Split-Face Vitamin C Comparison Consumer Preference Study

C-ESTA® Serum and CE Ferulic®

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INTRODUCTION

Vitamin C is commonly used to treat aged skin because of its regenerative effects on skin wrinkles, texture, strength, and evenness of tone through its roles as an antioxidant, tyrosinase inhibitor, and inducer of collagen synthesis. There are many vitamin C formulations on the anti-aging skin care market that vary by their pH, packaging, and vehicle, which can affect the absorption, and therefore, the efficacy of the product. The purpose of this study was to assess the subjective efficacy, wearability, tolerance and overall preference of two professional vitamin C topical serums and sunscreens in Caucasian females using a split-face method and to assess subject preferences.

METHODS

An online "virtual" split-face study of thirty-nine Caucasian women compared two popular vitamin C and SPF product combinations – C-ESTA® Serum and Marini Physical Protectant SPF 45 from Jan Marini Skin Research (Products A) and CE Ferulic® and Physical Fusion UV Defense SPF 50 from SkinCeuticals (Products B). The products were assigned to each subject's left or right side of the face in a split-face manner. Subjects rated / compared products on each side of the face through 5 online surveys at baseline, 24 hours, 3 days, 7 days and 14 days.

RESULTS

Thirty-five of the thirty-nine subjects completed the study. Over 86% of subjects preferred the smell and 83% preferred the feel / application of vitamin C Serum "A" over Serum "B". 71% of subjects preferred the application / feel of Sunscreen "A" over Sunscreen "B". Skin texture results showed significant difference between Products A and B with more than 3 times the number of subjects noting superior skin texture improvement with Products A as compared to Products B. Products A outperformed Products B in skin tone (brightness / luminosity) and trended higher for multiple additional categories. Products A also caused notably less irritation than Products B at all intervals.

CONCLUSION

Subjects noted superior improvement in skin texture with significantly less irritation on the Product A side of the face. Subjects also preferred the product smell, feel and application of both the vitamin C and SPF with Products A vs. Products B. Subjects did not note superior improvement with Products B in any measured category. Overall, subjects preferred Products A over Products B and were willing to pay more for Products A than Products B.

INTRODUCTION

Photo-aging is characterized by sagging and thinning of the skin, discoloration, fine lines, and skin fragility. It is mainly induced by sun exposure, including UVA and UVB rays. Clinical signs of photo-aging are caused by loss of elastin, hyaluronic acid (HA), and collagen. Loss of elastin tissues leads to skin sagging resulting in nasolabial fold (NL) wrinkles, sagging of the jaw line, and crow's feet wrinkles. Loss of collagen in skin leads to fine lines, thinness, fragility and textural change. Loss of hyaluronic acid in skin results in decreased skin plumpness and fine lines.

Protection against UV exposure helps prevent or minimize many of the visible signs of aging. The American Academy of Dermatology recommends daily use of a broad spectrum sunscreen with a minimum SPF of 30. While many consumers recognize the need for sunscreen, many are challenged by the smell or feel of sunscreens, resulting in non-compliance and loss of sun protection. Hence, a broad-spectrum sunscreen with high user appeal is critical to any anti-aging solution.

Collagen levels can be increased by using topical alpha hydroxy acids, retinoids and vitamin C.[1] Vitamin C has the added benefit of improving skin tone and color and providing antioxidant benefits in addition to its ability to increase collagen production. As humans are unable to synthesize vitamin C, thus the intake of dietary supplements or application of topical formulations of vitamin C is necessary to delay the process of aging or diseases related to vitamin C deficiency. Vitamin C is commonly used to treat aged skin because of its regenerative effects on skin texture, color, and inflammation through its roles as an antioxidant, tyrosinase inhibitor, and inducer of collagen synthesis.

HA is composed of repeated units of sugars (saccharides). The size of the HA molecule determines the ability of topically applied HA to penetrate into skin.[2] HA that is applied to the surface of the skin is a humectant; therefore it draws water into itself which can increase skin hydration in a humid environment.

Vitamin C is one of the most recognized antioxidants in consumer surveys and has had a surge in popularity over the last 10 years with many topical products entering the market making it difficult for the products to differentiate themselves to consumers. This study compares consumer preference between two commercially available topical vitamin C and sunscreen products.

Study Products

In this study, a combination of sunscreen and vitamin C from two different companies were compared in a split-face study to compare efficacy and consumer preference. Products A, by Jan Marini Skin Research, San Jose, CA, consisted of "C-ESTA Serum" ($93 retail) and "Marini Physical Protectant SPF 45" ($49 retail) – combined retail value of $142. Products B, by SkinCeuticals Inc., Garland, TX consisted of "CE Ferulic" ($159 retail) and "Physical Fusion UV Defense SPF 50" ($34) – combined retail value of $193.

"C-ESTA Serum" is an anti-aging and antioxidant product containing vitamin C (ascorbyl palmitate), dimethylaminoethanol (DMAE), hyaluronic acid (sodium hyaluronate), vitamins B5 (pantethine) and E (tocopheryl acetate), tyrosine and zinc. "CE Ferulic" is an anti-aging and antioxidant product containing vitamin C (L-ascorbic acid), vitamin E and ferulic acid (see Table 1 on p. 4).

"Marini Physical Protectant SPF 45" is an 80-minute water resistant broad spectrum SPF containing zinc oxide, titanium dioxide, green tea extract, alpha-bisabolol and CoEnzyme Q10 and microscopic oil-absorbing particles. "Physical Fusion UV Defense SPF 50" is a 40-minute water resistant broad spectrum sunscreen containing zinc oxide, titanium dioxide and artemia selina (see Table 1 on p. 4).

Antioxidants

Antioxidants have the capacity to neutralize free radicals by giving oxygen the missing electron it needs, reducing oxidative stress and their ability to cause damage. By neutralizing free radicals, antioxidants mitigate damage to the skin and lessen the effects of aging. Vitamin C and vitamin E are two antioxidants shown to significantly reduce the damage produced by free radicals. Free radicals are compounds formed when oxygen molecules combine with other molecules yielding an odd number of electrons. An oxygen molecule with paired electrons is stable; however, oxygen with an unpaired electron is "reactive" because it seeks and seizes electrons from vital components leaving them damaged.[3] DNA, cytoskeletal elements, cellular proteins, and cellular membranes may all be adversely affected by reactive oxygen species (ROS).[4,5]

Many factors need to be considered when selecting an optimal vitamin C. Nearly all forms of vitamin C, and L-ascorbic acid in particular, are sensitive to degradation from exposure to air and light.[6] Products exposed to air and light will lose efficacy over the life of the product. Ascorbyl Palmitate is a more stable form of vitamin C and the test product is packaged in an airless container to eliminate degradation over time.

Different forms of vitamin C also have different formulation requirements for efficacy. To penetrate the skin, L-ascorbic acid (a polar water-soluble molecule) must be applied in a high concentration with a low pH of 2.0 to 2.5. This low pH can cause skin stinging, redness and persistent irritation in some skin types. Ascorbyl Palmitate is a lipid soluble form of vitamin C, effective over a broader pH range, allowing for significantly greater penetration with less irritation.

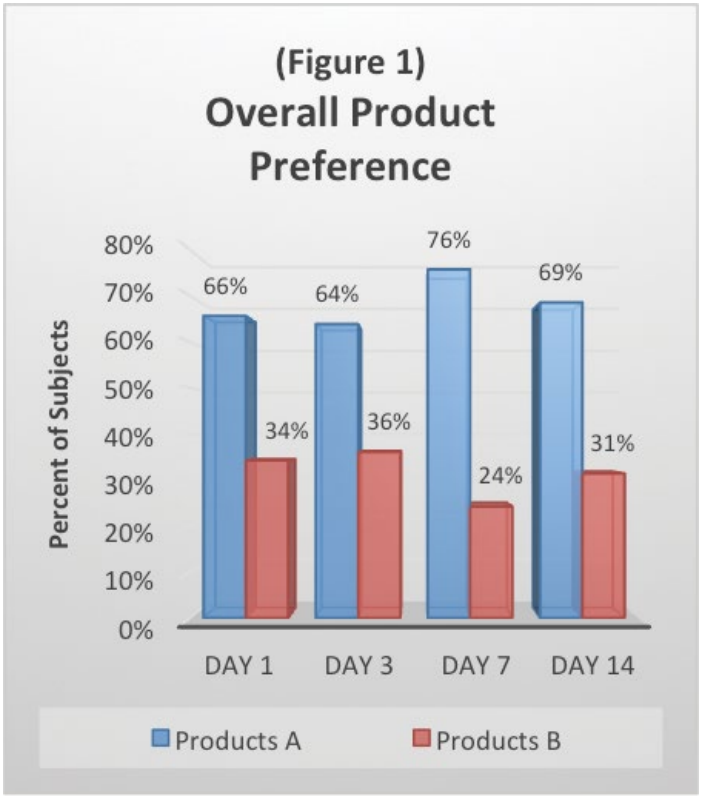
Ascorbyl Palmitate is shown to be effective as an intact molecule[7] in-vivo and in-vitro, and hydrolysis of

Ascorbyl Palmitate yields ascorbic acid in the skin with greater penetration due to its lipid soluble nature. Its increased absorption and ability to reside in the lipid portion of the cell membrane may give it a protective advantage over water soluble forms of ascorbic acid. In an oxidative stress induced tumor study, Ascorbyl Palmitate was found to be more than 30 times more effective than L-ascorbic acid and effective at significantly lower concentrations. This is hypothesized to be due mainly to the poor dermal penetration of the polar, water-soluble L-ascorbic acid.[8]

Ascorbyl Palmitate is further shown to have a photo-protective and anti-inflammatory benefit in-vivo. When applied post UV exposure, skin pre-treated with Ascorbyl Palmitate showed lower rates of erythema and required a higher minimum UV dosage to induce erythema. Further, in post-UV induced erythema, redness resolved 50% faster on areas treated with Ascorbyl Palmitate vs. untreated skin. Benefits were also observed in Asteatic Dermatitis, Psoriasis and dry skin.[9]

Green tea extract is a powerful antioxidant that significantly decreases the appearance of lines and wrinkles and is shown to reduce the damage from oxidative stress, thus decreasing cellular damage. This provides great benefits to photo-damaged and aging skin.[10]

DMAE, a precursor to acetylcholine which plays a role in proliferation, differentiation, locomotion, and secretion. A study by Grossman observed that topically applied DMAE facial gel resulted in improvement of multiple signs of skin aging including improvement in skin tensile strength, lip fullness and overall appearance of facial skin with improvement in the reduction of forehead lines and periorbital fine wrinkles.[11] These improvements remained after 2 weeks of cessation of the product. The mechanisms of action in the skin of acetylcholine and DMAE remain to be elucidated but evidence suggests that the skin is an active site of acetylcholine synthesis, storage, secretion, metabolism, and receptivity. Muscarinic acetylcholine receptors have been localized to keratinocytes, melanocytes and dermal fibroblasts, whereas nicotinic acetylcholine receptors have been found in keratinocytes.[12]



METHODS

Survey Subject Population

Subject screening was conducted via an online virtual trial. A total survey group of 40 subjects was completed to allow for dropouts while maintaining a minimum of 25 subjects at study completion. All subjects recruited for this study were Caucasian females between the ages of 30 and 65, and Fitzpatrick skin types II through IV. All subjects received 5 surveys at the following time points: baseline, 24 hours, 3 days, 7 days and 14 days.

The target population was defined as those who met the following criteria: 1) able to read, understand, and sign the approved informed consent; 2) able to limit their sun exposure and willing to daily wear sunscreen for the duration of the study; 3) able to avoid becoming pregnant, breast feeding, and willing to use a reliable method of birth control throughout the course of the study; 4) subjects who feel their skin was dull with a loss of radiance or have fine lines on the face; and 5) subjects who have uneven skin tone.

Survey Materials

Subjects received the study materials with home instructions to use throughout the two-week study period. Email notifications and reminders were provided to give instructions on how to fill out the 5 online surveys to determine the consumer preference for each of the products.

C-ESTA Serum and SkinCeuticals CE Ferulic were labeled as either Products A or B, and were used in combination with study-provided sunscreens. Subjects and investigators did not know the identity of Products A or B.

All subjects were instructed to apply Products A to one side of their face and Products B to the other side

(Table 1: Key Ingredient Function and Comparison)

	Product Name	Key Ingredients	Ingredient Benefits
Products A	C-ESTA Serum	Ascorbyl Palmitate (Vitamin C)	Lipid soluble, neutralizes free radicals, promotes collagen synthesis, greater product penetration
		Dimethylaminoethanol (DMAE)	Skin rejuvenation, tightens skin, reduces laxity and fine lines & wrinkles
		Sodium Hyaluronate (Hyaluronic Acid)	Skin hydration
		Tocopheryl Acetate (Vitamin E)	Neutralizes free radicals, inhibits UV-induced melanogenesis; has anti-inflammatory properties
		Zinc Sulphate	Skin Conditioner
		Tyrosine	Skin Conditioner
		Pantethine (Vitamin B5)	Skin Conditioner
	Marini Physical Protectant SPF 45	Zinc Oxide 8%	Broad spectrum sun protection
		Titanium Dioxide 6%	Broad spectrum sun protection
		Ubiquinone (CoEnzyme Q10)	Neutralizes free radicals, reduces UV induced damage, helps build new collagen and elastin. May be more effective than Vitamin E at preventing oxidative damage to tissue.
		Alpha-Bisabolol	Anti-inflammatory, anti-irritant
		Camellia Oleifera (Green Tea Extract)	Neutralizes free radicals, skin conditioner, reduces lines & wrinkles
		Microscopic Sponges	Absorbs oil on skin
Products B	SkinCeuticals CE Ferulic	L-Ascorbic Acid (Vitamin C)	Neutralizes free radicals, promotes collagen synthesis
		Alpha Tocopherol (Vitamin E)	Neutralizes free radicals, inhibits UV-induced melanogenesis; has anti-inflammatory properties
		Ferulic Acid	Antioxidant, neutralizes free radicals
	Physical Fusion UV Defense SPF 50	Zinc Oxide 5%	Broad spectrum sun protection
		Titanium Dioxide 6%	Broad spectrum sun protection
		Artemia Selina	Decreases UV induced damage Anti-inflammatory, anti-irritant

of their face. Products A and B were assigned to the left or right side of the face respectively. Subjects were also allowed to use daily facial cleanser and moisturizer and to continue wearing their makeup throughout the duration of the study.

Data Collection

Data was collected at baseline and days 1, 3, 7 and 14. Study surveys were provided to all enrolled subjects, ensure confidentiality of their individual responses and personal information. Surveys 2 to 5 for each respective time point allowed subjects to rate each product based on smell, feel and application as well as perceived impact on skin texture, pore size, skin tone, laxity, eye wrinkles and irritation / sensitivity with a final assessment of overall product preference.

Statistical Analysis

This report made use of statistics and graphics to draw inferences and conclusions. Choices were numerically coded to properly prepare for statistical testing with lower values representing negative skin perception and higher values representing positive skin perception. To assist in the visualization of results, some graphics used percentage even though statistical tests used numerical scores. A repeat measure Analysis of Variance (ANOVA) was used to test for significant difference at the $p = 0.05$ level. A paired two-tail t-test was used to compare preferences between products at each time interval.

RESULTS

Thirty-five subjects completed the full study. Overall, subjects significantly preferred Products A over Products B at all measured time intervals with a significant number preferring Products A at days 7 and 14 ($p<0.05$) (see Figure 1 on page 3). Nearly two thirds of subjects (22 vs 13) were willing to pay more for Products A vs. Products B and two times the number of subjects indicated a preference of over $20 more for Products A than vs. Products B (8 vs. 4).

Subjects significantly ($p<0.001$) preferred the application/feel and smell of Product A's vitamin C serum (C- ESTA Serum) vs. the Product B serum (SkinCeuticals CE Ferulic) at all measured time intervals (see Figure 2).

Subjects also significantly preferred the Product A physical sunscreen over the Product B sunscreen. With topical products, most consumers expect to see a difference in the skin in 4 weeks' time. In this study subjects saw a difference in skin texture as early as day 3. When assessing skin texture, Products A outperformed Products B at all data points with statistical significance at days 7 and 14 ($p<0.05$). 3X the number of subjects noted superior improvement in texture on the Products A side vs. the Products B side (43% vs. 14%) with 2/3 of subjects indicated superior or equal improvement on the Products A side. Only 14% of subjects indicated superior improvement in texture with Products B (see Figure 3 on p. 6).

Irritation between the two products was notably different at all measured time intervals with Products B exhibiting nearly two times the amount of irritation of Products A. However, due to the lower number of subjects experiencing irritation, the difference was not significant ($p=0.08$ at day 3) (see Figure 4 on p. 7).

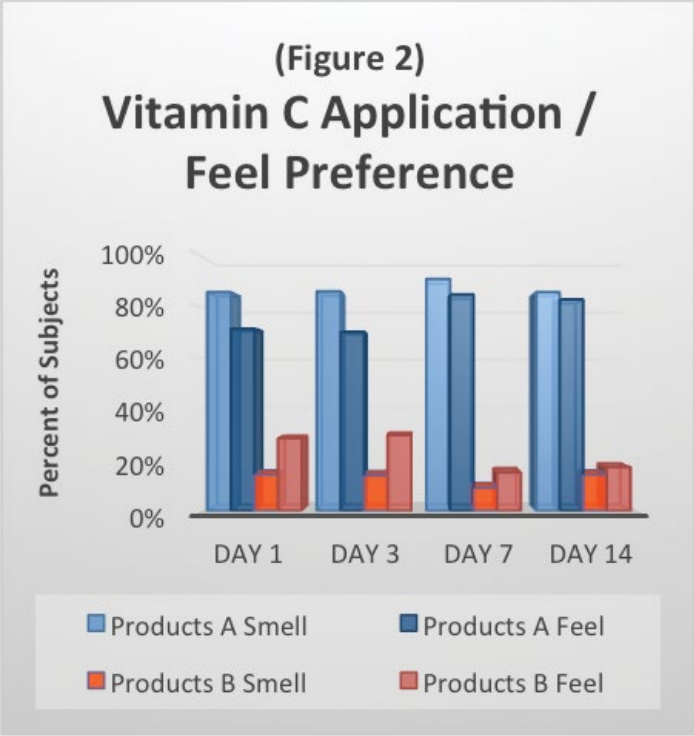
While not statistically significant, Products A trended toward superior performance at all measured time intervals for skin tone (brightness/ luminosity) (31% vs. 23% at day 14) and laxity (23% vs. 11% at day 14). Longer follow-up or a larger population size may show differences in these categories.

No meaningful difference or trend was observed regarding nasolabial folds and wrinkles under the eyes and pore size.

DISCUSSION

Overall, subjects preferred Products A over Products B. This was due to both superior results and superior aesthetic experience.

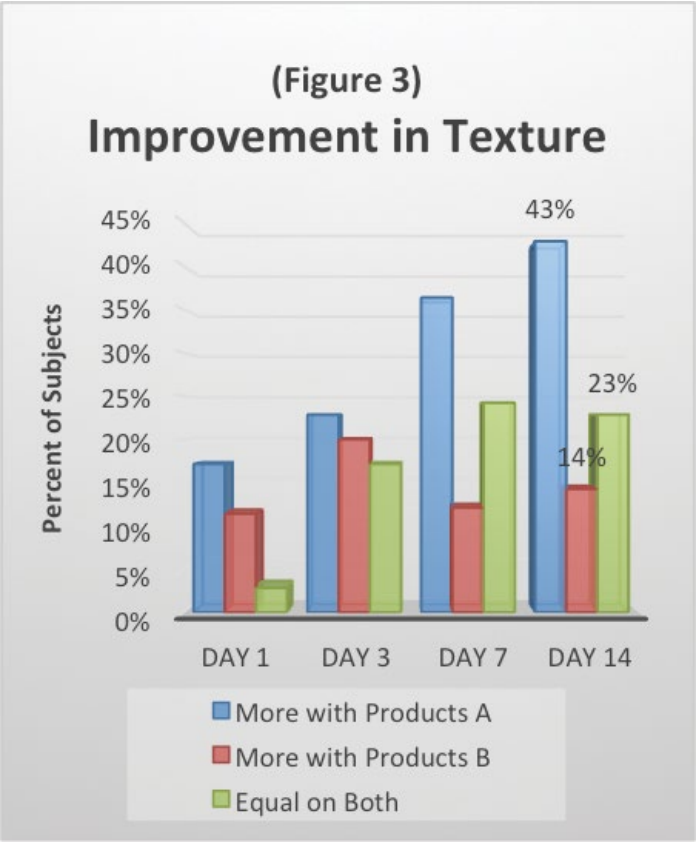
(Figure 2)



Application, feel and smell of a product play a large role in consumer preference, the ability to wear daily for best results and willingness to repurchase the product. In this study subjects preferred the smell and feel of Products A at all measured intervals with 86% and 83% respectively preferring Products A at Day 14. While a strong preference like this can lead to biases or a placebo effect on other questions, the notable percent of subjects indicating no improvement with either product for lifting, laxity and nasolabial folds suggests that the preference of the feel and smell of Products A did not bias the results of the survey.

Skin texture and associated fine lines are one of the most common visible signs of aging skin and showed the greatest difference between Products A and B in the study. Products A statistically outperformed Products B at day 7 and day 14 with increasing differentiation over time and the greatest difference observed at day 14. This question is the most targeted question in respect to the expected results with an anti-aging skincare regimen.

Changes over time were expected in both products due to the increased production of collagen by the fibroblasts (skin cells). Due to the low pH, exfoliation and secondary irritation and micro swelling of Product B we (principal investigator) incorrectly expected superior results with Products B. Products A, however, exhibited superior performance at all time-intervals despite its non-acidic



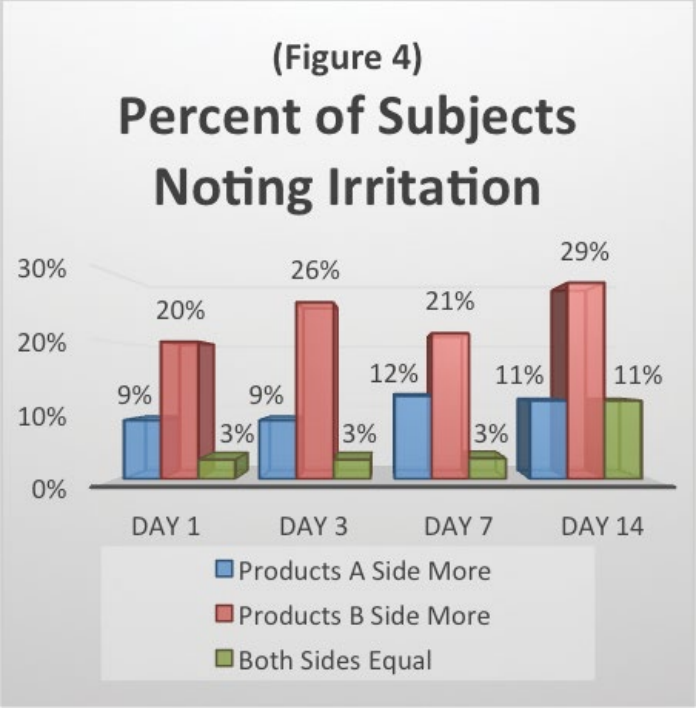
pH and significantly lower irritation rate. The superior improvement observed with Product A is likely due to a combination of increased collagen production, hydration from the HA, firming of skin from DMAE and skin conditioning from green tea extract, zinc, tyrosine and vitamin B6.

Wrinkles under the eyes can be improved by increased collagen production, increased skin hydration and slight skin swelling from irritation. Fine lines seen in photo-aging studies may improve based upon moisturizing and plumping ingredients in the formulation alone, however, improvement is often due to the additive effects of increased skin hydration and increased collagen production. As these lines are often deep and difficult to improve in a short study such as this, we did not expect significant improvement. Nearly 70% of subjects, however, noted improvement with either or both products, indicating the quality of both products.

Skin tone improvement is expected with vitamin C as it inhibits tyrosinase, which is needed to make melanin (skin pigment). If the ascorbic acid was efficacious, we would expect to see improvement in skin tone (color) over time but pigmentation studies usually note improvement at 8- 12 week time points. Surprisingly, when asked on Day 14 about skin tone, brightness and luminosity, subjects noted improvement. Products A performed slightly better than Products B (11 vs. 8 subjects) with and 9 subjects indicating both sides improved equally. Only 7 subjects said that neither side improved illustrating that changes in the appearance of skin pigmentation can occur earlier than can be explained by tyrosinase inhibition alone and may be partly due to effects of vitamin C, HA, green tea, vitamin E and or other key ingredients on hydration and reflectivity.

Pore size reduction may be observed due to tightening of skin, increased collagen production, astringent characteristics of ingredients or from swelling of the skin from irritation. On day 7 Products A had a greater effect on pore size than Products B but by day 15 there was no significant difference between Products A and B on pore size. As there was less irritation seen from Products A than Products B, irritation and swelling would not account for the improved appearance of the pores. A larger number of subjects would be needed to assess if there were a difference in the effects on pore appearance between the two groups.

Laxity, nasolabial folds and lifting along the jawline may be improved by increased collagen production as well as skin tightening. The magnitude of change



necessary to visually observe these changes, however, is not likely to occur in a short-term 14-day study. While there was a slight but consistent observed bias toward Products A across all of these observations, most subjects noted no improvement from either product. The observed bias may be due to superior collagen stimulation or a combination of stimulation with lifting effects and hydration due to DMAE and HA but a longer term study with a larger number of subjects would be required to demonstrate statistical significance.

The significant percent of subjects noting no improvement by either product (approximately 50% for each) or equal improvement with both products (15-20%) indicates integrity of the data on other measurements, as this shows a lack of bias and willingness to grade “no-response” for both products.

Irritation is commonly experienced with vitamin C products due to typically low-pH formulation. Notably fewer subjects reported irritation with Products A vs. Products B at all time-intervals during the study. Nearly two times the number of subjects indicated irritation on the Product B side at all measured intervals with very few subjects indicating equal irritation on both sides (Figure 4). While not statistically significant ($p=0.08$ on Day 3, $p=0.1$ on Day 14) the trend was notable. The lack of statistical significance is likely due to the small total number of people experiencing irritation.

The lack of irritation and improvement seen with Products A suggests rapid improvement mechanisms other than short term irritation and inflammation.

Price plays an important role in product selection and value and consumers are much more likely to repeat purchases where they perceive superior value.

In this study, 22 of 35 of subjects were willing to pay more for Products A than for Products B with nearly twice the number of subjects willing to pay over $20 more for Products A than Products B. The strong preference to pay more for Products A is amplified in the market where Products A cost significantly less than Products B ($142 vs. $193 respectively). This indicates a value gap of more than $50 between the two products.

CONCLUSION

Overall, Products A were significantly preferred over Products B. Statistical analyses showed that subjects observed significantly superior improvement in texture with Products A over Products B. Further, subjects significantly preferred application, feel and smell of both the vitamin C serum and the sunscreen of Product A over Product B. Finally, Products A caused less sensitivity and irritation. This combination lead to a clear user preference and willingness to pay more for Products A over Products B.

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