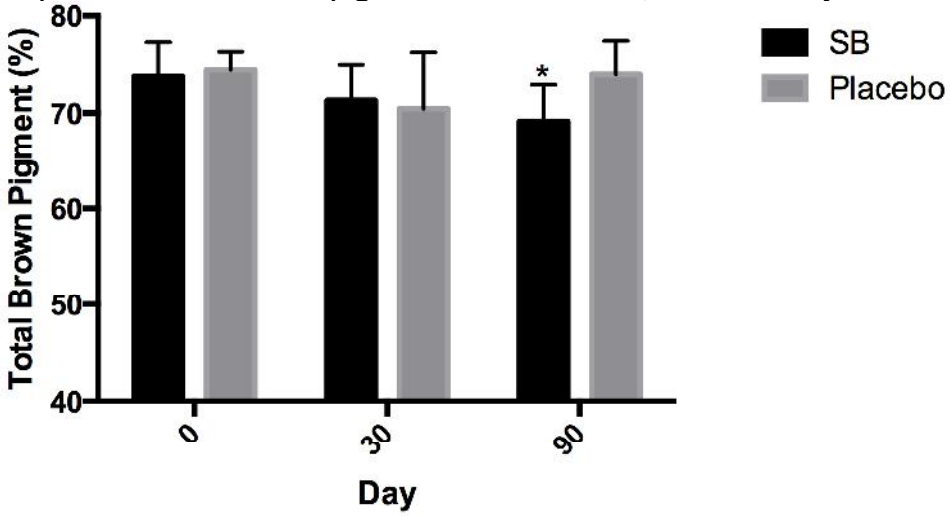
The participant's baseline mean total facial brown pigmentation score was 71.47%, with 13.91% dark brown. At 90 days of treatment, the mean total facial brown pigmentation score was 47.00%, with 0.24% dark brown.

Table 3: Mean brown pigmentation prior to and following treatment

	SB Group (*n*=13)			Placebo Group (*n*=6)		
Variable	**Baseline**	**30 days**	**90 days**	**Baseline**	**30 days**	**90 days**
Left cheek (%)	75.54 ± 12.54	77.39 ± 11.71	72.97 ± 15.33	74.42 ± 2.83	73.01 ± 13.26	72.26 ± 11.76
Right cheek (%)	78.54 ± 13.64	78.55 ± 14.75	74.38 ± 17.36	76.18 ± 5.24	75.11 ± 13.38	75.23 ± 13.65
Forehead (%)	73.61 ± 15.72	72.61 ± 16.47	65.96* ±11.49	78.67 ± 10.18	72.56 ± 17.09	76.37 ± 9.81
Chin (%)	71.56 ± 13.65	61.22* ± 21.74	68.60 ± 15.06	74.66 ± 4.44	66.66 ± 15.11	75.67 ± 9.63
Nose (%)	69.59 ± 18.47	66.74 ± 18.09	63.82 ± 15.83	68.37 ± 10.00	64.87 ± 17.46	70.35 ± 11.26
Total (%)	73.77 ±12.69	71.30 ± 13.25	69.15* ± 13.56	74.46 ± 4.57	70.44 ± 14.23	73.98 ± 8.45

* $p < 0.05$, in comparison with baseline (paired two-tailed *t*-test).

Figure 7: Comparison of total brown pigmentation at baseline, 30 and 90 days



Mean + SEM (standard error of the mean), * $p < 0.05$ for day 0 vs. day 90

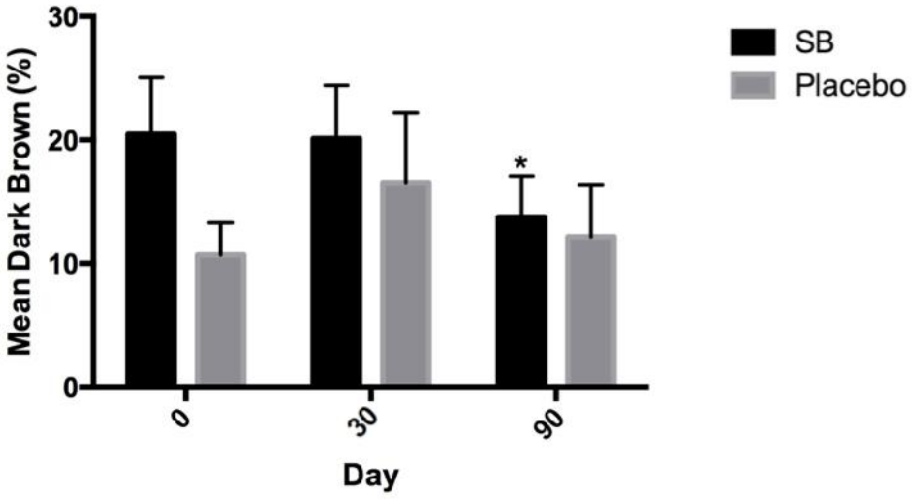
Following 30 days of treatment, chin region brown pigmentation scores were significantly decreased in the SB treatment group, although total facial brown pigmentation was not significantly lower in comparison with baseline measurements ($p = 0.19$). At 90 days, there was a modest, but significant decrease in baseline total brown pigmentation scores in the SB treatment group, with a decrease from 73.77 ± 12.69 to 69.15 ± 13.56 ($p = 0.042$). Pigmentation decreased in the forehead region ($p = 0.046$), but not in the left cheek ($p = 0.17$), right cheek ($p = 0.12$), chin ($p = 0.15$) or nose ($p = 0.11$). Total brown pigmentation scores were not significantly lower in the SB treatment group than the placebo group at 30 or 90 days ($p = 0.89$ and 0.44). Total brown pigmentation did not change significantly in the placebo group at either 30 or 90 days ($p = 0.48$ and 0.89). There were no significant changes in any of the facial regions at 90 days (left cheek $p = 0.68$, right cheek $p = 0.87$, forehead $p = 0.53$, chin $p = 0.70$ and nose $p = 0.66$).

Table 4: Mean dark brown pigmentation prior to and following treatment

	SB Group (*n*=13)			Placebo Group (*n*=6)		
Variable	**Baseline**	**30 days**	**90 days**	**Baseline**	**30 days**	**90 days**
Left cheek (%)	23.99 ± 20.72	24.92 ± 18.81	18.81 ± 16.97	10.53 ± 6.45	17.39 ± 12.62	15.80 ± 13.90
Right cheek (%)	29.95 ± 22.72	29.72 ± 22.36	23.06 ± 17.90	13.98 ± 7.70	21.29 ± 16.56	14.84 ± 13.62
Forehead (%)	23.31 ± 21.84	17.54* ± 17.63	10.05** ± 10.33	14.73 ± 18.85	22.00 ± 23.76	12.40 ± 16.4
Chin (%)	9.63 ± 11.81	16.84 ± 24.59	9.84 ± 14.47	9.32 ± 8.88	11.79 ± 18.38	11.30 ± 13.31
Nose (%)	15.49 ± 16.44	11.50 ± 13.98	7.04* ± 11.00	4.93 ± 4.18	10.30 ± 12.45	6.43 ± 8.60
Total (%)	20.47 ± 16.57	20.10 ± 15.63	13.76* ± 12.04	10.70 ± 6.34	16.55 ± 13.85	12.15 ± 10.44

* $p < 0.05$, ** $p < 0.01$, in comparison with baseline (paired two-tailed *t*-test).

Figure 8: Comparison of total dark brown pigmentation at baseline, 30 and 90 days



Mean + SEM (standard error of the mean), * $p < 0.05$ for day 0 vs. day 90

Total dark brown pigmentation scores decreased significantly in the SB group at 90 days of treatment ($p = 0.010$), but not in the placebo group ($p = 0.78$). The decrease in dark pigmentation occurred in the forehead ($p = 0.007$) and nose ($p = 0.029$) regions.

Skin Satisfaction Questionnaires

Table 5: DF group skin satisfaction 100 mm VAS responses prior to and following treatment

	DF Group (*n*=13)			Placebo Group (*n*=4)		
Variable	**Baseline**	**90 days**	***p***	**Baseline**	**90 days**	***p***
Radiance (mm)	50.5 ± 17.4	66.3* ± 19.7	0.018	4.3 ± 3.9	57.7 ± 21.6	0.32
Redness (mm)	44.8 ± 33.7	56.7 ± 23.5	0.40	41.3 ± 21.4	49.4 ± 21.1	0.84
Irritation (mm)	43.1 ± 34.5	52.4 ± 28.4	0.51	43.8 ± 14.4	57.4 ± 28.5	0.48
Brown spots (mm)	45.0 ± 27.3	61.0* ± 20.6	0.01	37.2 ± 22.3	57.4 ± 4.4	0.05
Softness (mm)	60.9 ± 18.6	70.1 ± 16.0	0.16	54.7 ± 7.8	66.5 ± 13.5	0.081
Dryness (mm)	34.8 ± 25.3	62.6*** ± 17.6	0.0008	54.2 ± 14.7	52.3 ± 13.7	0.77
Overall quality (mm)	59.2 ± 18.2	68.7 ± 17.1	0.19	36.2 ± 13.7	67.6 ± 16.5	0.086

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$ for comparison of baseline vs. 90 days (paired two-tailed *t*-test).

Skin satisfaction scores increased significantly in the DF treatment group for 3 variables, including radiance, brown spots and dryness at 90 days ($p = 0.018$, 0.01 and 0.0008), however perception of overall skin quality did not increase significantly with treatment ($p = 0.19$). No significant changes occurred in the placebo group ($p > 0.05$ for all variables).

Table 6: SB group skin satisfaction 100 mm VAS responses prior to and following treatment

	SB Group (*n*=13)			Placebo Group (*n*=6)		
Variable	**Baseline**	**90 days**	***p***	**Baseline**	**90 days**	***p***
Radiance (mm)	49.7 ± 20.3	69.0* ± 18.8	0.046	50.4 ± 20.0	64.9 ± 8.4	0.22
Redness (mm)	50.7 ± 29.7	63.7 ± 24.9	0.35	47.5 ± 30.4	42.5 ± 22.3	0.54
Irritation (mm)	58.8 ± 28.4	65.7 ± 29.2	0.62	47.4 ± 29.7	51.7 ± 28.9	0.92
Brown spots (mm)	38.3 ± 30.3	60.4 ± 30.0	0.057	38.0 ± 18.0	67.0* ± 6.7	0.017
Softness (mm)	55.7 ± 24.2	73.5* ± 12.1	0.019	60.2 ± 19.1	75.0 ± 9.2	0.14
Dryness (mm)	40.3 ± 23.4	53.3 ± 26.3	0.22	54.8 ± 27.5	73.4* ± 28.2	0.029
Overall quality (mm)	44.0 ± 20.5	73.3*** ± 16.7	0.0006	45.9 ± 14.4	65.9 ± 10.2	0.13

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$ for comparison of baseline vs. 90 days (paired two-tailed *t*-test).

Skin satisfaction scores increased significantly in the SB treatment group for 3 variables, including radiance, softness and overall quality at 90 days (p = 0.046, 0.019 and 0.0006). Skin satisfaction scores also increased significantly in the placebo group for 2 variables, including brown spots and dryness (p = 0.017 and 0.029).

Discussion

Despite the reduction in red pigmentation observed in the DF group's facial images, participants did not perceive any significant change in their skin's redness following treatment. However, the improvement in brown spot VAS scores could be associated with a reduction in facial inflammation, which may be of particular benefit in the treatment of acne symptoms. When exposed to the acne-causing bacteria *Propionibacterium acnes*, epidermal cells produce superoxide anions, which have been identified as critical in the development of acne inflammatory lesions.[43] The inflammation caused by acne lesions often results in brown spots due to the process of post-inflammatory hyperpigmentation, which can last for up to one year.[44] As patients with acne have decreased SOD activity and higher levels of oxidative stress in comparison with healthy controls,[45] increasing SOD levels could potentially reduce the amount of acne-related post-inflammatory hyperpigmentation. In addition, the decrease in brown spots may also be associated with a more youthful appearance, as uneven color uniformity and brown spots play a significant role in determining perceived age.[46]

Considering that total brown spot and dark brown pigmentation only improved in the SB group's facial images, the placebo group's improvement in brown spot VAS scores may be attributed to placebo effect. It's unclear why there was no improvement in perceived appearance of dark spots in the SB group, although the study duration and seasonal period may be contributing factors. One of the SB formula's active ingredients is a lycopene-rich tomato extract: while lycopene has been shown minimize UV photodamage, the photoprotective effects may only accumulate after a minimum of 10-12 weeks of supplementation.[33-35] As the study was conducted during the fall and winter seasons, the minimization of photodamage may be more pronounced during summer when UV exposure is higher.

Conclusion

Supplementation with DF and SB for 90 days significantly reduced total facial erythema and hyperpigmentation, respectively, as determined by pigment analysis. Participant skin satisfaction scores for several attributes also improved significantly with both treatments.

Acknowledgments

The study was funded by a grant from Isocell North America Inc., the manufacturer of GliSODin® products.

Appendix – Changes in Brown and Red Pigmentation Following Treatment

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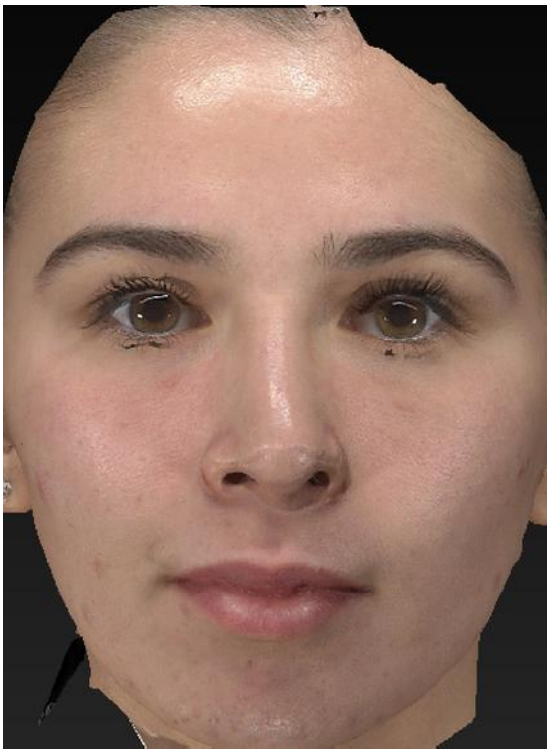
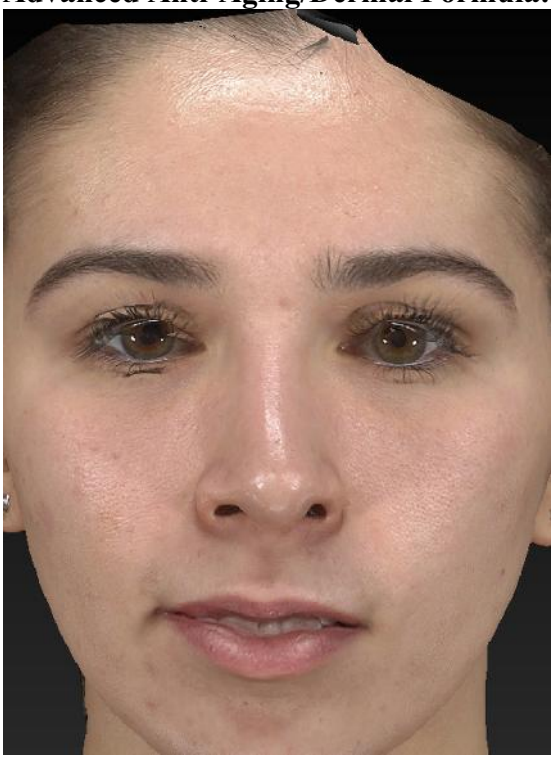
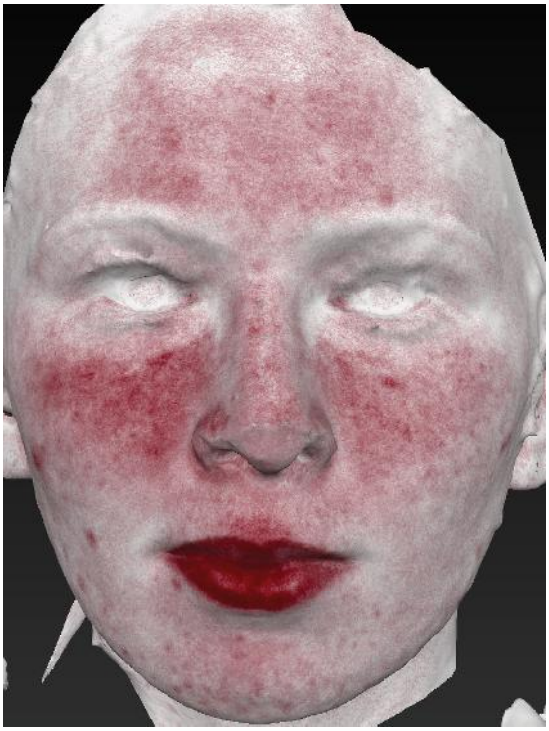
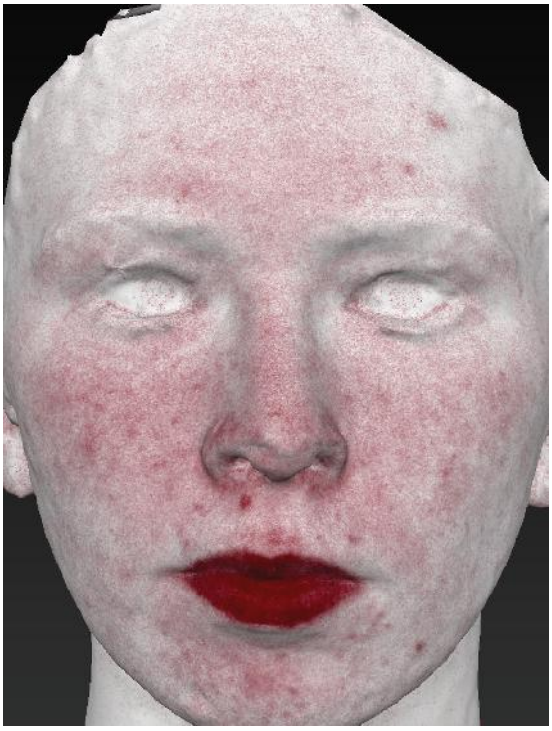
Before:



After 90 days of treatment with GSN Advanced Anti-Aging/Dermal Formula:







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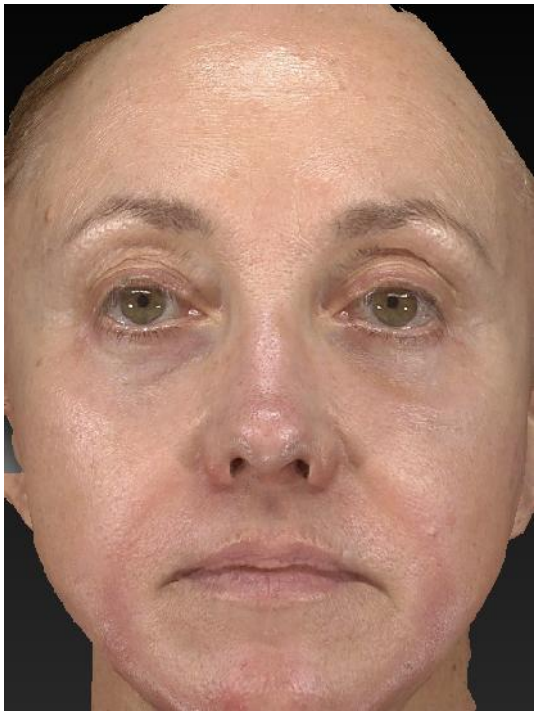
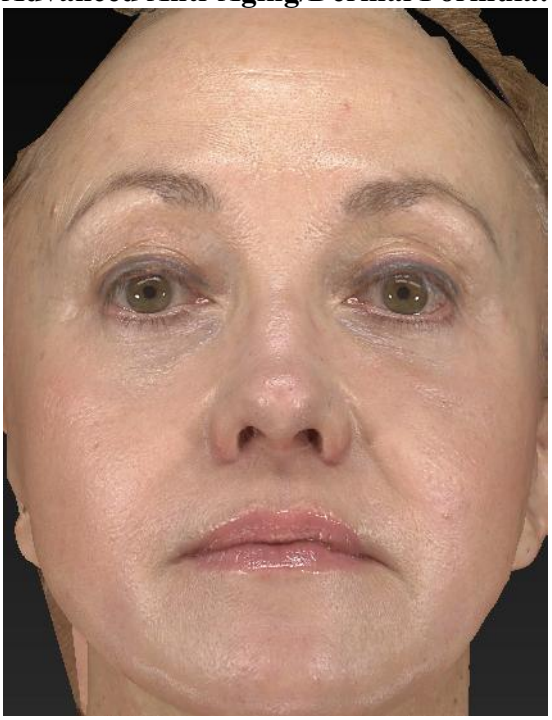
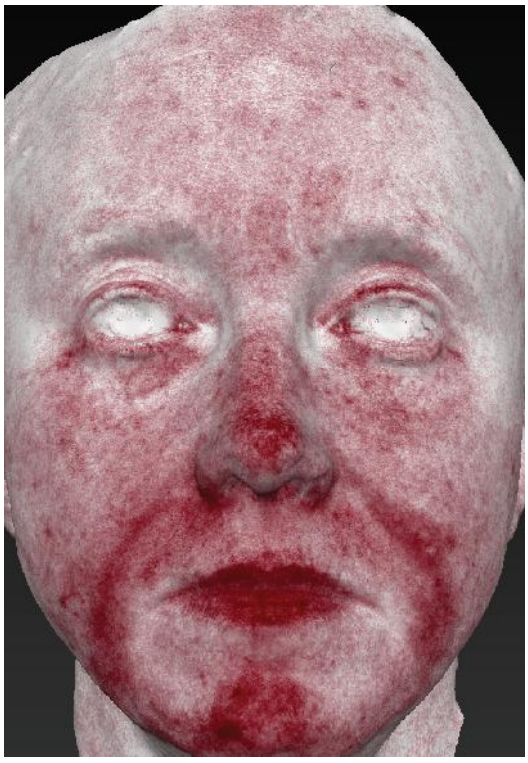
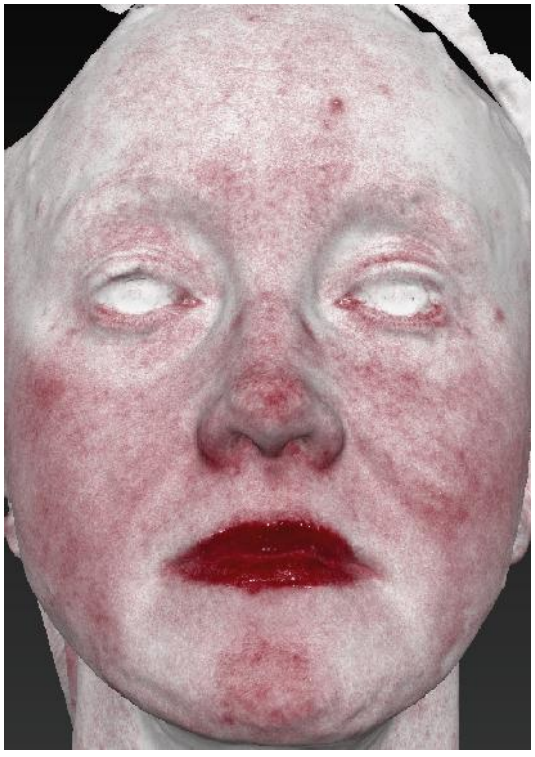


After 90 days of treatment with GSN Advanced Anti-Aging/Dermal Formula:







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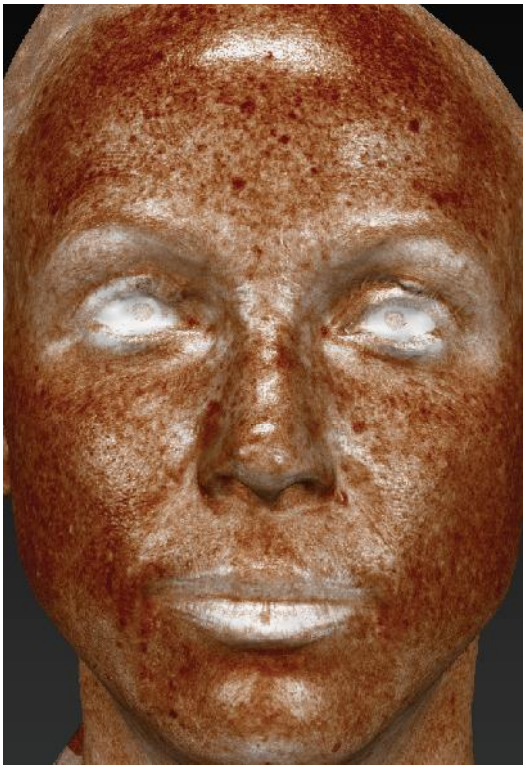
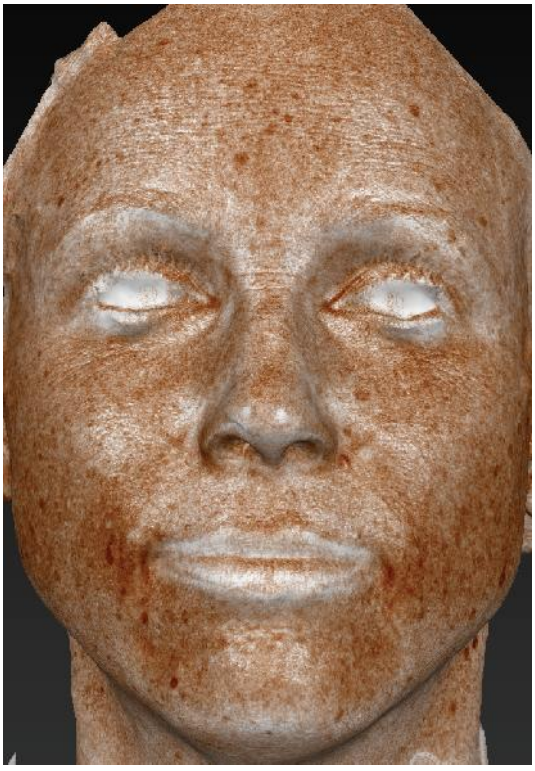


After 90 days of treatment with GSN Advanced Skin Brightening Formula:



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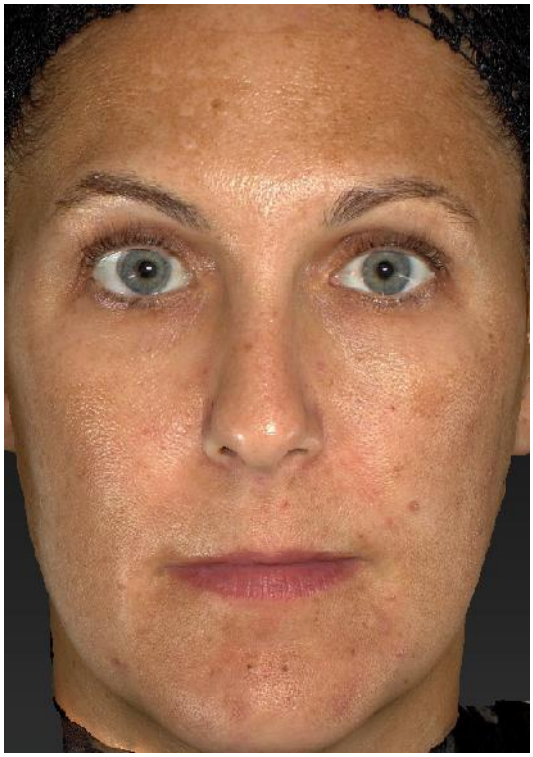

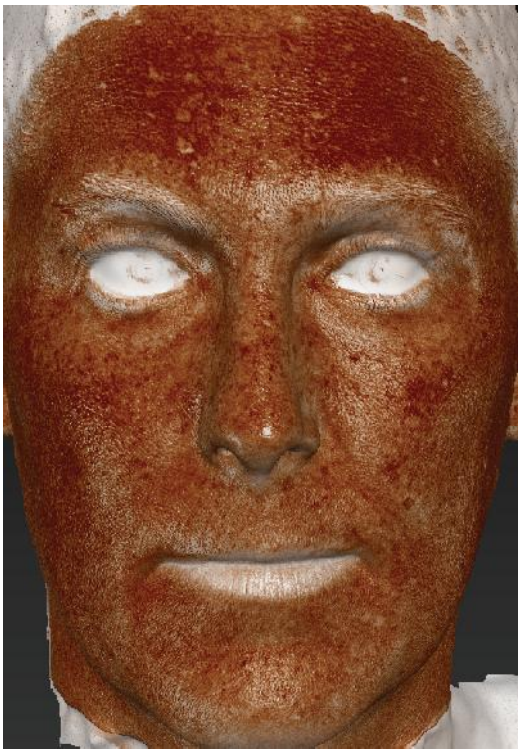

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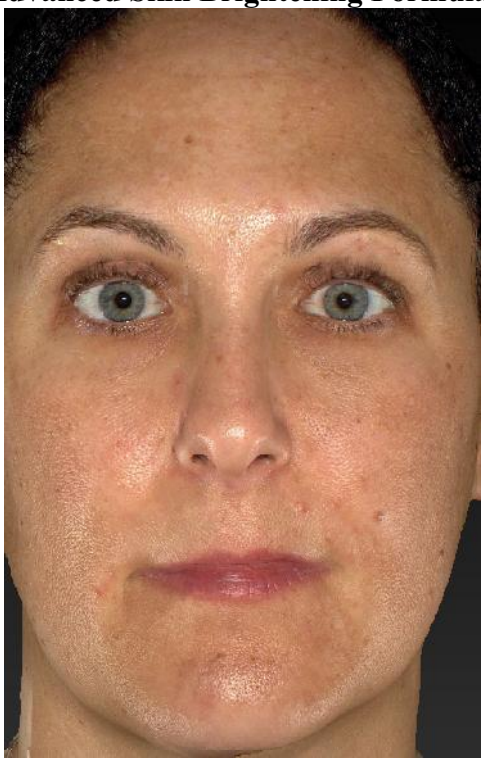

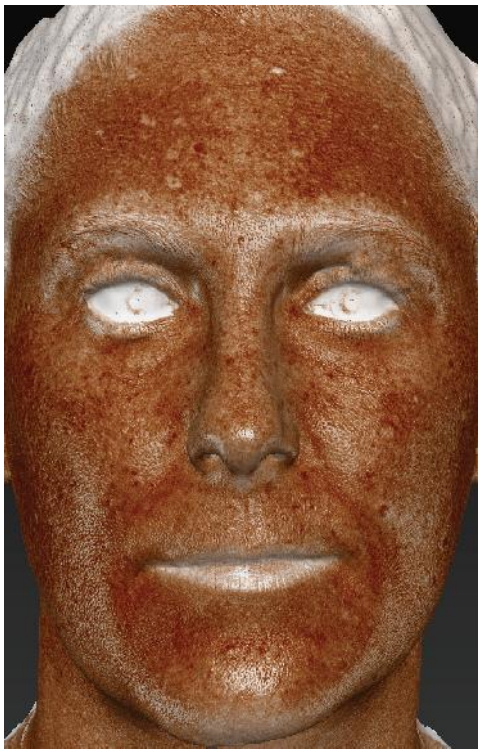

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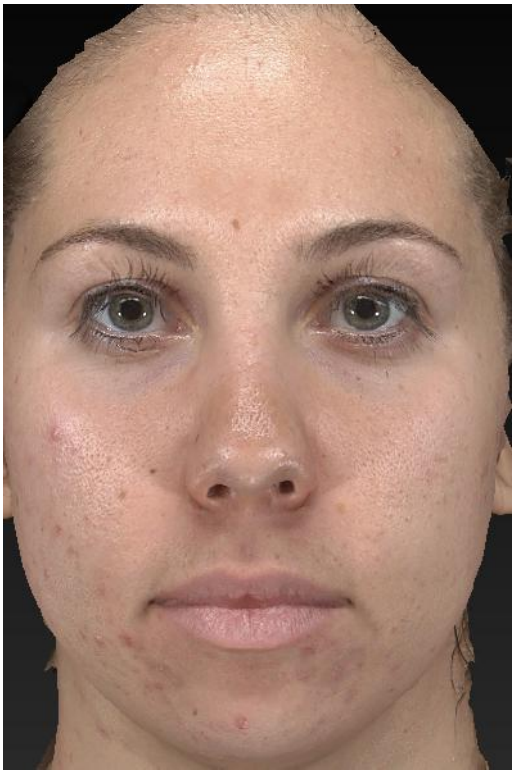

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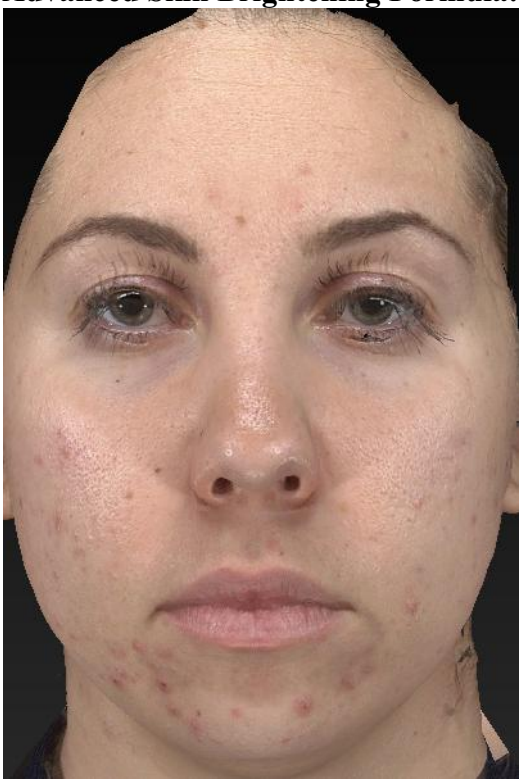

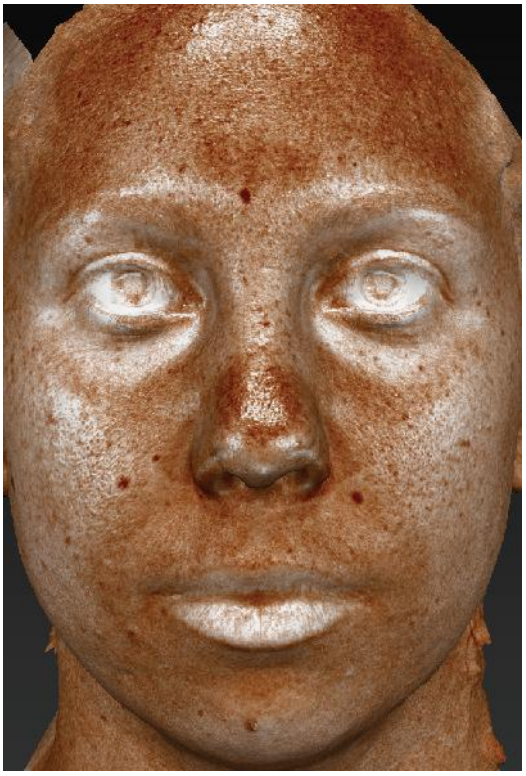

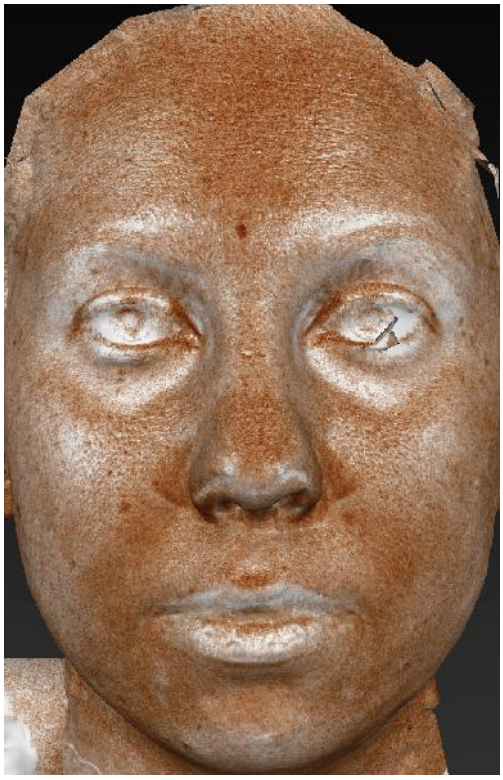

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