High Concentration (15%) Vitamin C (Ascorbic Acid) Stabilized in Unique Aqueous Vehicle with Feverfew, Polyhydroxy Acid (PHA), and Epigallocatechin Gallate (EGCG) Provides Clinical Benefits for Hyperpigmentation in a Diverse Population

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Introduction

AA (vitamin C) is widely used in skincare for its antioxidant and skin brightening properties. Anhydrous AA formulations are not as effective in delivering AA as aqueous systems. However, stability in an aqueous vehicle is challenging as water increases oxidation kinetics for AA and optimal efficacy has been shown at low pH.

A holistic formulation approach to skin brightening was utilized that included the addition of feverfew, gluconolactone, and EGCG for multi-mechanistic benefits including antioxidant protection and surface exfoliation.

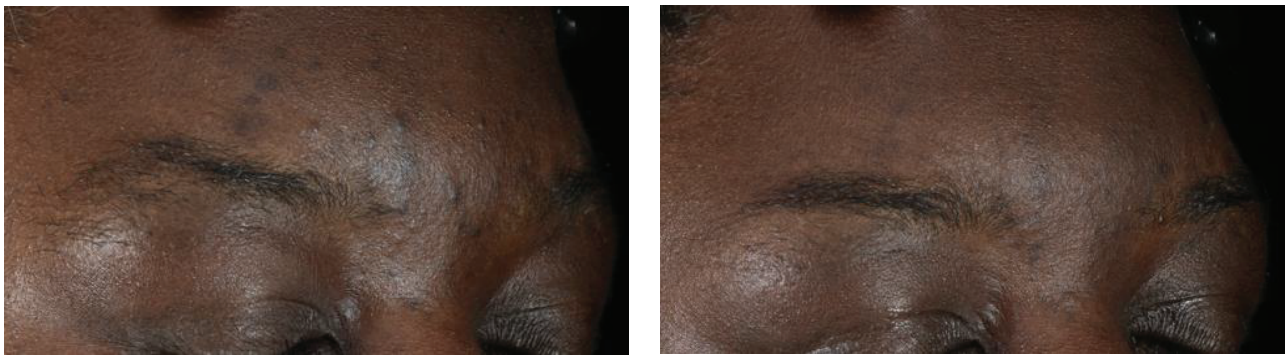
AA, ascorbic acid; EGCG, epigallocatechin gallate; PHA, polyhydroxy acid

Clinical Photography

Visible improvement in pigmentation and texture are shown as average to above average examples in **Figures 1, 5,** and **6**. A face serum containing AA, Feverfew, PHA, and EGCG was used once daily for 12 weeks in a diverse population

Figure 1. Improved Pigmentation, More Even Skin Tone

Black/African American, Fitzpatrick Skin Type VI



Baseline | 12 Weeks

Development of Stabilized, Aqueous Ascorbic Acid Serum With Multi-Mechanistic Benefits

Formulation Background and Ingredient Selection

Table 1. Skin Benefits of Selected Ingredients

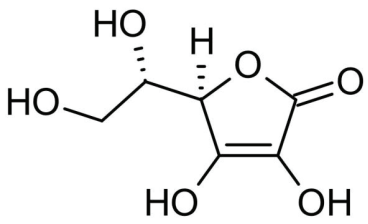
	AA	Gluconolactone	Feverfew	EGCG
Antioxidant	●	●	●	●
Pigmentation	●	●	●	
Humectant		●		
Exfoliation		●		
Chelation		●		
Anti-inflammatory			●	●
Increase Glutathione			●	

- PHAs can chelate the metal ions found in the environment that lead to reactive oxidative species (ROS) generation, oxidative stress and pigmentation. The chelation of copper, a known factor in melanin production, by Gluconolactone (PHA) leads to an improvement in skin pigmentation and overall skin tone[1]
- Feverfew (*Tanacetum parthenium*) is a botanical extract that significantly reduces pollution-induced melanin content and ROS, specifically caused by environmental pollutants such as particulate matter <2.5 µm in diameter (PM 2.5)[2]
- EGCG is derived from green tea and provides antioxidant and anti-inflammatory benefits

Formulation Development

- The efficacy of AA is formulation dependent
- Pure AA is hydrophilic, yet highly unstable in aqueous systems. The chemical structure of AA is shown in **Figure 2**
- It is imperative to formulate skin care products at the proper pH and concentration for efficient stability and efficacy
- A unique formulation was created balancing AA in an aqueous vehicle to determine the optimal ratio for solubility and efficacy

Figure 2. Chemical Structure of Ascorbic Acid



Formulation Challenges

Method

- Experiments were conducted on various aqueous formulations containing AA, Gluconolactone, Feverfew, and EGCG with differing pH levels and concentrations of water
- Initial experiments were completed to determine the optimum pH range for AA solubility. Samples were evaluated visually for AA solubility at 4°C and noted by the absence or presence of AA crystals, as shown in **Figure 3**
- Based on the pH data, additional formulations were prepared with varying water content, and AA stability was monitored at 25°C/60% RH and 40°C/75% RH. Samples were measured by HPLC analysis for the concentration of AA at initial and several timepoints over 12 weeks and any visual, insoluble AA was recorded

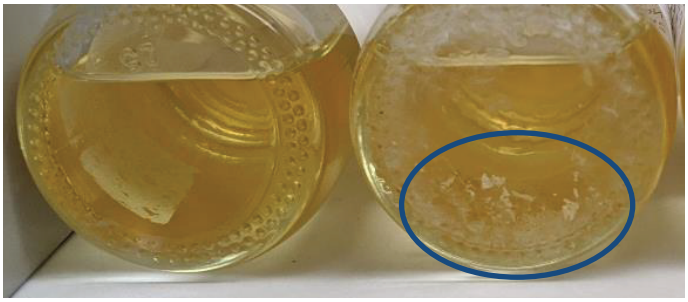
Results

- AA was both stable and soluble in the formulation containing the medium level of water concentration, as shown in **Table 2**

Table 2. AA Solubility and Stability in Formulations With Varying Water Content

	Water Content		
	Low	Medium	High
Solubility	Insoluble	Soluble	Insoluble
Stability	Stable	Stable	Degrades

Figure 3. Formulation Indicating Insolubility of AA



AA, ascorbic acid; EGCG, epigallocatechin gallate; PHA, polyhydroxy acid

Clinical Study of Face Serum With Vitamin C, Feverfew, PHA and EGCG Provides Benefits to Hyperpigmentation Across All Skin Tones

Clinical Study Methodology

Design

- 12-week, Institutional Review Board approved, single center, prospective clinical study with direct comparison to baseline condition

Population

- Females, ages 30–60 years with Fitzpatrick Skin Types I-VI
- Key inclusion criteria: moderate score for lack of clarity and radiance and mild to moderate uneven skin tone on the global face (modified Griffith's scale); textural parameters such as fine lines and wrinkles were included as appropriate to ensure inclusion of all skin tones

Evaluation Tools

- Clinical grading for pigmentation and textural attributes and tolerability were collected as well as self-assessment questionnaires and digital photography

Statistics

- Clinical grading scores were compared to baseline scores for each subject at each visit using a Wilcoxon signed-rank test, $p \leq 0.05$. Percent changes from baseline calculated from mean delta scores are presented. Self-assessment scores were tabulated

Test Product

- The face serum containing AA, Feverfew, PHA, and EGCG was applied once daily in the morning; bland day SPF 35 and night moisturizers were provided to standardize the regimen

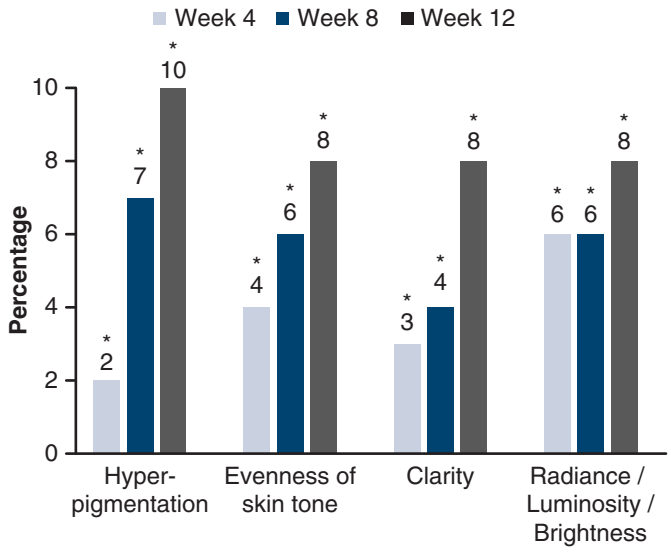
Results

44 racially and ethnically diverse women representing all Fitzpatrick Skin Types (I-VI) completed the study; 43% Black/African American, 18% Asian, 37% Caucasian, 2% Multi-racial with 9% being Hispanic/Latino

Clinical Grading

- All 12 clinically graded parameters showed significant improvement at Week 12, $p \leq 0.05$. (**Figure 4, Table 3**)
- Eight of the 12 parameters, including all pigmentation/brightening parameters in **Figure 4**, significantly improved at Week 4 and continued through Week 8 and Week 12, $p \leq 0.05$

Figure 4. Clinical Improvement to Pigmentation Parameters



*p≤0.05

Table 3. Clinical Improvement in Texture and Firmness Parameters

	Week 4	Week 8	Week 12
Fine lines	9%	11%	21%
Wrinkles	NS	5%	17%
Pore size	3%	3%	7%
Laxity / Lack of firmness	NS	6%	11%
Global lift	NS	7%	13%
Tactile roughness / smoothness	10%	12%	18%
Visual roughness / smoothness	4%	6%	8%
Overall photodamage / appearance	NS	6%	14%

NS, Not Significant

Results (cont'd)

Self-Assessment

Early Benefits Noticed ***After 1 Week***

- 98% brighter complexion, more radiant
- 100% smoother texture

Favorable Scent Attributes

- 90% pleasant scent
- 95% no lingering scent

Multiple Benefits to Hyperpigmentation and Texture ***After 12 Weeks***

- 100% skin is more brilliant
- 95% complexion is dramatically brighter
- 95% skin feels protected against environmental stressors
- 95% fine lines are less visible
- 93% skin tone is dramatically more even
- 90% dark spots are less apparent

Tolerability

- **Serum was well tolerated** with no statistically significant increases from baseline for edema, erythema, dryness, burning, stinging, itching, tightness.
- One adverse event (possibly related) for mild erythema, dryness, and moderate itching on the cheeks was reported; subject discontinued study.

Clinical Photography (cont'd)

Obvious improvements to hyperpigmentation along with benefits to brightness, texture, and antiaging parameters provide visual support for the clinical and consumer perceived benefits (**Figures 5–6**)

Figure 5. Improved Pigmentation & Lines/Texture

Caucasian, Fitzpatrick Skin Type II

Baseline 12 Weeks

Figure 6. Improved Skin Clarity & Radiance

Caucasian/Latino, Fitzpatrick Skin Type III

Baseline 12 Weeks

Conclusions

- A holistic formulation was developed with selected ingredients to provide **exfoliation, even skin tone** and **boosted antioxidant** activity in the skin
- An aqueous-based face serum was **optimized for enhanced bioavailability of AA (Vitamin C)** based on pH range and AA stability
- Favorable scent attributes were noted for this elegant AA (Vitamin C) serum **including scent was pleasant and scent did not linger**
- The high strength **15% Vitamin C serum with Feverfew, PHA and EGCG**, formulated to provide multiple mechanisms for **effective facial pigment evening and brighter skin**, delivered clinically and consumer perceivable benefits for overall facial skin brightening **in a diverse population representing all skin tones**

AA, ascorbic acid; EGCG, epigallocatechin gallate; PHA, polyhydroxy acid

References

1. Dufort M, et. al. Chelation properties demonstrated by a novel analytical method help elucidate polyhydroxy acids benefits for environmental oxidative stress and pigmentation. Poster Exhibit; 79th Annual Meeting of the American Academy of Dermatology, Virtual: April 2021.
2. Yang A, et. al. Particulate Matter 2.5 (PM2.5) as a model of pollution induces hyperpigmentation in melanocytes potentially via oxidative stress. Poster Exhibit; 78th Annual Meeting of the American Academy of Dermatology, Denver: March 2020.

Scientific Poster presented at the *American Academy of Dermatology Annual Meeting*, 25–29 March 2022.