
Novel Dual-Chamber Anti-aging and Acne Solution Utilizing 10% Benzoyl Peroxide and 1% Retinol

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INTRODUCTION

Acne and anti-aging are two of the most significant skin concerns affecting the population today. Nearly 54 million people in the US alone are affected with acne each year, and anti-aging is recognized as the primary driver for the entire cosmetic skin care industry. With nearly 50% of female adults experiencing acne, an increasing rate of adult acne and ever increasing attention on new anti-aging technologies, there is a significant demand for a combination acne and anti-aging solution for adults.

METHODS

This study investigates a new acne and anti-aging product capable of simultaneously delivering stable formulations containing 10% Benzoyl Peroxide (BPO), 1% retinol, antioxidants and peptides. Twenty-one adult patients were enrolled in a 12-week, open label, non-placebo controlled study. Patients were assessed at each visit by a dermatologist to determine improvement in acne and photo-aging. Pre- and post- photographic assessments were conducted by four independent dermatologists reviewing global acne and skin quality. Finally, patients completed pre and post self-assessments to determine perceived improvement and satisfaction.

RESULTS

Acne lesion counts improved in 100% of all patients. Improvement was statistically significant by week 4 ($p < 0.0001$) and continued to improve through study completion. Average lesion reduction was 64% ranging from a low of 36% to a high of 78%. Global acne assessment scores improved significantly ($p < 0.0001$) with an average reviewer assessment of 70% of patients improving by 1 or more grades. Improvement in photo-aging was significant ($p = .02$) with photographic review indicating significant improvement in skin quality ($p < 0.0001$) in 100% of all patients. Patient assessment showed significant improvement in both skin quality ($p < 0.0001$) and acne ($p < 0.0001$). Patient satisfaction was high with no reported cases of irritation or excessive drying.

CONCLUSION

The simultaneous application of BPO, retinol, antioxidants and peptides delivered statistically significant improvement in acne and anti-aging without the common acne medication side-effects of skin irritation and excessive drying. Lesion count improvement was comparable or superior to prescription topical medications and over 70% of patients improved by at least one full grade using the 4-point global acne assessment scale. Skin quality improvements were significant by both patient self-assessment and investigator assessment. The tested solution represents a new and highly effective acne and anti-aging solution for adults with mild to moderate acne vulgaris.

INTRODUCTION

Acne and anti-aging are two of the most significant skin concerns affecting the adult population today with nearly 54 million people affected each year in the US alone. In an effort to control acne, American physicians write nearly eleven million prescriptions (The Lewin Group, 2004) with an estimated annual cost of \$2.2 billion. In terms of dollars spent to control a skin condition, acne is second only to hair and nail diseases. In fact, it is estimated that acne patients are willing to spend an average

of \$4.00 per day to alleviate their acne conditions, indicating a potential market of \$12 billion (The Lewin Group, 2004).

Anti-aging is the primary driver for the cosmetic industry and, now more than ever, adults in all age categories are seeking solutions to address the visible signs of aging. Among the many technologies used for anti-aging benefits, three of the most common topical solutions are retinoids, peptides and green tea. These technologies have been shown to enhance

collagen production, increase dermal thickness and reduce inflammation, abnormal pigmentation and diffuse redness (Fowler JF Jr., 2010) (Atkin DH, 2010) (Fu JJJ, 2010).

Acne, while often thought of as an adolescent condition, greatly affects the adult population and the prevalence is growing. In recent years the average age of individuals with acne has increased from 20.5 to 26.5 years of age (Goulden V, 1999), with the typical age ranging between 15-42. Studies show that approximately 50% of women between 20-29 years old and 25% of women 40-49 years old are affected by some form of acne with 12% of all adult women having clinically significant acne (Goulden V, 1999). Self-assessment data show that for the age groups of 20-29, 30-39 and 40-49, respectively, acne affects 50.9%, 35.2% and 26.3% of women and 42.5%, 20.1% and 12.0% of men (Collier CN, 2008). Studies also show that this disease can have a dramatic influence on a patient's quality of life (QOL), more so even than psoriasis. 25% of all people with acne suffer from anxiety and 13% exhibit depression ranging from mild to severe (The Lewin Group, 2004).

Two of the first-line solutions to treat acne are retinoids (vitamin A derivatives) and benzoyl peroxide (BPO) (Zaeinglein AL, 2006) (Sinclair W, 2005). Retinoids are highly keratolytic thereby enhancing desquamation of the follicular epithelium, reducing the number of microcomedones. They also exhibit significant anti-inflammatory properties (Zaeinglein AL, 2006) and are used very successfully as a primary treatment for inflammatory acne (Sinclair W, 2005). Finally, retinoids can help enhance the penetration of other topical drugs such as BPO and antibiotics (Zaeinglein AL, 2006) (Gollnick H, 2003) (Mills OH Jr., 1978).

BPO is a potent antibacterial agent, which also has mild anti-inflammatory and keratolytic effects. Because of its ability to rapidly destroy *P. acnes* bacteria, it is an important component of acne therapy as both a stand-alone technology and in combination with many other acne treatments. For severe acne treated with oral and topical antibiotics, BPO and retinoids are recommended to be used in combination to enhance efficacy, suppress the emergence of resistant strains of *P. acnes* bacteria and sustain results after a course of antibiotics (Zaeinglein AL, 2006) (Sinclair W, 2005) (Gollnick H, 2003).

Over time, the oxygen created by BPO breaks down retinoids – preventing stable combination formulations. Because of this, many protocols prescribe separate application of retinoids and BPO in an AM/PM routine. These protocols are sub-optimal as they limit the number of applications of both retinol and BPO, require multiple products and complicate the application process leading to decreased compliance. A recent study disproved the need for separate application protocols finding no difference in efficacy or skin irritation when both BPO and retinoids were applied in the AM vs. separate AM/PM applications (Pariser D, 2010).

Additional technologies such as anti-bacterial peptides and green tea are also becoming more popular treatments to control acne. Green tea is shown to have anti-inflammatory characteristics and functions as a 5-alpha reductase to help control inflammatory and hormonal acne. Since oxidative stress

is speculated to be a factor in the pathogenesis of acne, green tea and other antioxidants that reduce reactive oxygen and oxidative stress in the skin (Elsaie ML, 2009) (Katiyar SK, 2001) can independently improve acne (Elsaie ML, 2009).

The product under investigation is a new combination acne and anti-aging solution (Age Intervention Duality by Jan Marini Skin Research). This new product utilizes a dispensing system with independent internal chambers comprised of stable formulations of 10% BPO and 1% Retinol plus antioxidants (green tea, bisabolol and Chrysin), an anti-bacterial peptide, anti-aging peptides and moisturizers. The ingredients in this new acne and anti-aging product are specifically designed to maximize results in acne and anti-aging improvement without drying or excessive irritation to the skin.

METHODS

Twenty-one adult subjects were enrolled in a 12-week, open-label, non-placebo controlled acne study with a total of 5 office visits (initial, 2 weeks, 4 weeks, 8 weeks and 12 weeks). Inclusion criteria specified individuals with mild to moderate acne of both genders between the ages of 20-65, in good health, non-smoking and with no known diseases or conditions causing their acne.

Subjects in the study used the investigational BPO, retinol and anti-aging formulation with The Skin Care Management System (Jan Marini Skin Research). The Skin Care Management System is a complete pre-packaged skin care system consisting of a glycolic cleanser, a Vitamin C serum, a resurfacing gel, a hydrating product and a sunscreen. The complete system was used to ensure uniform incorporation of a daily skin care regimen, including cleanser, moisturizer and sunscreen as each of these components could affect results. An acclimation period of 2-weeks was utilized to minimize skin sensitivity with patients applying Duality MD every other evening during week one, every evening during week two finally twice daily for weeks 3-12. The protocol followed recommended procedures for the Skin Care Management System.

Assessments included principal investigator review, patient self-assessment, and blinded photographic review at study completion by four independent dermatologists. Quantification of acne was determined by both total lesion count (TLC) and global acne assessment. TLC quantified the total number of non-inflammatory lesions, inflammatory lesions (papules / pustules) and nodules / cysts (>5mm) on the forehead, right cheek and mouth/chin/nose area. Global acne assessment was determined following the FDA Guidance for Industry Acne Vulgaris: Developing Drugs for Treatment (Table 1).

Improvement in anti-aging was determined by the principal investigator using a 10-point scale for overall photo-damage (pigmentation, wrinkles, elastosis, elasticity, etc.), overall skin pigmentation (including hyperpigmentation from acne), and overall appearance of skin quality (texture, luminosity, tone and general appearance).

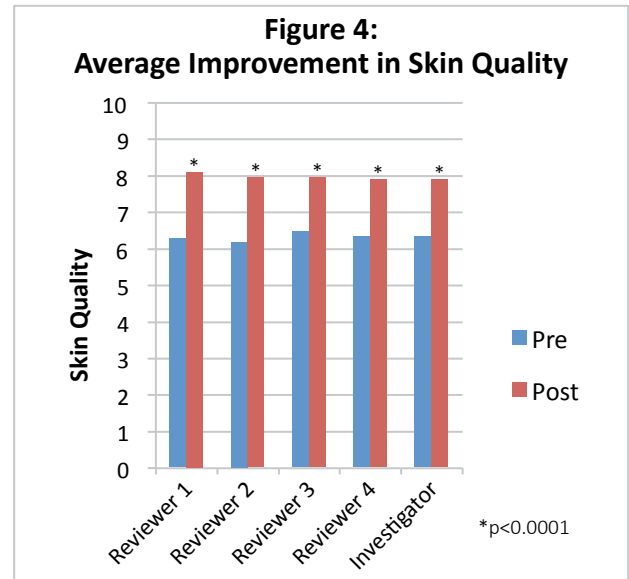
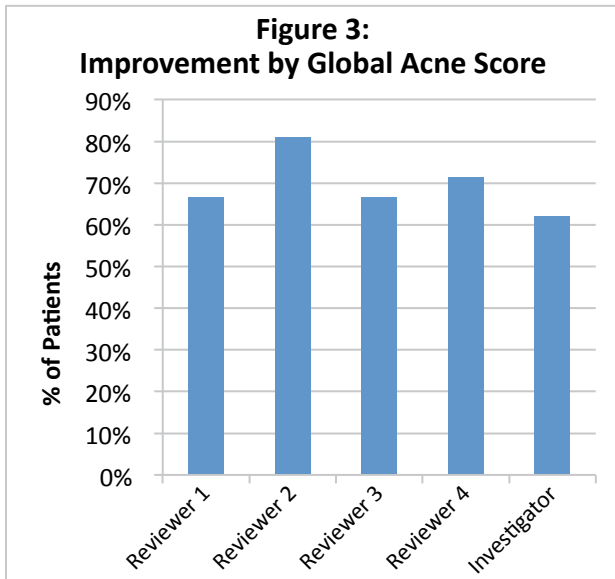
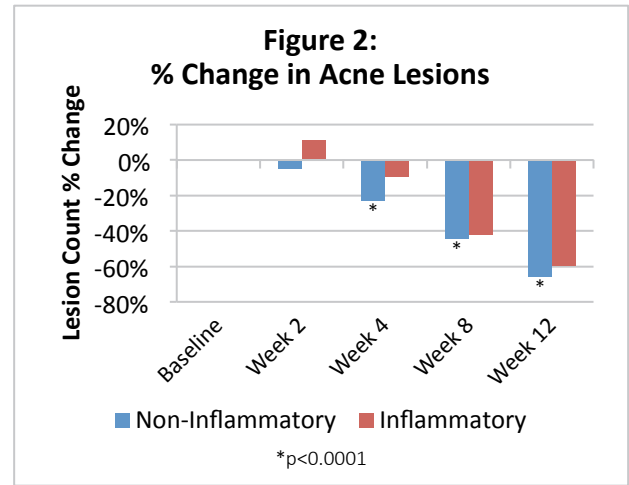
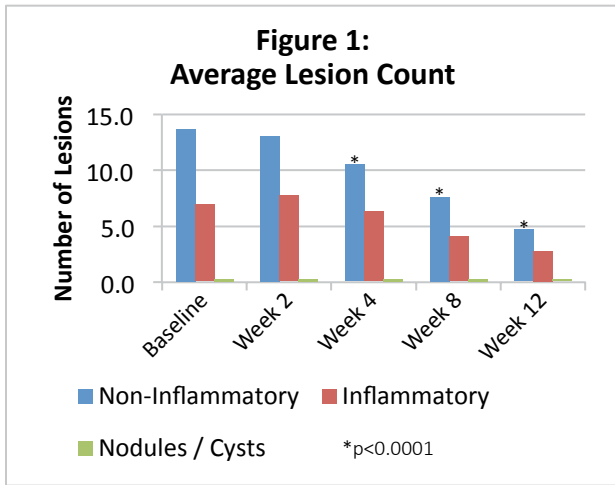


TABLE 1 – INVESTIGATORS GLOBAL ACNE ASSESSMENT

1	Clear skin with no inflammatory or non-inflammatory lesions
2	Almost clear; rare non-inflammatory lesions with no more than one small inflammatory lesion
3	Mild severity; greater than Grade 1; some non-inflammatory lesions with no more than a few inflammatory lesions (papules / pustules only, no nodular lesions)
4	Moderate severity; greater than Grade 2; up to many non-inflammatory lesions and may have some inflammatory lesions but no more than one small nodular lesion
5	Severe; greater than Grade 3; up to many non-inflammatory and inflammatory lesions but no more than a few nodular lesions

Photo-aging was also assessed using a published multi-factorial 4-point scale developed by Dr. Macrene Alexiades-Armenakas published in *JDD* Sept. 2006 for assessing photo-aging pre- and post-non-ablative laser treatments. This scale was used in place of a standard wrinkle score due to its increased granularity to measure changes in texture, erythema, elastosis and wrinkles.

To determine patient satisfaction, patients were asked to complete pre -and post- study questionnaires. Finally, upon study completion, patients were asked to rate their perceived degree of improvement in acne, discoloration, rosacea, wrinkles, skin texture, pore size, skin smoothness, elasticity and luminosity / brightness of the skin.

Statistical significance was determined by paired t-test. Unless otherwise specified, statistical significance was determined by comparing pre and post-treatment data. A p value of less than 0.05 was used to determine significance.

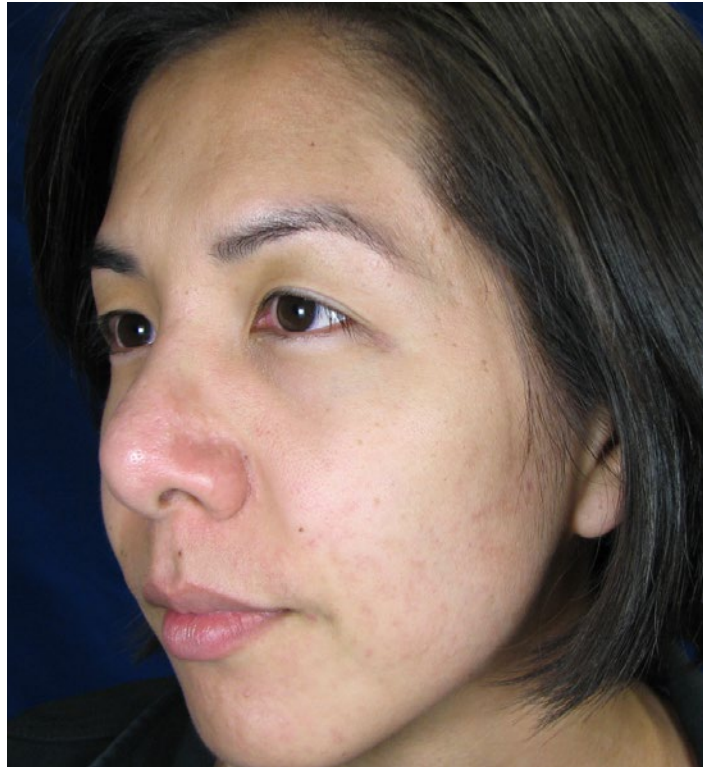
RESULTS

Patient compliance was extremely high with no reports of drying or skin irritation. There were also no drop-outs in the

PHOTOGRAPHIC EVALUATIONS



BEFORE



AFTER | 3 MONTHS



BEFORE



AFTER | 3 MONTHS

PHOTOGRAPHIC EVALUATIONS



BEFORE



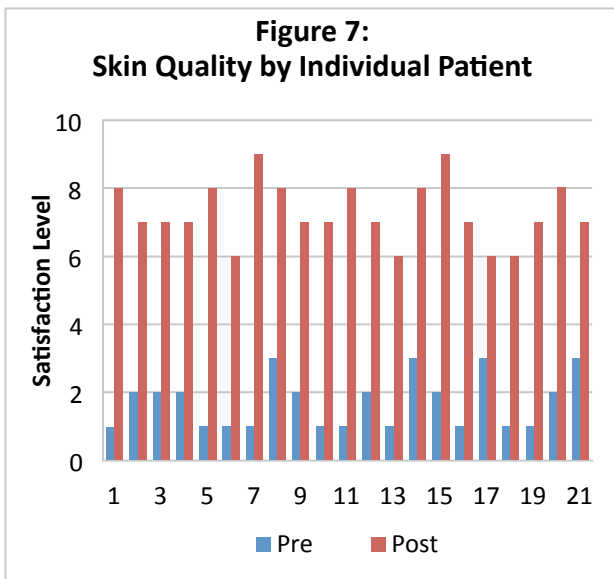
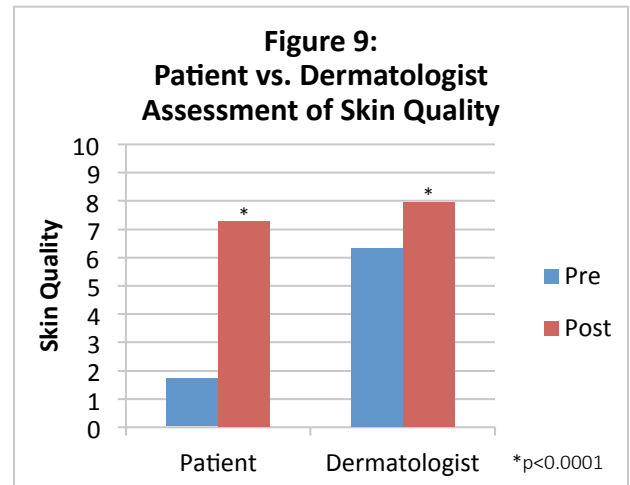
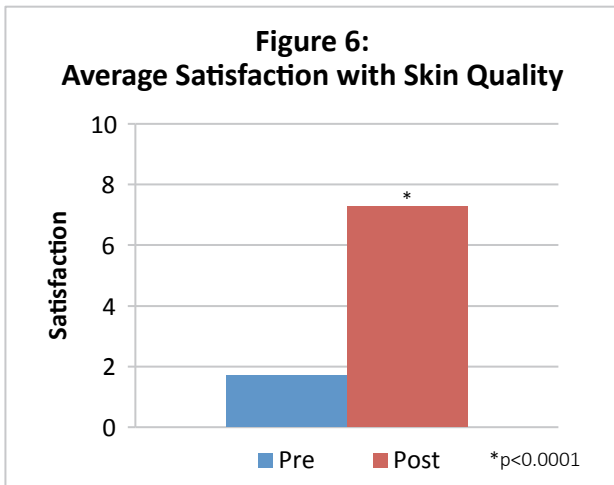
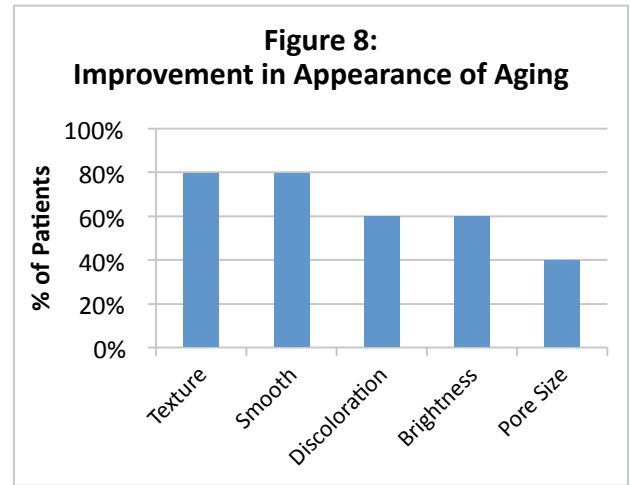
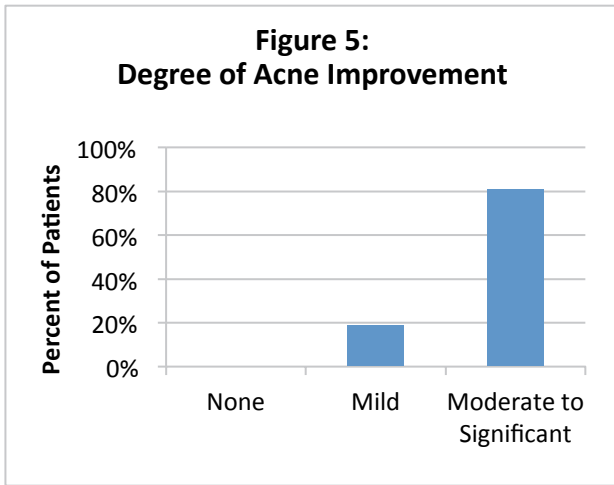
AFTER | 3 MONTHS



BEFORE



AFTER | 3 MONTHS



The average per-patient reduction was 64% ranging from a minimum reduction of 36% to a maximum of 78%. Average lesion counts and % improved significantly by week 4 ($p<0.0001$) and increased in significance through week 12 (Figures 1 and 2).

Acne improvement using the 4-point global assessment scale was determined by 5 individual dermatologists (4 blinded photographic reviewers plus the principal investigator). Data showed statistically significant improvement ($p<0.0001$) in all reviewers with an average of 70% of patients improving by at least one full grade (Figure 3). Anti-aging measurements all showed statistically significant improvement. Both assessments using the published photo-aging scale and 10-point assessment of skin quality by all five dermatologists showed statistically significant improvement ($p<0.0001$). Improvement in pigment was also statistically significant ($p=0.002$).

Blinded physician reviewers were asked to identify the correct before and after image and then grade the skin quality in both before and after images. There was a 100% success rate selecting before and after images by all four investigators. Correlation between the reviewers and the principal investigator was also high (Figure 4).

PATIENT SELF-ASSESSMENT

100% of patients noted an improvement in acne ranging from mild to significant. Measurements grading acne pre and post study showed a statistically significant improvement

study - all patients initially enrolled completed the study. Enrollment consisted of twenty one individuals between the ages of 20-29. Nineteen of the enrolled patients were female and two were male. Data is separated into two categories, physician assessment and patient self-assessment.

PHYSICIAN ASSESSMENT

Reduction in lesion count was significant ($p<0.0001$) with 100% of patients showing a significant reduction in lesion count.

($p < 0.0001$) in self-assessed acne (Figure 5). Periodic acne flare-ups were reduced in both frequency and severity.

Additionally, 100% of patients showed significant improvement in overall skin quality ($p < 0.0001$) with very high consistency in degree of perceived improvement. Average satisfaction increased from 1.7 pre-treatment to 7.3 post-treatment on a 10 point scale (Figure 6). Degree of improvement was significant among all individuals with very high patient-to-patient consistency (Figure 7). Anti-aging scores using the published multi-factorial score also showed significant improvement ($p = 0.028$).

DISCUSSION

The primary limiting factors to the use of both BPO and retinoids is typically skin irritation. Skin irritation will often result in decreased compliance including: discontinued usage, sporadic usage, use only when acne is present or spot treatment to acne lesions only. Any form of non-compliance can significantly decrease treatment efficacy. The lack of a single product and different AM/PM routines further complicates therapy and reduces compliance. The tested solution has the ease of use of a single product with 2X daily application leading to greater patient compliance.

This study was conducted between the months of November and March in Edmonton, Alberta with average monthly temperatures of -4° , -8.7° , -13.9° , -5.4° and -3.6° Celsius for each of the sequential months. In this climate, dry irritated skin is a significant problem and concern even without medications. Acne medications, in particular, tend to be drying and irritating to the skin, particularly in harsh climates. This issue is particularly true for BPO and retinol. One of the most notable findings from this study was the complete lack of irritation or sensitivity associated with use. In fact, many patients commented that the formulations were not overly drying, but rather moisturizing, and very tolerable compared to OTC products and topical prescription retinoids. Fourteen of the subjects in the study previously tried OTC and prescription products and services to treat acne – nine ProActiv, two Clindoxyl Gel, two chemical peels and one Stievamycin Gel. Finally, cosmetic elegance was high with patients commenting that the formulations felt smooth and elegant to apply and had a pleasant odor. These observations and results further increase the probability of compliance and lasting acne maintenance.

Patient satisfaction with this product and protocol was extremely high with 100% study retention and 18 patients (86%) indicating intent to purchase and or recommend the product to a friend or family member. All three patients that did not indicate intent to purchase observed improvement by both dermatologist and self-assessment but had the lowest percent improvement in acne and post-treatment skin quality perceptions.

Anti-aging improvement assessed by both dermatologist and self-assessment were statistically significant. When patients with mild or greater pre-study photo-damage were broken out as a subset, the improvement was significantly more notable. Of the twenty-one patients, only ten showed minor photo-damage with cumulative photo-aging scores of 4-5 out of 20 by dermatologist assessment (5 categories with a 0-4 scale

each). These ten patients when viewed as a subset (Figure 8) witnessed a significant improvement in the appearance of key components commonly associated with aging.

An interesting observation was the variation in pre-treatment perception of skin quality between patients and the reviewing dermatologists (Figure 9). Pre-treatment, the average patient assessment had an average score of 1.7 out of 10 compared to an average score of 6.3 by the principal investigator and independent reviewing dermatologists. The variation between scores was far less notable post-treatment (after acne improvement) where patient self-perception of skin quality much more closely matched that of the reviewers. The excessively low perception of skin quality pre-treatment by patients compared to trained reviewers is presumably due to the presence of acne and exemplifies the significant impact of acne on QOL and self-perception.

The dual-chamber dispensing solution utilized in this study effectively combined BPO and retinol plus antioxidants, peptides and moisturizers in a single product eliminating the problem of multiple and incompatible products. Additionally the protocol studied combinatory application in both the AM and PM and found highly effective results. This indicates that the formulations in this product are stable and effective when simultaneously applied to the affected area.

CONCLUSION

The technologies tested in this skin care regime yielded statistically significant improvement in acne and anti-aging as assessed both by test subjects and multiple dermatologists. The dual chamber packaging solution effectively eliminates the challenges of simultaneously delivering and dispensing these key acne and anti-aging technologies and the specific formulations combine to yield results with little to no skin irritation. Patient satisfaction was exceptionally high with 100% of patients experiencing a significant reduction in the number of acne lesions (average = 68% reduction, ranging 36% to 78% reduction) and 100% experiencing significant improvement in skin quality with no cases of skin irritation or drying.

Age Intervention Duality MD with the Skin Care Management System effectively treats adult acne and offers statistically significant anti-aging improvement with little to no skin irritation. Acne improvement is statistically significant by week 4 and continues to improve through week 12.

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