

The Effects of Celadrin™ Topical Cream Treatment to Improve Facial Skin Appearance

Robert L. Hesslink, Jr., Kristee Emens-Hesslink and David W. Armstrong III

Imagenetix, Inc., San Diego, CA 92127

INTRODUCTION

The aging American population has drawn considerable interest from the marketing world as witnessed by the numerous skin care products on store shelves and the plethora of infomercials shown daily on television. However, upon scrutiny of these products one is struck by the lack of standardized testing. The typical product endorsement includes a pre- and post-photograph showing a remarkable improvement in fine lines, wrinkles and overall appearance. Rarely do we see solid, scientific information presented to document these successes.

The majority of OTC skin care creams, gels and emollients contain non-drug ingredients such as common anti-oxidants (vitamin C and vitamin E) combined with newer compounds such as lipoic acid. Little, if any, standardized clinical investigations into these products has been conducted. The bulk of reports in the scientific literature pertaining to skin appearance improvement are primarily focused on one single ingredient: retinaldehyde or retinoic acid (4,5,7,9,11).

The current investigation was conducted to obtain preliminary information regarding the use of Celadrin™ topical application for improving facial skin. The main criteria for this study were to establish the safety of the product and demonstrate improvement in visible signs of aging.

METHODS

Subject Recruitment

Subjects were recruited by Life Management Group, a clinical research organization from La Jolla, CA. Participants were staff and faculty of the University of California, San Diego plus the surrounding San Diego and La Jolla area. The protocol was reviewed and approved by an IRB board convened by Life Management Group for its studies.

Twenty-nine subjects were recruited, screened, and enrolled between the ages of 25 and 65 years of age; the mean age was 45 years. One subject dropped out due to non-medical, non-study related reasons. Twenty-one of the 29 subjects had been using commercial face cream products prior to enrolling in the study.

Face Cream Application

Participants applied a topical cream daily for 21 days. Each participant completed a washout period of ten (10) days to cleanse the face and neck with nothing but moisturizing soap and water and used no other products during the washout or during the research study. The participants continued their regular routine, which included their normal diet, sleep pattern, physical activity, medications, and multivitamin consumption. The participants were to drink a minimum of eight eight-ounce glasses of water per day. The participants were to limit sun exposure to casual/incidental during daily activity. During the twenty-one day research study, the participants were to apply 42 applications of the facial cream on the face and neck areas. These were applied twice daily: once in the morning upon rising and once in the evening before retiring. Participants were instructed to be particularly careful to keep the cream application from getting in their eyes.

Face Cream Formulation

The face cream contained proprietary esterified fatty acids (e.g. Celadrin™) in addition to purified water, carbomer, methylparaben, propylparaben and fragrance, glycerin and glyceryl stearate.

Questionnaire

The questionnaire consisted of 19 questions anchored by a Likert-type scale: “1 = Not at all or None”; “2 = Somewhat or Few”; “3 = Moderately or Moderate”; and “4 = Very or Many.” The questionnaire was completed by the subject prior to and at the end of 21 days. In addition, the investigators interviewed each subject and completed the questionnaire using their own observations. See Appendix I for complete questionnaire details.

Statistics

Cochran-Mantel-Haenszel Tests, stratified by subject, were conducted of pre- vs. post-responses to all 19 questions, a subset of 11 questions concerning the face and a subset of 9 questions concerning the neck. All tests were significant at $P < .0001$. Although the response variables are not a continuous numeric, for comparative purposes, we report the mean response score \pm SD pre and post for all questions, the subset of questions for face and neck Pre-Interviewer (Pre-I), Post-Interviewer (Post-I), Pre-Subject (Pre-S) and Post-Subject (Post-S).

RESULTS

The Celadrin cream was favorably perceived by the subjects from their anecdotal statements. Participant comments focused on the lightness and hydrating quality of the cream, and the fact that the cream spread easily and that they only had to use a small amount. In addition, 93% of the subjects reported no adverse affects of the cream. Two subjects reported small blemishes during the first few days of application which abated over time.

Analysis of the questionnaire scores revealed that the “interviewer” noted overall improvement ($p < 0.01$) after 21 days of application (figure 1). As shown in figures 2 and 3, both the “subject” and “interviewer” noted significant ($p < 0.001$) improvement after visual inspection. The neck area showed improvement ($p < 0.01$) with cream application as determined by the “subject” and “interviewer” questionnaire responses although with less statistical power. This may reflect the difference between facial and neck dermal layers.

DISCUSSION

The present investigation shows the benefit of using Celadrin™ for treating age-related facial problems. In this preliminary trial, subjects and investigators reported significant observable improvements after 21 days of application. The number of clinical trials reported for facial improvement products is limited. The primary studies in the scientific literature deal with the use of retinoic acid compounds. There are only a small number of trials looking at products with natural ingredients.

The few studies that are in the literature discuss prescriptive drugs. In 1996 and 1997, Gilchrist reviewed skin aging and medical therapies. The synergy between normal aging and environmental influences were shown to elicit a thickened epidermis and increased melanogenesis with even greater changes in the dermis (6,7). However, treatment with tretinoin cream for 4-6 months suggested a reparative process. Further changes were noted in histological sections after 12 months in both the dermis and epidermis. Kligman and Draeos (9) reported in 2004 that high strength tretinoin was tolerated well by patients and shortened the time required for clinical response. In this trial 32 female subjects applied the cream nightly for 30 days. Investigators reviewed photographs and assessed three main criteria: fine lines; mottled hyperpigmentation and surface texture/roughness. The authors noted that most subjects experienced mild to moderate improvement. The majority of trials conducted on retinoic acid-based creams tend to focus on epidermal and dermal thickening, coarse wrinkling, roughness, and elasticity (4,5,11). These trials ranged from 24 to 52 weeks of daily treatment. In most cases, patients tolerated the cream without adverse events and achieved some benefit in skin thickening and photodamaged aging. It is noteworthy that these studies failed to include investigator and patient survey instruments for subjective assessment of treatment.

An extensive review was recently published by Chiu and Kimball in the British Journal of Dermatology (3). These authors reviewed the popular vitamins, minerals and botanicals used in topical creams today. These ingredients included antioxidants and anti-inflammatories. It was concluded that even though these agents have a long history of use, the rigorous studies to validate them were still lacking. However, there are a small number of trials investigating alternative ingredients (e.g. ascorbic acid, vitamin E) that adhere to stringent scientific experimentation.

Due to its high level of antioxidant activity, ascorbic acid has been investigated more frequently than others. The use of ascorbic acid (3%) in a topical cream was recently studied in 25 human subjects for 12 weeks (12). Compared to placebo there was a significant reduction in facial wrinkles. This study corroborates an earlier study showing efficacy and safety of a 5% ascorbic acid application over a 6-month period (8). Another highly regarded anti-oxidant was tested by Beitner (2). In this study, a 5% solution of alpha-lipoic acid was investigated for improving measures associated with aging facial skin. Thirty-three women enrolled in a unique design in which one-half of their face was treated twice daily with the alpha-lipoic acid cream and the other half with control cream. After 12 weeks, the treated side exhibited improvements in all measures including subject self-evaluation, photographic evaluation and laser profilometry. The treated side showed an average decrease in skin roughness by 50.8%.

The current study investigated the effectiveness of a proprietary compound composed of esterified fatty acids. It has been well-established since 1961 that fatty acids increase skin permeability through a number of mechanisms (13). In addition, preliminary animal and human research on Celadrin™ has suggested the potential efficacy in ameliorating facial skin roughness and wrinkling. After 21 days, participants in our study indicated through self-evaluation a noted improvement in their facial area with modest improvement in the neck region. These observations were corroborated by the investigators through their own pre- and post-assessment. The participants in the present study noticed that their skin seemed more hydrated and more firm. The observations reported herein are supported by a recent study using another fatty acid: date palm kernel extract (1). In this study, ten healthy women applied the date palm cream twice per day for 5 weeks. There was a significant reduction in total surface wrinkles as determined by silicon replica analysis. In addition, this clinical measure was confirmed through visual inspection in over 60% of the patients.

While newer methodology such as silicon replica analysis (e.g. profilometry) offer great insights for scientific documentation purposes a recent methodological study reported an 87 percent correlation between subjective assessments of wrinkle improvement versus that measured via profilometry (10). This information suggests that the results obtained in the present study offer preliminary support for Celadrin™ as a product for improving skin appearance.

In summary, it is evident that the findings of the current study are preliminary and need further elucidation. However, it does appear that 21 days of application using Celadrin™ can improve face and skin appearance. These results are encouraging and warrant continued investigation using new clinical assessment tools such as silicon replica analysis.

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Interviewer Mean Response All Questions

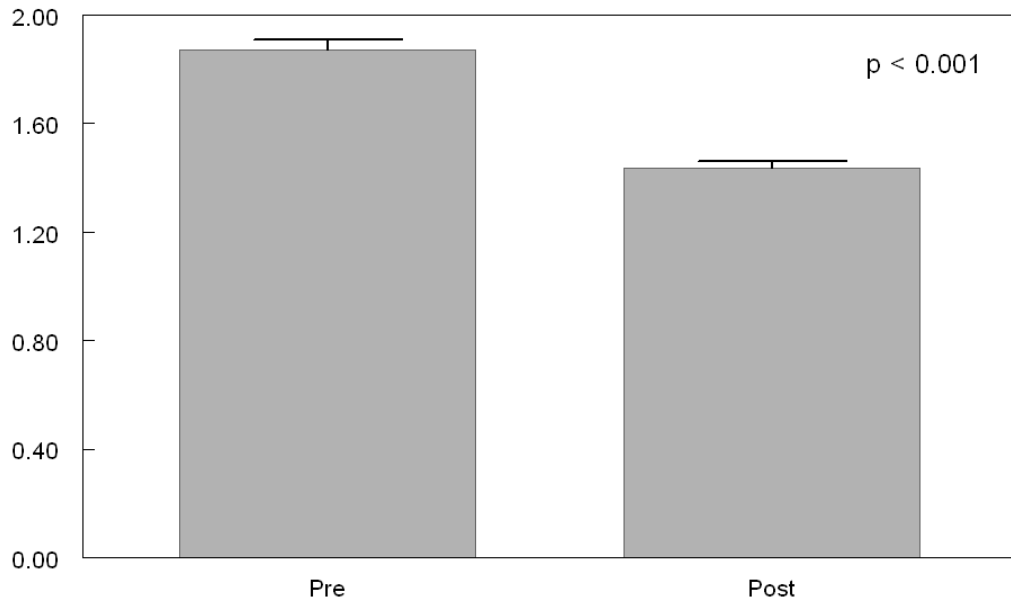


Figure 1

Interviewer Mean Response Face Questions

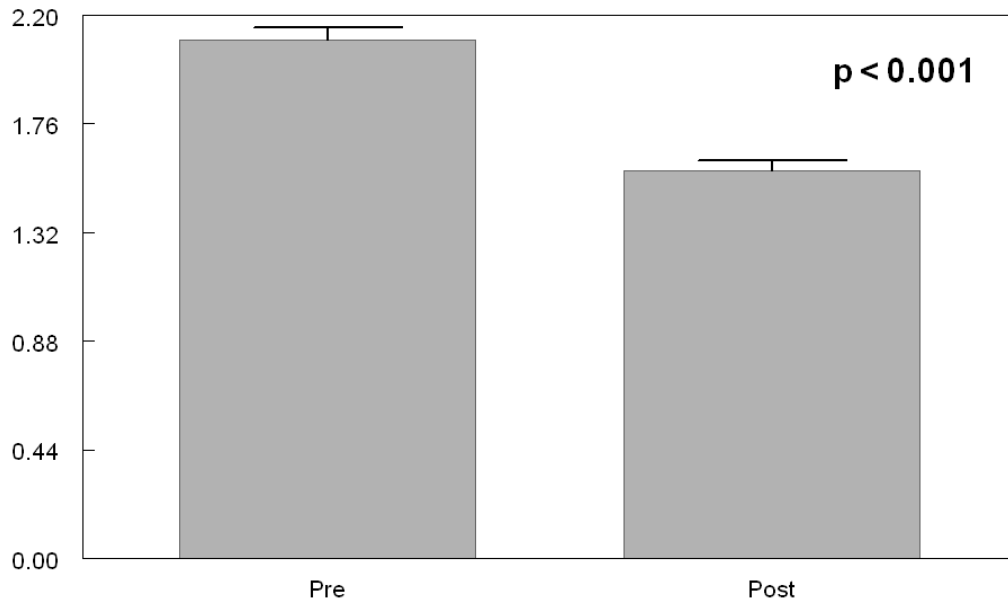


Figure 2

Subjects' Mean Response Face Questions

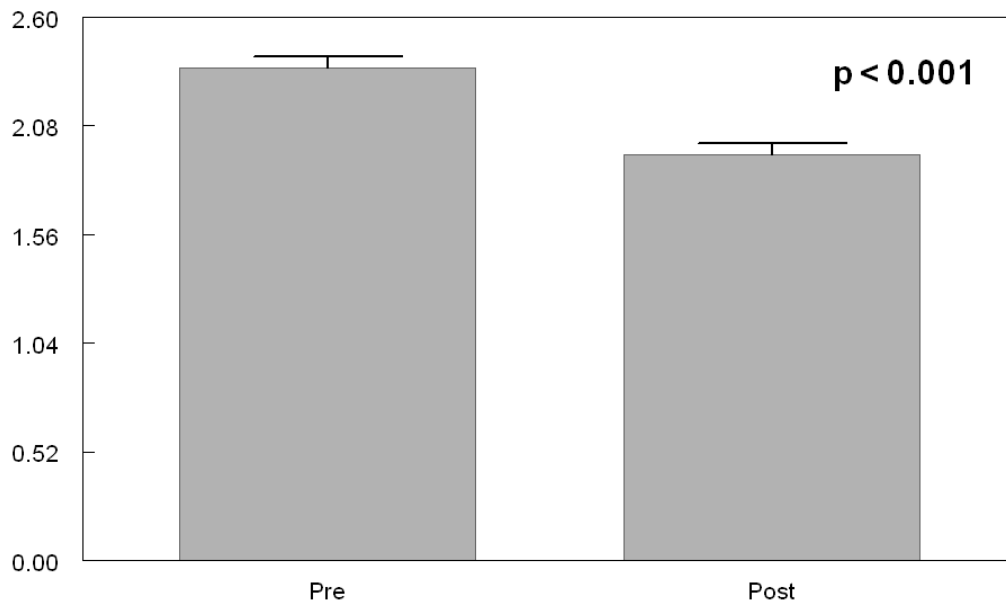


Figure 3

Interviewer Mean Response Neck Questions

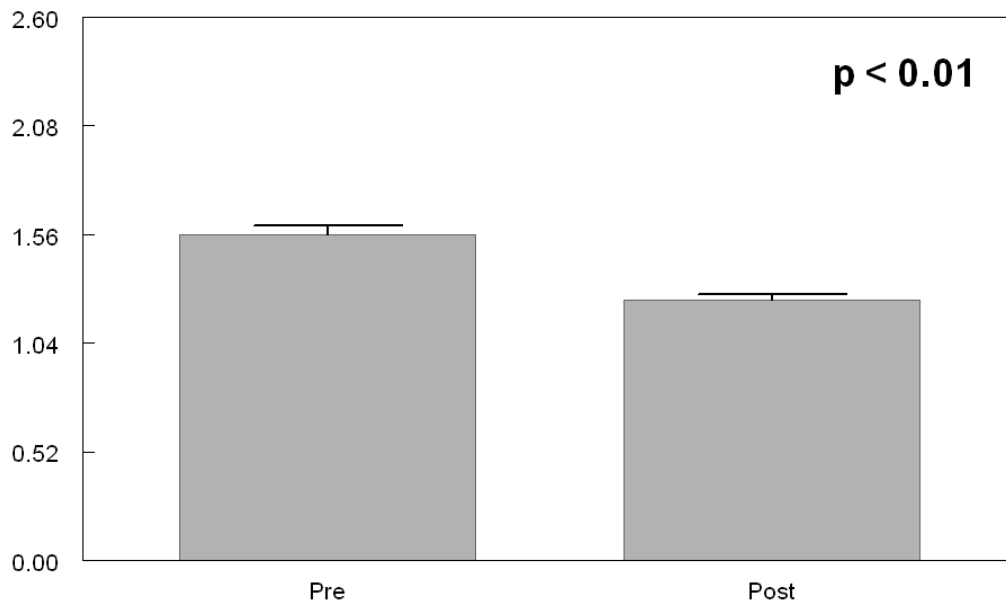


Figure 4

Subjects' Mean Response Neck Questions

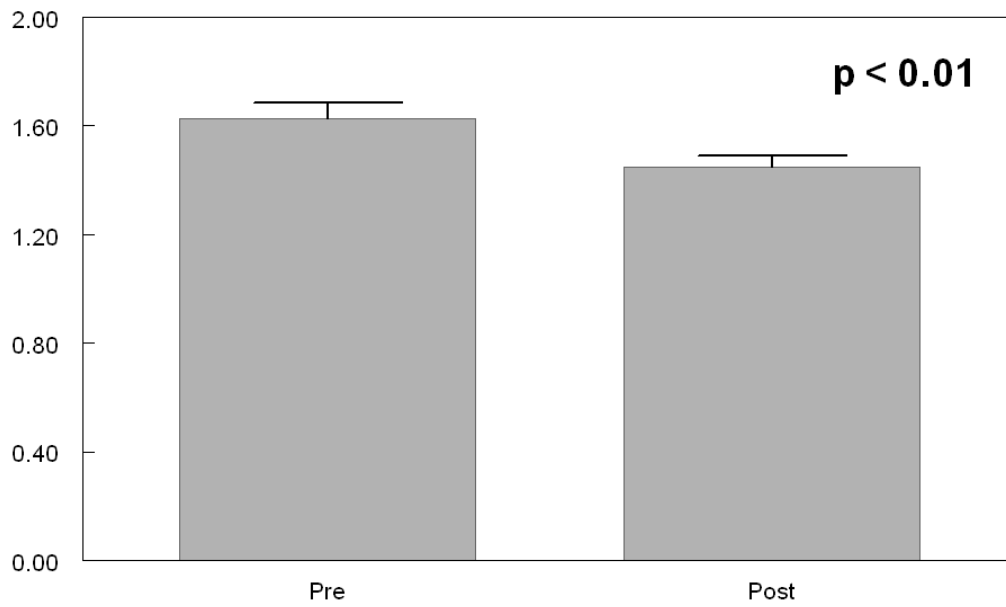


Figure 5

Appendix I: Face Cream Questionnaire

1. Please place an 'X' next to areas of your face & neck you consider a problem:

- | | | | |
|------------------|---------------------|-----------|---------------------|
| A._Forehead | D._Between Eyebrows | G._Nose | J. _Bags Under Eyes |
| B._Sides of Nose | E._Chin | H._Cheeks | K._Mouth |
| C._Sides of Face | F._Jawline | I._Neck | L._Eyes |

2. How concerned are you about the following conditions that affect your skin as you age?

- | | Not at all
1 | Somewhat
2 | Moderately
3 | Very
4 |
|---------------|-----------------|---------------|-----------------|-----------|
| a. Age spots: | _____ | _____ | _____ | _____ |
| b. Wrinkles: | _____ | _____ | _____ | _____ |
| c. Sagging: | _____ | _____ | _____ | _____ |

3. Please describe the number of fine lines on your face:

- | | | | |
|-----------|------------|---------------|-----------|
| None
1 | A Few
2 | Moderate
3 | Many
4 |
|-----------|------------|---------------|-----------|

4. Please describe the number of deep lines/coarse wrinkles on your face:

- | | | | |
|-----------|------------|---------------|-----------|
| None
1 | A Few
2 | Moderate
3 | Many
4 |
|-----------|------------|---------------|-----------|

5. Please describe the number of large pores on your face:

- | | | | |
|-----------|------------|---------------|-----------|
| None
1 | A Few
2 | Moderate
3 | Many
4 |
|-----------|------------|---------------|-----------|

6. Please describe the number of acne blemishes on your face:

- | | | | |
|-----------|------------|---------------|-----------|
| None
1 | A Few
2 | Moderate
3 | Many
4 |
|-----------|------------|---------------|-----------|

7. In the last 21 days, how often did your face break out with blemishes:

- | | | | |
|------------|-------------------|-----------------|-------------|
| Never
1 | Occasionally
2 | Frequently
3 | Always
4 |
|------------|-------------------|-----------------|-------------|

8. Please describe any dryness on your face:

- | | | | |
|-----------|-------------|---------------|-------------|
| None
1 | Slight
2 | Moderate
3 | Severe
4 |
|-----------|-------------|---------------|-------------|

9. Please describe any oiliness on your face:

- | | | | |
|-----------|-------------|---------------|-------------|
| None
1 | Slight
2 | Moderate
3 | Severe
4 |
|-----------|-------------|---------------|-------------|

Appendix I: Face Cream Questionnaire (cont.)

10. Please describe the texture of the skin on your face:

Smooth	Slightly Rough	Moderately Rough	Severely Rough
1	2	3	4

11. Please describe the number of fine lines on your neck:

None	A Few	Moderate	Many
1	2	3	4

12. Please describe the number of deep lines/coarse wrinkles on your neck:

None	A Few	Moderate	Many
1	2	3	4

13. Please describe the number of large pores on your neck:

None	A Few	Moderate	Many
1	2	3	4

14. Please describe the number of acne blemishes on your neck:

None	A Few	Moderate	Many
1	2	3	4

15. In the last 21 days, how often did your neck break out with blemishes:

Never	Occasionally	Frequently	Always
1	2	3	4

16. Please describe any dryness on your neck:

None	Slight	Moderate	Severe
1	2	3	4

17. Please describe any oiliness on your neck:

None	Slight	Moderate	Severe
1	2	3	4

18. Please describe the texture of the skin on your neck:

Smooth	Slightly Rough	Moderately Rough	Severely Rough
1	2	3	4