Original Article

The effects of a daily facial lotion containing vitamins B3 and E and provitamin B5 on the facial skin of Indian women: A randomized, double-blind trial

Hemangi R. Jerajani, Haruko Mizoguchi[1], James Li[1], Debora J. Whittenbarger[1], Michael J. Marmor[1]

Department of Dermatology, L.T.M. Medical College, L.T.M. General Hospital, Mumbai, India, [1]The Procter and Gamble Company, Sharon Woods Technical Center, Cincinnati, OH, USA

Address for correspondence:
Dr. Haruko Mizoguchi, The Procter and Gamble Company, Sharon Woods Technical Center, 11510 Reed Hartman Highway, Cincinnati, OH 45241-9974, USA. E-mail: mizoguchi.h@pg.com

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ABSTRACT

Background: The B vitamins niacinamide and panthenol have been shown to reduce many signs of skin aging, including hyperpigmentation and redness. **Aims**: To measure the facial skin effects in Indian women of the daily use of a lotion containing niacinamide, panthenol, and tocopherol acetate using quantitative image analysis. **Methods**: Adult women 30-60 years of age with epidermal hyperpigmentation were recruited in Mumbai and randomly assigned to apply a test or control lotion to the face daily for 10 weeks. Effects on skin tone were measured using an image capturing system and associated software. Skin texture was assessed by expert graders. Barrier function was evaluated by transepithelial water loss measurements. Subjects and evaluators were blinded to the product assignment. **Results**: Of 246 women randomized to treatment, 207 (84%) completed the study. Women who used the test lotion experienced significantly reduced appearance of hyperpigmentation, improved skin tone evenness, appearance of lightening of skin, and positive effects on skin texture. Improvements versus control were seen as early as 6 weeks. The test lotion was well tolerated. The most common adverse event was a transient, mild burning sensation. **Conclusions**: Daily use of a facial lotion containing niacinamide, panthenol, and tocopheryl acetate improved skin tone and texture and was well tolerated in Indian women with facial signs of aging.

Key words: Hyperpigmentation, Niacinamide, Skin tone

INTRODUCTION

Recent studies have noted the beneficial effects of topical niacinamide in aging skin, including improved barrier function, decreased appearance of signs of photoaging, and reduced sebum production.[1-5] Although previous studies have evaluated the effects of niacinamide in Japanese[1,6] and Caucasian women,[6] no study has been conducted in Indian women.

In this study, we have utilized state-of-the-art imaging capture and analysis methodology to evaluate changes in a number of skin parameters in Indian women following daily use of a facial lotion containing niacinamide, panthenol, and tocopheryl acetate. The study was approved by the Independent Scientific and Ethics Committee of the Kelkar Education Trust's Scientific Research Center.

METHODS

Subjects

Women 30-60 years of age and in good health were recruited at the Kelkar Education Trust's Scientific Research Center in Mumbai, India, between January and April, 2007. To be eligible, women had to have epidermal hyperpigmented spots on the cheeks and facial skin tone with a chromameter reading of >51 in the L-value. All subjects provided written informed consent. Women were excluded if they were pregnant or lactating, had skin cancer or a history

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of recent treatment for skin cancer, had clinically significant skin disease or any condition associated with changes in pigmentation, or had diabetes or immune system-related disease. Recent use of anti-acne, skin lightening or bleaching products, recent facial medical treatments (e.g., collagen treatments, chemical peels, etc.), current participation in another clinical trial, and use of anti-inflammatory medications were also grounds for exclusion.

Test products

After a 2-week period during which all women cleaned their faces with the same commercial face wash (Olay foaming face wash, Procter and Gamble, Cincinnati, OH, USA) and applied the same pre-treatment product (control lotion), the subjects were randomly assigned to use either a moisturizing lotion or a control lotion. The moisturizing lotion contained 4% niacinamide, 0.5% panthenol, 0.5% tocopheryl acetate, sunscreen, and glycerol in addition to other cosmetic ingredients that made up the control lotion. Age (30-47 and 48-60) and facial pigmentation level (low, medium, high) were used as stratification variables in the randomization. Both subjects and evaluators were blinded to the product assignments. Women used the assigned test product twice daily (morning and night) after washing their face with Olay foaming face wash for 10 weeks. They were instructed to refrain from using any topical products on their face except lipstick, eye makeup, and non-medicated facial powder or exposing their face to tanning lights and excessive outdoor sunlight.

Facial imaging methodology

Hyperpigmentation and skin lightening were measured using digital images captured at baseline and weeks 6, 8, and 10. The images were taken using the same imaging equipment under the same conditions (lighting, distance, head position) at all time points. The equipment utilizes a combination of two cameras (Fuji F2 Pro digital SLR camera and SuperCircuits PC-33C CCD video camera) to capture both study images and repositioning images. Using the image software (UltraGrab) to capture these two images, the imaging system allows a trained system operator to reposition a subject into the same position at each imaging session during the course of the study period. Facial illumination is provided by two JTL Versalight D 1000 flash units. The cameras and flash units are mounted onto the imaging head of the system, which also incorporates a fixed color chart for the "on-the-fly" color calibration and color correction of study images. Cross-polarized lighting was used to capture changes in facial skin tone (hyperpigmentation and evenness).

All the images were taken after the subjects washed with the face wash and acclimated to the controlled temperature (18-22ºC) and humidity (40-60%) room for approximately 30 min. Hair and clothing were covered with black drapes during imaging to minimize visual distractions and maximize consistency across all the images. The resulting digital images from the system were analyzed for hyperpigmentation using image analysis. This method utilizes a computerized mathematical program to objectively quantify the amount of hyperpigmented areas within the defined cheek area. The program sums the area of hyperpigmentation and then divides it by the defined cheek area for each subject. The resulting fraction is referred to as "spot area fraction." In addition, the captured digital images were subjected to chromophore-specific image processing (Non-contact SIAscopy, NC2) to identify and quantify eumelanin-based features of the skin. NC2 has been validated as a new method to quantify eumelanin using specially calibrated cameras and lighting and patented algorithms that take into account cutaneous optics.[7] These NC2 melanin-concentration maps were used to assess the changes in hyperpigmentation and overall skin evenness. Skin lightening was measured by image analysis of L**a***b* using the captured images without further processing and image analysis of melanin map gray scale (related directly to melanin concentration) using the images that had undergone chromophore-specific processing.

Expert grading of skin fine lines, wrinkles, and texture

Digital images were visually evaluated by expert graders using a visual perception system (VPS). The expert graders viewed the image at baseline and an image taken post-treatment and rated the extent of improvement or worsening on the following scale: 0 = no difference, 2 = slight, 4 = moderate, 6 = large, and 8 = extensive. Improvement and worsening relative to baseline were scored as positive and negative changes, respectively. Before unblinding and statistical analysis, the images were examined for their suitability for visual assessment via VPS analysis (e.g., no expression change, no extraneous features that confound evaluation) and only those deemed suitable were evaluated by VPS.

Facial skin integrity (transepidermal water loss)

TEWL measurements were made at baseline and at weeks 4, 6, 8 and 10 during product use by means of a Tewameter (MPA 580; Courage-Khazaka, Cologne,

Germany). Duplicate measurements were taken on each side of the face from two areas on the cheek: Below the center of the eye and below the outer corner of the eye. All measurements were made below any visible signs of fine lines or wrinkles while keeping the Tewameter probe on the cheek bone.

Statistical analysis

Measurements from the two sides of the face were averaged unless one side of the face did not meet the minimum criteria for hyperpigmentation at baseline (i.e., hyperpigmentation level of 1). In that case, only the side that met the minimum criteria was used for analysis. Changes from baseline were calculated and analyzed using a mixed model for repeated measures. The statistical model included treatment, week, treatment-by-week interaction, and age as variables. Baseline was added to the statistical model as a covariate when it existed. Comparisons between groups were based on the intent-to-treat population.

Significance was declared at $\alpha = 0.05$ using a one-sided test. No multiplicity adjustment was made as more than one parameter may be used to measure one attribute and previous studies have shown that these parameters are often correlated with each other.

RESULTS

Subject characteristics and disposition

Of 252 subjects enrolled in the pre-treatment period, 246 were randomized (test product, 124; control, 122) and 207 (84%) completed the study (test product, 99; control, 108). Baseline characteristics were similar in the two treatment groups [Table 1]. Of the 39 subjects who were randomized but did not complete the study, the reasons for withdrawal included non-compliance with product usage ($n = 30$), voluntary withdrawal ($n = 7$), use of excluded medications ($n = 1$), and participation in another clinical trial ($n = 1$). No subject withdrew as a result of an adverse event.

Table 1: Characteristics of the randomized population

Characteristic	Group	
	Test product (*n* = 124)	Control (*n* = 122)
Age, years (mean + SD) (range)	39.2 + 6.4 (30-58)	39.1 + 6.3 (30-59)
Age distribution-*n* (%)		
30-47 years old	111 (90)	110 (90)
48-60 years old	13 (10)	12 (10)
Hyperpigmenation level-*n* (%)		
Low	27 (22)	29 (24)
Medium	73 (59)	70 (58)
High	24 (19)	22 (18)

Hyperpigmentation

Levels of hyperpigmentation were quantified as spot area fraction and the changes from baseline in the spot area fraction were used to compare treatment effects. Women using the test product experienced significant reductions in the level of pigmentation in hyperpigmented spots compared with women using the control lotion. The difference between the groups was significant by the first post-treatment measurement at week 6 [Figure 1, left panel]. Changes in the test product group were also significantly reduced compared with baseline values whereas no significant change from baseline was observed in the control group. Images of the cheek area at baseline (left) and after 10 weeks (right) of treatment with the test product are shown in Figure 2. These same images, at baseline (left) and after 10 weeks (right) of treatment, with the outlines of pigmented areas as detected by image analysis are shown in Figure 3.

The data were also examined to determine the effect on melanin-specific spots as measured by NC2 [Figure 1, right panel]. The test product group experienced significant reductions in melanin-specific spots compared with baseline and with control lotion at all time points. In contrast, melanin-specific spots increased significantly during use in the control group.

Evenness of skin tone

Evenness of skin tone was examined by analyzing the variance in tone in the NC2 melanin concentration maps. Use of the test product resulted in significantly improved evenness of skin tone compared with baseline and with control lotion at all time points [Figure 4].

Skin lightening

Analysis of L-values showed that use of the test product resulted in significant overall lightening of the skin during use compared with baseline and the control lotion [Figure 5, left panel]. In contrast, the skin of women using the control lotion darkened significantly during the period of use.

Skin lightening was also evaluated by analyzing the NC2 melanin concentration maps. Consistent with the analysis of overall color changes measured by L-values, the melanin-specific images also demonstrated significant lightening during use of the test product compared with the control lotion [Figure 5, right panel].

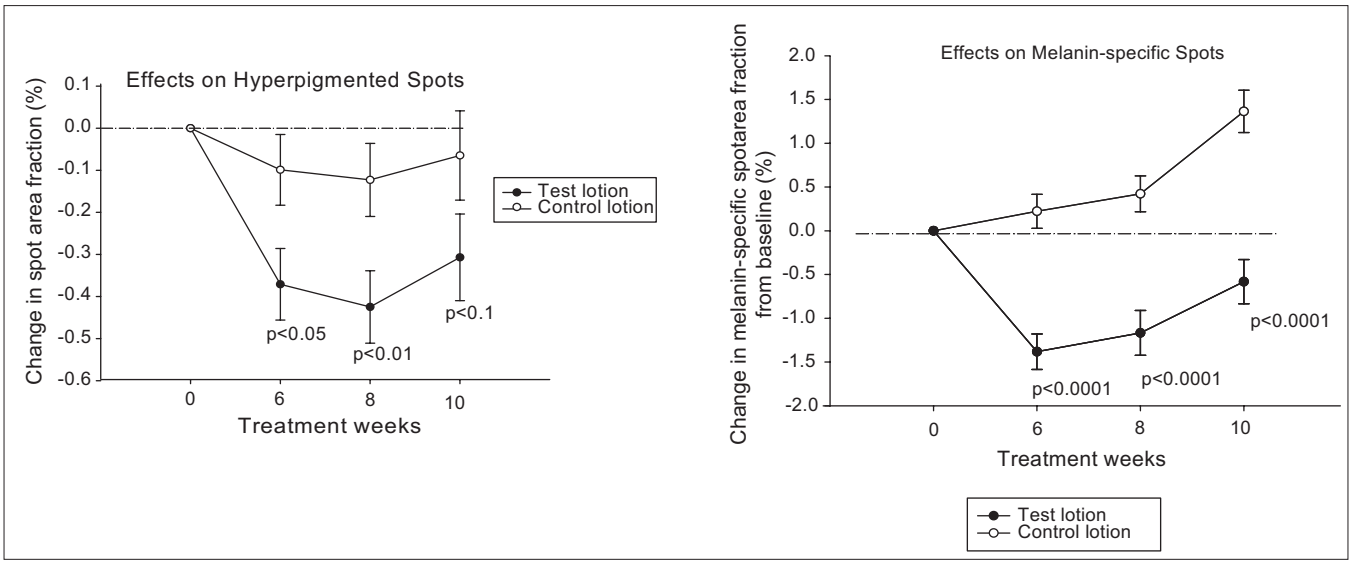

Figure 1: Changes in hyperpigmented spots (left panel) and melanin-specific spots (right panel) during the study. *P*-values represent between-group comparisons

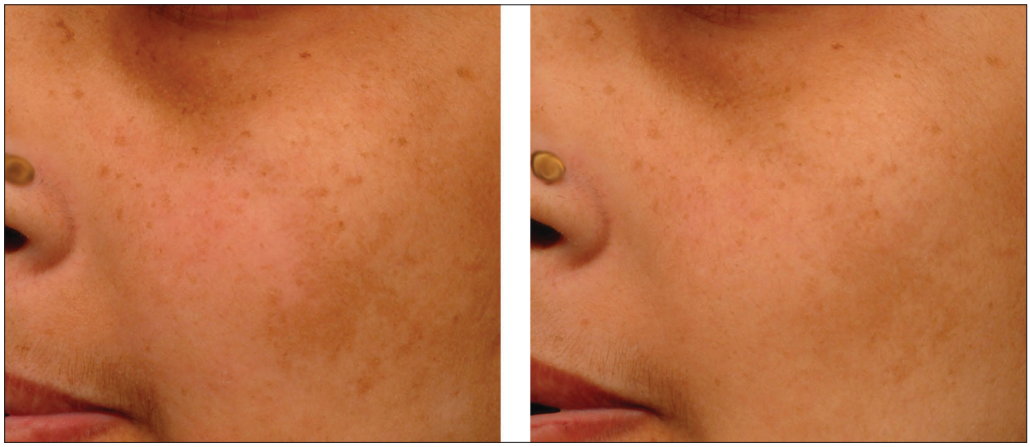

Figure 2: Images showing hyperpigmentation at baseline (left) and after 10 weeks (right) of treatment

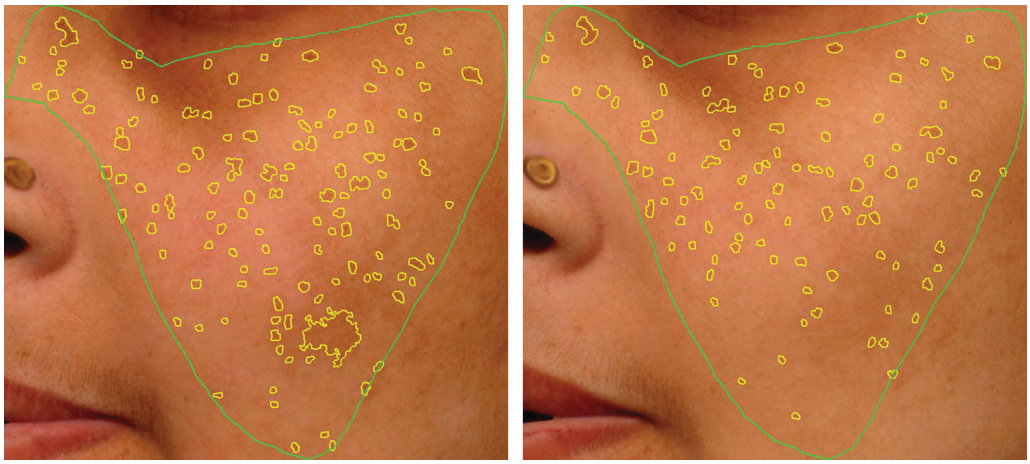

Figure 3: Outlines of pigmented areas as detected by image analysis are shown at baseline (left) and after 10 weeks (right) of treatment

Expert grading of skin texture

The expert grader assessments using the VPS were analyzed to determine the effects of product use on fine lines and wrinkles and on overall texture. Compared with baseline, fine lines and wrinkles increased during use of the control lotion. This effect was attenuated by the use of

the test product [Figure 6, left panel]. Similar effects were seen for texture, which worsened in the control group but not in the test product group [Figure 6, right panel].

Facial skin integrity

Skin barrier function was analyzed by examining the effect of product use on TEWL measurements. These values decreased in both groups, indicating a trend toward improved integrity. A significant difference between groups was seen at week 8 when subjects using the test product experienced a greater reduction in TEWL than subjects using the control lotion [Figure 7].

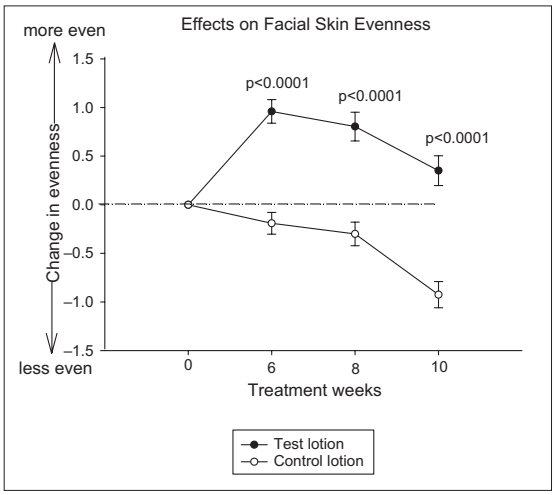

Figure 4: Changes in skin tone evenness during the study. *P*-values represent between-group comparisons

Adverse events

A total of 10 subjects (eight in the test product group and two in the control group) reported adverse events during use. The most common adverse effect was a mild, transient burning sensation following application (six subjects in the test product group and two subjects in the control group). The other adverse events were dryness of facial skin and exacerbation of acne, both of which were reported by one subject in the test product group. None of the subjects discontinued study participation because of an adverse event.

DISCUSSION

In this double-blind, randomized study, use of a facial skin lotion containing niacinamide, panthenol, and tocopheryl acetate by Indian women produced a significant improvement in a number of skin parameters associated with aging, including significantly reduced hyperpigmentation, improved skin tone evenness, and improved skin texture. Some evidence of a beneficial effect on barrier function was also observed. The product was well tolerated.

These results are consistent with those previously reported using niacinamide.[1-5] The effects of niacinamide in reducing skin pigmentation may be attributed to its ability to inhibit the transfer of melanosomes from melanocytes to keratinocytes.

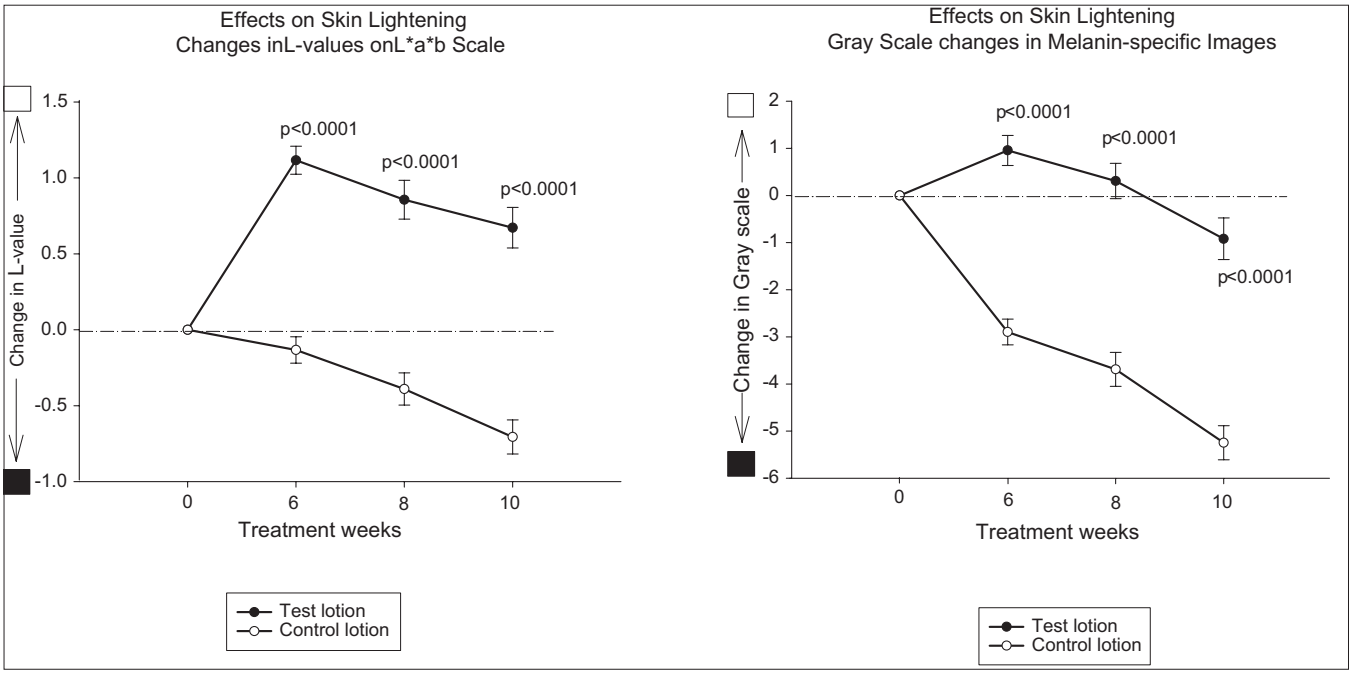

Figure 5: Changes in skin lightness during the study (left panel, overall L-value; right panel, melanin-specific values). *P*-values represent between-group comparisons

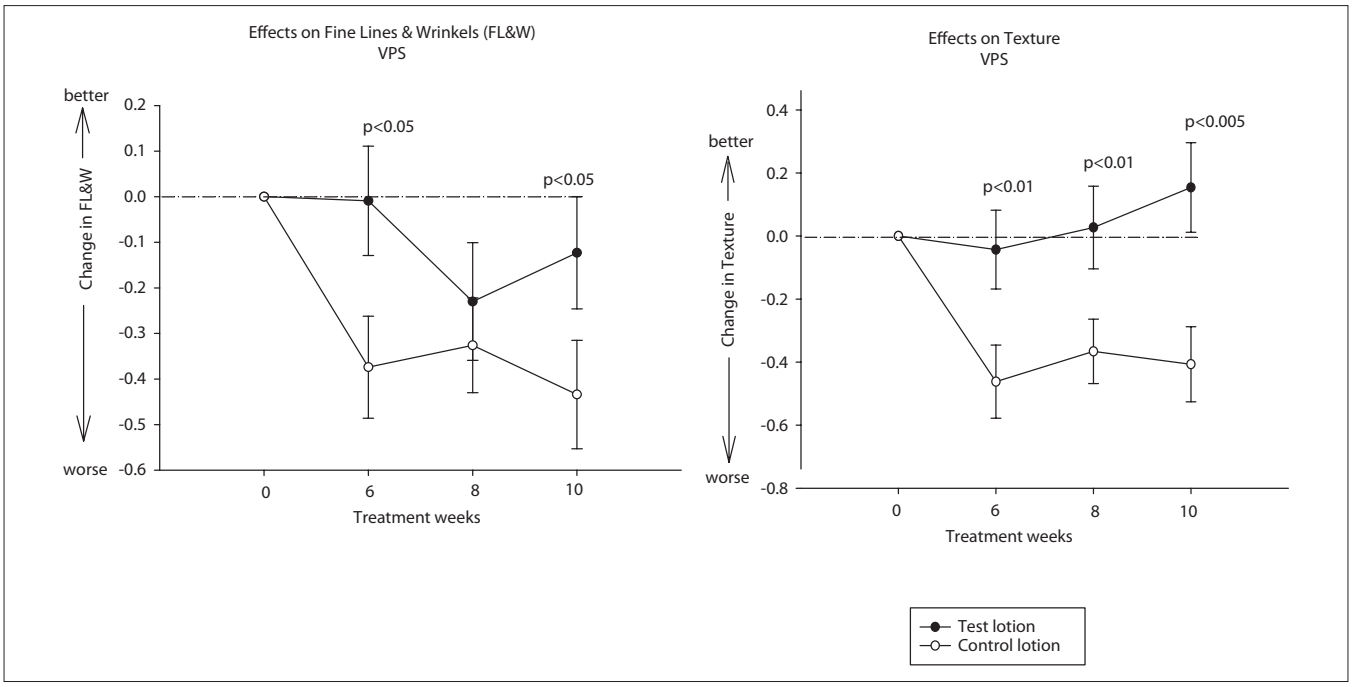

Figure 6: Changes in expert grader-assessed skin texture during treatment (left, fine lines, wrinkles; right, overall texture). *P*-values represent between-group comparisons

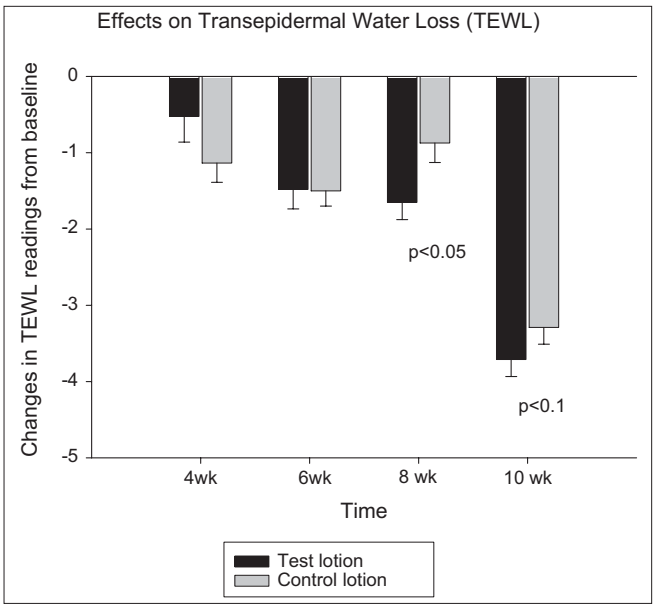

Figure 7: Changes in skin integrity as measured by transepidermal water loss during the study. *P*-values represent between-group comparisons

A study by Hakozaki *et al*. found that niacinamide decreased melanocyte transfer by 35-68% in a keratinocyte/melanocyte coculture method.[1] The same authors reported that niacinamide significantly reduced hyperpigmentation and increased skin lightening in a group of Japanese women.[1] Similarly, panthenol has also been shown to have beneficial effects on the skin.[8,9]

In addition to demonstrating the usefulness of this formulation in reversing the skin effects of aging, this study also demonstrates the general utility of our facial imaging system and its associated clinical model in evaluating facial treatments in Indian women. Our results also illustrate the sensitivity of the NC2 chromophore mapping technique in quantifying melanin-related study endpoints. The methodology employed in this study offers a new approach for investigating facial skin conditions in Indian women and for assessing the performance of cosmetic products in a scientifically sound and controlled setting.

In interpreting some of the changes observed in this study, it is worth noting that the daily UV index in Mumbai rose steadily (from approximately 7 to 12) over the period during which the study was conducted. This seasonal increase in exposure to UV light would be expected to cause increases in skin pigmentation. In fact, gradual increases in pigmentation were evident in the melanin-related measurements [Figure 1] and skin-lightening measurements [Figure 5] over the course of the study. Despite this seasonal effect, a clear benefit in reducing skin pigmentation was observed with the test product.

In this study, we investigated the effects of the test lotion on subjects with a chromameter reading of 51 or greater in L-value. We employed this criterion in order

to assure that the images captured by the facial imaging system could be processed properly using the current analysis program. Overcoming this methodological limitation would allow us to evaluate the facial skin conditions and impact of facial skin products among Indian women across the entire spectrum of skin color. Our focus in this study was to evaluate a facial lotion containing certain vitamins/provitamin together with sunscreen because these types of ingredients are not widely used among Indian women. Further investigation will be needed to examine how each component is contributing to the benefits observed in this study.

Our results suggest that products containing niacinamide, panthenol, and tocopheryl acetate are useful in improving a number of facial skin parameters that are associated with aging.

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